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Poster Abstracts

PO001 | Haemophilia a use case scenarios for a portable testing device in Europe

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Introduction: A portable multi-parameter blood coagulation analysis device (EnzySystem) is being developed to improve the diagnosis and management of patients with haemophilia A (PwHA). It simultaneously measures factor VIII activity and thrombin generation in 100 μL of capillary whole blood within 1 h. This study surveys use case scenarios for the EnzySystem in Europe.

Methods: Use-case analysis was performed with healthcare professionals (HCPs) and patients to determine their preferences regarding the use of the EnzySystem. Data was acquired using questionnaires and (online) interviews.

Results: Most respondents (61%) were excited about the portable testing device. Both near-patient use (37%) and home-use (48%) were identified as attractive applications of such a device. The interest in (clinical) laboratory use (15%) was limited.

In Western and Northern Europe, diagnosis and clinical laboratory testing are considered in place. Haemophilia treatment centres are accessible to all patients despite the great distances in some Northern European countries. PwHA would use the home-testing device to guide haemophilia A management in a (severe) bleeding situation and in unstable conditions. HCPs would prefer to gain experience with testing in a near-patient setting before advising patients to use the device at home. HCPs see added value of a near-patient device for use in remote areas as well as in emergency situations when laboratory testing is unavailable. 80% of the HCPs would consider the portable testing device for their daily routine.

In some Eastern European countries, the use of the device for diagnosis of haemophilia A is mentioned as not all PwHA have been diagnosed and haemophilia treatment centres are not accessible to all patients.

Discussion/Conclusion: From the interim data analysis it can be concluded that the recommended use case scenario for Western and Northern European countries is the management of haemophilia A with a home-use device. Additionally, it was suggested to first raise awareness using the near-patient device. For some Eastern European countries, the near-patient device for diagnosis is put forward.

As the input is still limited and not equally distributed over the regions of interest, we will continue collecting information in Europe.

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PO002 | Extravascular distribution of factor IX: A pharmacological evaluation?

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Introduction: The treatment of haemophilia B is based on the use of factor IX concentrates (FIX) whose pharmacokinetic (PK) properties are strongly influenced by their nature [plasma derived (pdFIX), recombinant (rFIX) or recombinant extended half-life]. The half-life and the through level are important factors in assessing the haemostatic capacity of these products. However, FIX has a significant extravascular distribution linked to its binding to collagen IV (Col4), which could have a beneficial influence on its efficacy. Our aim was to compare the distribution profiles of different FIX concentrates.

Methods: Monte Carlo simulations were carried out to determine the FIX activity profiles in different distribution compartments using SimulX (Monolix Suite). Based on the literature, population PK models were collected for pdFIX, rFIX, FIX linked to human albumin (rIX-FP), FIX Fc fusion protein (rFIXFc) to simulate steady state administration in 1000 patients of 40 IU/kg twice weekly (pdFIX, rFIX) and once weekly (rIX-FP, rFIXFc).

Results: The PKs of FIX are described according to two- or three-compartment models. These compartmental approaches demonstrate different levels of distribution of FIX concentrates. The first compartment represents the blood stream, the 2nd compartment, could corresponds to the rapid binding of FIX to subendothelial vascular Col4 and 3rd compartment could represent the extravascular distribution of FIX. The 2nd compartment, present for all concentrates, corresponds to the rapid binding of FIX to subendothelial Col4, capable of very quick in situ coagulation. The 3rd compartment

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is found here for all FIX concentrates except rIX-FP. This compartment PK profile is superimposed on that of the first phase of the 1st compartment (peak then rapid decrease). Significant differences were observed for the volumes of the 2nd compartment (15.8–87 dL) of the different FIX concentrates. The consequences in terms of exposure, evaluated by the mean concentration in this compartment, were 10.4, 5.9, 6.9 and 10.4 IU/mL for pdFIX, rFIX, rFIXFc and rIX-FP, respectively. The estimated mean FIX residence times were 42.3, 34.4, 137.0 and 217.4 h respectively for these same products.

Discussion/Conclusion: This simulation shows significant variations in distribution between the different FIX concentrates. This study could help to determine the dosage regimens of FIX concentrates in real life, by taking this characteristic into account.

Disclosure of Interest: X. Delavenne Speaker Bureau of: XD has received honoraria for participation in symposia by CSL Behring, Shire, Octapharma and Sobi., B. Guillet Consultant for: BG has been a consultant for Baxter/Baxalta/Shire/Takeda, CSL Behring, LFB, Novo Nordisk, Octapharma, Roche-Chugaï and Sobi.

PO003 | Measurement and Interferences of emicizumab up to six months after last infusion during laboratory follow-up in two cases of acquired haemophilia A

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Introduction: The use of emicizumab has been reported for the treatment of bleeding in acquired haemophilia A (AHA). Emicizumab interferes with factor VIII activity (FVIII:C) chronometric assays (OSA) and FVIII inhibitors measurement requiring specific monitoring by chromogenic assays (CSA). We report here the biological follow-up of two patients treated for an AHA and who received emicizumab treatment.

Methods: The first case was a 78-year-old male patient (P1) with a lymphocytic lymphoma, referred for a spontaneous psoas hematoma. At admission he had a FVIII:C < 1 IU/dL and FVIII inhibitor at 246 BU/mL. The second case was a 78-year-old female patient (P2) referred for recurrent spontaneous hematomas with FVIII:C < 1 IU/dL and FVIII inhibitor at 70 UB/mL. Bleedings were initially treated with by-passant agent and immunosuppressive therapy was initiated. Despite inhibitor titre decrease, bleedings persisted, thus emicizumab was administered at 3 mg/kg/week for 5 weeks (w) (P1) or 4w (P2). Emicizumab was measured on STAR MAX with CK-PREST® (STAGO) and r2 diagnostics calibrator (CRYOPEP). CSA was performed with SIEMENS FVIII Chromogenic reagent.

Results: Haemostatic efficacy was quickly achieved with a reduction of the hematoma size and no more haematuria for P1 and a cessation of bleeding in 48 h for P2. When FVIII inhibitors decreased, FVIII:C level progressively increased and interfered with the measurement of emicizumab since 10 IU/dL. We therefore evaluated an equation allowing us to subtract endogenous FVIII:C to calculate emicizumab concentration without overestimation. For P1 FVIII:C > 50 IU/dL was achieved 104 days (d) after emicizumab initiation, FVIII inhibitor was still detectable at 1.9 BU/mL and emicizumab concentration at 25 μg/mL (after correction). For P2, FVIII:C > 50 IU/dL was achieved 73 days after initiation of emicizumab, FVIII inhibitor was at 4 BU/mL and emicizumab at 42 μg/mL (after correction). Emicizumab was still detectable up to 6 months (m) after infusion, allowing only at this time the measurement of FVIII:C by OSA. FVIII inhibitor were undetectable 9 m (P1) and 7 m (P2) after the diagnosis.

Discussion/Conclusion: Emicizumab is an interesting therapy in the management of AHA, despite the lack of consensus on treatment regimens and monitoring.

Complex biological monitoring and interference on dosages can disrupt follow-up until at least 6 m after the last administration.

Disclosure of Interest: None declared.

PO004 | A single centre assessment of the frequency and clinical relevance of discrepant factor VIII assays both in persons without a disorder of haemostasis and in those with haemophilia A

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Introduction: Discrepant 1-stage and chromogenic factor VIII (cFVIII) assays in haemophilia A (HA) are widely reported. We investigated discrepant FVIII assays in an unselected population without HA to define the incidence of discrepant FVIII assays. We then investigated discrepant assays and bleeding in persons with HA.

Methods: Unselected persons with a normal 1-stage FVIII had a cFVIII performed. A one-proportion Z test was performed (H_0: $p = p_0$, H_1: $p > p_0$) to determine the association between the proportion of patients who had normal 1-stage FVIII activity and those with cFVIII within the mild HA range (0.06–0.40 IU/mL). To determine the normal range for 1-stage to cFVIII ratio, we calculated the mean one-stage to cFVIII ratio and a 95% CI using two standard deviations from the mean. To correlate discrepant assays with bleeding, we analysed persons with mild HA. We assessed bleeding with the ISTH Bleeding Assessment Tool (BAT). We used the published cut-off of more than 1.5-fold difference in FVIII assays to define FVIII discrepancy.

Results: Of 120 samples from persons not known to have HA with a normal 1-stage FVIII none had an abnormal cFVIII. The mean/median 1-stage FVIII was 0.91/0.87 IU/mL whilst the mean/median cFVIII was 0.94/0.90 IU/mL ($p = .32$, two-tailed t-test). The range for the ratio of 1-stage to cFVIII was 0.72–1.24. Of 107 HA persons (66 mild HA, 24 females with low FVIII and 7 HA carriers with normal FVIII), 30 (28%)

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had discrepant results and of these 24 (22%) had a *FVIII* mutation. Thirteen had a classical discrepancy (1-stage FVIII > cFVIII assay), 17 had inverse discrepancy (1-stage FVIII < cFVIII assay). Among patients with genetic mutations, 15 had c.1094A > G p.(Tyr365Cys) associated with inverse discrepancy. 5 had c.2149C > T p.(Arg717Trp) and 1 had c.5320C > T p. His1755Try, both associated with classical discrepancy. Three novel F*VIII* mutations were found. Patients with classical discrepancy experienced bleeding (BAT score of 4–8). Patients with inverse discrepancy did not bleed (BAT score of 0–2).

Discussion/Conclusion: In patients without a bleeding disorder 1-stage FVIII and cFVIII results are closely correlated. 1-Stage FVIII is sufficient to screen for HA but if normal and a bleeding disorder suspected then a cFVIII should be performed. In our population, inverse discrepancy may be more frequent than previously realised.

Disclosure of Interest: None declared.

PO006 | Clot waveform analysis in haemophilia A carriers

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Introduction: The activated partial thromboplastin time (aPTT)-based clot waveform analysis (CWA) is a simple global haemostasis test available on optical system analysers. The aim of this study was to evaluate the usefulness of aPTT-CWA in haemophilia A carriers.

Methods: A cross-sectional study was carried out in the biological haematology department over a period of 10 months from June 2021 to March 2022 including haemophilia A carriers and controls (healthy women). Laboratory assessment included aPTT-CWA and FVIII activity (FVIII:C).

The software program for the analysis for the aPTT-CWA allows the associated first and second derivative curves (DCs) to be displayed. The first derivative curve (D1) corresponding to the velocity of clot formation and the second derivative curve (D2) corresponding to the acceleration of clot formation.

Three CWA parameters were noted:

-**Max1:** maximum velocity (reflecting the 'thrombin burst' and bleeding risk)

-**Max2:** maximum acceleration (detecting any coagulation factor deficiency)

-**Min2**: maximum deceleration

Results: We recruited 26 haemophilia A carriers and 30 women as control group.

The medians of T max1 and T max2 were significantly higher in female carriers of haemophilia A (40.8–33.7 s) compared to controls (37.50–33s; $p < .001$). The medians of Max1 and Max2 were significantly lower in female carriers of haemophilia A (180.04; 526.08) compared to controls (213.5—760.01; $p < .05$). The median of Min2 was lower in female carriers of haemophilia A compared to controls (−246.96, −16.83; $p = .124$) but this difference was not significant.

The correlation of FVIII:C with max1 was not significant ($r = 0.24$; $p > .05$). The correlation of FVIII with max2 was positive and significant ($r = 0.51$; $p < .001$). The correlations of FVIII with Tmax1, Tmax2 and min2 were negative and significant ($r = -0.67$, $r = -0.6$ and $r = -0.6$) ($p < .001$).

Discussion/Conclusion: Additional research efforts are warranted to explore the potential of clot waveform analysis (CWA) for identifying haemophilia carriers. Especially as CWA is an affordable and easily accessible tool integrated into coagulation analysers equipped with optical detection systems.

Disclosure of Interest: None declared.

PO007 | FVIII inhibitors can be accurately determined in haemophilia A plasma in the presence of mim8

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Introduction: Mim8 (denecimig; Novo Nordisk) is an FVIIIa mimetic bispecific antibody in development for the treatment of haemophilia A with or without inhibitors. This study investigated if FVIII inhibitors can be accurately measured using bovine FIXa/FX FVIII chromogenic substrate assays (CSA) in the presence of Mim8 in haemophilia A plasma.

Methods: A FVIII inhibitor kit (Precision BioLogic) and two FVIII CSA kits using bovine FIXa/FX reagents, Factor VIII Chromogenic Assay (Siemens Healthineers) and Chromogenix Coatest® SP4 FVIII (Chromogenix) were used with Mim8 at 5, 10, 20 and 40 μg/mL (final concentration) and FVIII inhibitor (Affinity BioLogicals) spiked in pooled congenital FVIII deficient plasma (George-King Bio-Medical) at 0.2, 1.0 and 4.8 Bethesda units (BU)/mL (final concentration). FVIII inhibitor samples were prepared from a solution with a potency of 11.8 BU/mL (Siemens CSA). Mim8 interference was defined as a negative result (<0.6 BU/mL) becoming positive for samples containing 0.2 BU/mL of FVIII inhibitor, and a result ±25% (%RE) of unspiked sample for samples containing 1.0 or 4.8 BU/mL FVIII inhibitor.

Results: No Mim8 interference was observed at any FVIII inhibitor level, and all Mim8 spiked samples fell within ±25% of target. Siemens CSA inhibitor samples at 0.2 BU/mL remained negative (<0.6 BU/mL), with no results reported >0.4 BU/mL. Inhibitor samples with targets of 1.0 or 4.8 BU/mL recovered 0.96, 0.97, 0.98 and 0.97 BU/mL and 5.66, 5.88, 5.66 and 5.62 BU/mL, as Mim8 concentrations increased, compared to unspiked samples at 1.01 and 5.74 BU/mL, respectively. Spiked samples at 1.0 and 4.8 BU/mL recovered within −5.0 to −3.0%, and −2.1 to 2.4% of unspiked sample. Unspiked 1.0 and 4.8 BU/mL samples recovered within 1.0% and 19.6% of target, respectively. Chromogenix CSA recovered 0.90, 0.92, 0.94 and 0.84 BU/mL, as Mim8 concentrations increased, compared to 0.88 unspiked sample at 1.0 BU/mL. At 4.8 BU/mL, results were 5.22, 5.52, 5.57 and 5.72 BU/mL compared to

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unspiked sample of 5.07 BU/mL. Spiked samples at 1.0 and 4.8 BU/mL recovered within −4.5%–6.8%, and 3.0%–12.8% of unspiked sample. Unspiked 1.0 and 4.8 BU/mL samples recovered within 12.0% and 5.6% of target, respectively.

Discussion/Conclusion: Using FVIII CSAs with bovine reagents, FVIII inhibitor levels up to at least ~5.0 BU/mL were accurately measured in haemophilia A plasma in the presence of up to 40 μg/mL Mim8.

Disclosure of Interest: K. Weldingh Shareholder of: Novo Nordisk A/S—equity holder in publicly-traded company, Employee of: Novo Nordisk A/S, W. Pickering Shareholder of: Laboratory Corporation of America Holdings Englewood—equity holder in publicly-traded company; Fortrea—equity holder in publicly-traded company, Employee of: Laboratory Corporation of America Holdings Englewood, M. Robinson Shareholder of: Laboratory Corporation of America Holdings Englewood—current equity holder in publicly-traded company, Consultant for: Pfizer & Sanofi—honorarium received, Employee of: Laboratory Corporation of America Holdings Englewood, C. Cogswell Shareholder of: Laboratory Corporation of America Holdings Englewood—equity holder in publicly-traded company, Employee of: Laboratory Corporation of America Holdings Englewood, M. Ezban Consultant for: Novo Nordisk A/S—consultant in last 24 months, Employee of: Novo Nordisk A/S—employee in last 24 months.

PO008 | Challenges in determining the severity of haemophilia A: An insight in discrepancies between factor VIII assays

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Introduction: A 31-year old male patient diagnosed with minor to moderate haemophilia A consulted the haemophilia treatment centre of the Cliniques universitaires Saint-Luc in Brussels, Belgium to clarify the severity of his disease. In the past, he had hemarthrosis in multiple joints and was treated with DDAVP and factor (F)VIII concentrate on demand.

Methods: The FVIII one-stage assay (OSA) was analysed with SynthasIL reagent and HemosIL FVIII deficient plasma (Werfen, Barcelona, Spain). Two chromogenic substrate assays (CSA) were executed: one CSA with human FIXa and FX reagents (Hyphen Biomed, Neuville-sur-Oise, France) and one CSA with bovine FIXa and FX reagents (Coamatic, Werfen). All assays were performed on an ACL-TOP 750 (Werfen).

Results: We took blood samples at three moments over 1.5 years. The FVIII OSA varied between 6 and 10 IU/dL. For the CSA with human reagents we found FVIII activities of <1 and 1 IU/dL. For two blood samples we also performed the CSA with bovine reagents which varied between 4 and 5 IU/dL. Von Willebrand factor was normal. Genetic analysis of the F8 gene revealed the presence of a missense mutation, at hemizygous state, c.854T > G, p.(Val285Gly).

Discussion/Conclusion: Discrepancies between the different FVIII assays were striking. The missense mutation, found in this patient, was already linked to a mild to moderate phenotype in two articles (Higushi et al in 1991 and Arruda et al in 1995). Clinical symptoms were however compatible with a moderate to severe phenotype. It was already hypothesised that mutations, located at the interface of domain A1 and A2, could lead to a more rapid dissociation of domain A2 resulting in reduced stability of the FVIII heterodimer and FVIIIa heterotrimer. In contrast to the OSA, where FVIIIa is only generated during the rapid clotting stage, FVIIIa is formed in the CSA in a longer incubation step. For the assays used in our laboratory, the incubation step was longer for CSA with human reagents compared to CSA with bovine reagents. Dissociation of the A2 domain, resulting in inactivation of FVIII, could therefore be more pronounced in CSA (human reagents) > CSA (bovine reagents) > OSA. This case demonstrates that for some haemophilia cases it is still difficult to predict disease severity. At diagnosis, it is important to perform both one-stage and chromogenic assays.

Disclosure of Interest: None declared.

PO009 | Laboratory monitoring of prolonged recombinant porcine FVIII treatment of 3 successive surgeries in the setting of acquired hemophilia

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Introduction: Recombinant porcine factor VIII (rpFVIII) is an approved therapeutic option of acquired haemophilia (AH) in the absence of anti-human FVIII auto-antibodies cross-reacting with porcine FVIII. The advantage of rpFVIII over bypassing agents is the possibility of laboratory monitoring. The pivotal study used a loading dose of 200 IU/kg based on prior data in patients with congenital haemophilia A with inhibitors. However, data on subsequent rpFVIII treatment and monitoring is sparse. We report the case of a 72-year-old man with AH who required rpFVIII for three consecutive surgeries of forearm compartment syndrome.

Methods: The 3 surgeries were: (1) one hematoma drainage and fasciotomy (Day-1 rpFVIII), (2) a necrosectomy (Day-6) and (3) a forearm amputation (Day-7). As per rpFVIII label, the posology and frequency of rpFVIII infusions after the initial bolus of 200 IU/kg were adapted to FVIII plasma levels using a 1-stage clotting assay (OSA) with a specific rpFVIII calibration (FVIII:Cp) as reference method. Concurrently, other FVIII measures were compared using OSA or chromogenic assays (CSA) with specific rpFVIII or standard calibration.

Results: The anti-human FVIII titre at diagnosis was 8 BU, without cross-reactivity to rpFVIII. rpFVIII was administered for 11 days. For each surgery, an initial 200 IU/kg bolus followed by repeated infusions of 150 IU/kg every 5 h allowed to maintain FVIII:Cp > 50% until Day-10 of treatment where a loss in efficacy was observed. rpFVIII recovery after each loading dose were 0.41% (Day-1), 0.73 (Day-6) and 0.55% (Day-7), respectively. Treatment was relayed by recombinant activated factor VII on day 11 before the detection of anti-rpFVIII antibodies.

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There was no bleeding complication during rpFVIII treatment and the 2 weeks follow-up.

The different measurement methods were compared on a total of 27 blood samples using FVIII:Cp as reference. In the absence of a specific rpFVIII calibration, FVIII levels by OSA were overestimated by 1.3–2.2 folds whereas they were underestimated by 50% when using CSA. With a specific rpFVIII calibration, CSA overestimated FVIII activity levels by 1.1–1.4 folds.

Discussion/Conclusion: This case underlines the importance of an appropriate and close biological monitoring of rpFVIII, using a OSA with a specific calibration, even when rpFVIII is used as first-line therapy and without detectable porcine inhibitor.

Disclosure of Interest: None declared.

PO010 | Synonymous variants in haemophilia A and its clinical correlation: Our experience at La Paz University Hospital

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Introduction: Limited literature addresses synonymous variants in haemophilia A (HA) and their potential role in factor VIII (FVIII) splicing and mRNA stability. Historically overlooked, these variants require comprehensive exploration at both clinical and molecular levels to enhance patient care and genetic counselling. This study seeks to elucidate the impact of synonymous variants on FVIII expression, clinical haemorrhagic outcomes and inhibitor development.

Methods: Retrospective descriptive study including 17 patients and genetic testing at HU La Paz's Department of Hematology, EAHAD/CDC databases.

Results: We present 17 patients with low FVIII levels and synonymous variants in FVIII gene. All variants were located within exonic regions:

- Ten patients carried the exon 2 variant c.222G > A previously associated with mild HA and conflicting splicing impact. Seven males exhibited FVIII levels consistent with mild HA. Among them, three males experienced clinical haemorrhagic symptoms, such as post-surgical bleeding, mucosal bleeding and superficial hematomas. Three female carriers presented FVIII levels over 60 IU/dL and remained asymptomatic.
- Five patients carried the exon 19 variant c.6066C > T, previously linked with mild HA. Three males exhibited FVIII levels corresponding to a mild HA diagnosis. One of them experienced bleeding symptoms, such as epistaxis and superficial hematomas. Two female carriers presented FVIII levels of over 70 IU/dL and remained asymptomatic.
- One male patient carried the exon 9 variant c.1443G > A previously associated with mild to moderate HA. This patient exhibited FVIII levels of 3 IU/dL (moderate HA). He experienced hematomas due to minor trauma, and received on-demand FVIII.
- We identified a male patient with FVIII levels at 42% carrying a synonymous variant not described previously, c.1636 C > A This variant is under investigation for its potential involvement in splicing or mRNA stability.
- No joint bleeding episodes or inhibitor development were observed.

Discussion/Conclusion: We present 17 cases of patients with synonymous variations in the FVIII gene correlated with low FVIII levels.

The synonymous variants c.222G > A and c.6066C > T are associated with mild HA, along with mild to absent haemorrhagic symptoms.

The synonymous variant c.1443G > A is associated with moderate HA and moderate haemorrhagic symptoms.

The synonymous variant c.1636C > A is not described in the database and requires further studies.

Disclosure of Interest: None declared.

PO011 | Blood viscoelastic testing could support the management of patients with haemophilia A

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Introduction: Measurement of factor VIII activity is decisive for the bleeding management of patients with haemophilia A in emergency situations. However, in most laboratories the determination of factor VIII activity takes several hours and is not available as an emergency parameter especially during holidays and weekends. Thrombelastography is a point-of-care method that provides data on different coagulation parameters in whole blood samples. It is well established so that the coagulation system can be monitored in emergency situations using this easy to use method. It gives a rapid overview of all phases of coagulation and fibrinolysis. Most results are available within a few minutes. In this paper, we report on the use of thrombelastography in the management of patients with haemophilia.

Methods: Consecutive nine patients with haemophilia A were included in this retrospective study. Whole blood samples of patients with and without substitution of different factor VIII preparations were investigated by using a viscoelastic test system to assess coagulation and fibrinolysis systems. Additionally, standard routine coagulation testing and factor VIII activity were performed.

Results: Twenty-seven samples from nine patients were tested in this study. Thrombelastographic measurements revealed longer clotting time in haemophilia patients compared to healthy donors (clotting time in IN-test: 198.7 ± 38.9 vs. 146.7 ± 12.0 s respectively, $p < .0001$). Interestingly, viscoelastic parameters were corrected after factor substitution (clotting time in IN-test: 157.8 ± 23.7 vs. 146.7 ± 12.0 s, respectively, $p = .1016$). Significant correlations between factor VIII activity as measured by the routine aPTT-based clotting test and the clotting time of the intrinsic ($r = -0.7188$, $p = < .0001$) and also the extrinsic test ($r = -0.3887$, $p = .0451$) were observed. Maximum of clot firmness and maximum lysis in both assays did not correlate with factor

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VIII activity. Interestingly, also lysis time of the formed clot and factor VIII activity correlated significantly ($r = -0.4759$, $p = .0252$).

Discussion/Conclusion: Our data support that viscoelastic testing could be useful to diagnose factor VIII deficiency and to support the management of coagulation treatment of patients with haemophilia A in emergency situations.

Disclosure of Interest: None declared.

PO012 | Stability of eptacog beta after reconstitution

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Introduction: Eptacog beta is a recombinant activated factor VII (rFVIIa) for the treatment of bleeding episodes in patients (≥12 years old) with congenital haemophilia A/B with inhibitors, and bleed prevention during surgeries/invasive procedures (EU/UK indications). Its formulation development was driven by the following objectives: sterile freeze-dried form for intravenous administration; single-dose vials of 1 mg/2 mg/5 mg of product; stability for ≥36 months at +30°C, and 24 h after reconstitution at +30°C. It was therefore necessary to stabilise the gamma-carboxyglutamic acid-rich domain and prevent product degradation via oxidation or aggregation. A pre-formulation screening study was conducted to evaluate excipients and to propose a lead formulation, which was confirmed by a qualitative/quantitative study of the proposed excipients and validated by a stability study. Eptacog beta is formulated with arginine hydrochloride, isoleucine, trisodium citrate dihydrate, glycine, lysine hydrochloride, polysorbate 80 and hydrochloric acid at an optimised pH. We depict here the stability data of 1 mg/5 mg vials up to 30 months of storage and subsequent reconstitution.

Methods: Single-dose vials containing 1 or 5 mg of eptacog beta powder were stored at +30°C (30 ± 2°C and 75% ± 5% relative humidity). Analyses were performed from the first day of storage (T0), then after 6 (T6) and 30 (T30) months of storage at +30°C; samples were reconstituted according to the pack instructions and stored at +30°C for 0, 4 or 24 h under ambient light exposure. The quality, purity and strength of the product were analysed at each timepoint. At T0, the 1 mg batch and the 5 mg batches had already been stored at 15–25°C respectively for 9 and 12 months prior to study start.

Results: We depict here the stability data of 1 and 5 mg vials up to 30 months of storage and subsequent reconstitution. No substantial changes in clarity (no visible particles), pH (5.8–6.2), oxidised forms (≤6%), cleaved forms (≤12%), aggregates (≤5%), rFVIIa concentration (0.90–1.20 mg/mL) or coagulation activity (35,000–60,000 IU/mL) were observed for both 1 and 5 mg vials at any timepoint (0, 4 or 24 h under ambient light exposure) after reconstitution for T0, T6 and T30.

Discussion/Conclusion: Reconstituted eptacog beta remained chemically and physically stable for up to 24 h at +30°C upon initial reconstitution, even following 30 months of prior storage in the lyophilised state at +30°C.

Disclosure of Interest: None declared.

PO013 | Laboratory markers of bleeding in haemophilia

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Introduction: The hallmark of haemophilia is inadequate strong bleeding in response to injuries. We hypothesise that the risk of bleeding in haemophilia results in aberrant wound healing and increased inflammation. This could affect the development of arthrofibrosis following joint bleeds, which remains an unsolved problem for haemophilia patients and their health care providers.

Methods: Recognising the role of macrophages in wound healing, we systematically assessed macrophage function and blood-induced inflammation in haemophilia patients. We then analysed blood-induced inflammation and arthrofibrosis in knee joints of transgenic mice with haemophilia A compared to coagulation-competent wildtype mice.

Results: Our studies revealed a deficit in regenerative macrophage markers in connection with reduced wound healing in monocytes isolated from the blood of a randomly selected cohort of haemophilia patients. In haemophilia mice, we observed a delayed influx and reduced phagocytic activity of haemophilia macrophages after joint bleeding, which resulted in delayed resorption of blood and increased inflammation due to neutrophil persistence. Blood-induced inflammation coincided with vastly increased interleukin-6 levels in blood samples from haemophilia mice, which subsided after hematoma resorption. Paralleling these results, we found a marked increase of interleukin-6 in the plasma of haemophilia patients with acute bleeding episodes while haemophilia patients that did not experience recent bleeding had IL-6 blood levels similar to healthy controls. We did not find increased IL-6 in haemophilia patients with arthropathy or infectious disease.

Discussion/Conclusion: Our data suggest that IL-6 could be a useful biomarker for joint bleeds in haemophilia patients. Therefore, further prospective studies are warranted.

Disclosure of Interest: None declared.

PO014 | FVIII post-infusion monitoring surveys: Results and analysis from the updated UK NEQAS BC haemophilia programmes 2023

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Introduction: New therapeutic factor VIII (FVIII) treatment products for patients with haemophilia A have been introduced to improve patient quality of life. When performing laboratory monitoring, the

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FVIII activity results can be misunderstood and affect clinical patient management.

Methods: In this updated UK NEQAS BC FVIII post infusion monitoring survey, 65 participating centres were distributed a maximum of five FVIII product spiked lyophilised plasma samples at varying concentrations. Each centre registered for the FVIII products that they were able to routinely measure within their laboratory using recommended (by manufacturer/published data) methods/reagents. The five FVIII product samples included: Advate, Elocta/Eloctate, Esperoct, Novoeight and Refacto AF.

Results: Data were returned from 52 centres. Centres performed either one-stage assays (OSA) or chromogenic assays (CA) when laboratory measuring. The overall medians and coefficient of variation (CV) for each sample was:

OSA: Advate median value 7.15 IU/dL, with CV = 12.4%, Elocta median value 55.7 IU/dL, with CV = 12.3%, Esperoct median value 27.7 IU/dL, with CV = 20.4%, Novoeight median value 7.1 IU/dL, with CV = 12.2% and Refacto AF median value 8.2 IU/dL, with CV = 23.3%.

CA: Advate median value 6.7 IU/dL, with CV = 37.3%, Elocta median value 63.5 IU/dL, with CV = 20.4%, Esperoct median value 35.5 IU/dL, with CV = 12.2%, Novoeight median value 8.0 IU/dL, with CV = 23.3% and Refacto AF median value 7.0 IU/dL, with CV = 26.7%.

NEQAS sample potency recoveries differed from overall submitted results for some FVIII products by >50% (range 7.0%–123.3%) Centres who used a non-recommended method/reagent were provided with a comment against their result.

Discussion/Conclusion: The UK NEQAS BC FVIII post infusion monitoring surveys are a valuable tool to highlight to participating centres the types of recommended method/reagents that should be used when laboratory measuring a particular FVIII treatment product. The surveys show the potential over- or under-estimation of results when using a non-recommended method/reagents due to the different sensitivities of reagent compositions in either OSA or CA kits.

Disclosure of Interest: None declared.

PO015 | Association of thrombin activatable fibrinolysis inhibitor (TAFI) with the severity of haemophilia B

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Introduction: Thrombin activatable fibrinolysis inhibitor (TAFI) is an enzyme that downregulates fibrinolysis. It is activated by thrombin generated during the coagulation process and represents the molecular link between coagulation and fibrinolysis. The aim of this study was to investigate activities and antigen concentrations of TAFI in patients with haemophilia B (HB) in order to found out a possible association with the severity of the disease.

Methods: The study group consisted of 41 HB patients (2–84 years), divided according to FIX activities into two groups: HB1-severe (FIX < 0.01 kIU/L; $N = 17$) and HB2-non severe (FIX 0.01–0.40 kIU/L; $N = 26$), and 41 healthy male controls (HMC, 6–76 years). FIX activities were measured by the one-stage clotting assay (Actin FS, Atellica-COAG360, Siemens). TAFI activity was measured by using Stachrom TAFI chromogenic assay (Diagnostica Stago, France) on Sysmex CS-2500 (Siemens). Activated and inactivated TAFI antigen (TAFIa/TAFIai) concentrations were measured using Asserachrom TAFIa/TAFIai ELISA (Diagnostica Stago). The MedCalc® Software was used for statistical analysis.

Results: TAFIa/TAFIai differed significantly between groups ($p = .010$) with lowest values observed in HMC (median 20.1 ng/mL; range: 16.3–24.3 ng/mL) that gradually increased in non-severe (median 22.3 ng/mL; range: 20.8–26.5 ng/mL) and severe HB patients (median 23.6 ng/mL; range: 18.6–29.9 ng/mL). However, the difference of TAFIa/TAFIai concentrations between HB1 and HB2 was not statistically significant ($p = .822$). Regarding TAFI activity, despite slightly higher activities found in HB1 (median 125.8%; range: 114.1%–135.3%) than in HMC (median 124.5%; range: 106.7%–135.8%) and HB2 group (median 121.2%; range: 113.8%–130.6%), no statistically significance ($p = .902$) was encountered between investigated groups.

Discussion/Conclusion: Obtained TAFIa/TAFIai results suggest the association of TAFI with the severity of HB. On contrary, the same association was not found for TAFI activities. Further investigation of other fibrinolytic parameters is needed to clarify the impact of fibrinolysis in HB patients.

Disclosure of Interest: None declared.

PO016 | Comparison of clot-based and chromogenic assays for measurement of factor VIII inhibitors in haemophilia A patients

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Introduction: The development of neutralising antibodies (inhibitors) to infused factor VIII (FVIII) is a major complication of haemophilia A (HA) treatment. Detection and validation of factor VIII inhibitors remain a challenge for most diagnostic laboratories, especially in the era of emicizumab that interferes with the FVIII one-stage assay (OSA). Aim: To evaluate the analytical performance and utility of chromogenic substrate assay (CSA) in detecting inhibitors in HA patients compared to the currently used OSA.

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Methods: Prospective and comparative study carried out in the Biological Hematology Department at Aziza Othmana Hospital over a period of 1 year from June 2022 to June 2023 including 76 specimens from 62 HA patients (40 severe, 18 moderate and 4 mild) receiving either plasma-derived or recombinant FVIII.

Inhibitor detection was performed using the Bethesda assay. After incubation, factor VIII was measured simultaneously with both OSA and CSA. OSA was carried out using HemosIL® Factor VIII deficient plasma (Instrumentation Laboratory) while we used HemosIL® ELECTRACHOME factor VIII kit for the CSA. Both assays were performed on ACL TOP® analyser.

Results: Both methods showed good correlation in screening for anti-FVIII inhibitors with a Pearson's correlation coefficient of 0.578 ($p < .0001$) and a Spearman's correlation coefficient of 0.562 ($p < .0001$).

All specimens with negative screening by OSA results ($n = 52$) showed negative results by CSA.

Among the three specimens that tested positive in the OSA screening, two exhibited positive results, while one yielded a doubtful result in the CSA screening.

Sixteen specimens with doubtful screening with OSA also had a negative screening with CSA and were termed discordant. Only five samples had a doubtful screening with both methods.

Despite the result's disparity in the doubtful group, OSA and CSA were significantly correlated ($r = 0.682$, $p = .001$).

For the discordant cases, recovery studies as well as screening with the Nijmegen-Bethesda assay and Lupus anticoagulants testing were recommended.

Discussion/Conclusion: Multiple laboratory tests are now available for detecting and understanding inhibitors, CSA might offer a good alternative for classical OSA in screening, showing good correlation despite few disparities. More studies are mandatory to validate the CSA, as emicizumab will require the intervention of this assay for monitoring purposes.

Disclosure of Interest: None declared.

PO017 | The thrombin generation assay as a method for monitoring haemophilia A patients using emicizumab and FVIII treatment

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Introduction: Severe haemophilia A (SHA) patients receive prophylactic treatment to prevent spontaneous bleeds. Standard treatment consisted of standard factor VIII (FVIII) replacement concentrates (SHL) or extended half-life FVIII products (EHL). Emicizumab is a new non-factor replacement therapy (NFRT) which mimics FVIII activity. In case of bleeding, additional FVIII is given, interfering with emicizumab. Conventional laboratory tests are unreliable for monitoring emicizumab, especially when combined with FVIII. Thrombin generation (TG) may be promising as a laboratory test to monitor the effectiveness of emicizumab and the combination with FVIII. We aimed to investigate the performance of a thrombin generation assay in assessing FVIII and emicizumab activity levels.

Methods: In vitro experiments were performed using FVIII deficient plasma (Siemens®), spiked with different doses of SHL, EHL and NFRT. Left over plasma samples were used from 18 SHA-patients, which were collected in different situations. TG was measured using PPP reagent LOW by Callibrated Automated Thrombogram (CAT) method (Stago).

Results: Thrombogram curves from in vitro experiments with emicizumab concentrations showed dose–response curves with a gradually increasing velocity index (VI) and peak hight (PH). Increasing dose–response curves were also seen in combined samples. In SHA-patients, FVIII levels by one stage clotting assay showed the best correlation with TG ETP% and PH% with Spearman correlation coefficients (r) of both 0.8. Emicizumab had a moderate correlation with ETP% ($r = 0.042$) and PH% ($r = 0.58$). In patients with emicizumab and SHL, the correlation between FVIII by bovine CSA was also moderate (ETP% $r = 0.47$; PH% $r = 0.50$). Lowest ETP% and PH% were suggested in patients in their through levels. Patients on emicizumab have higher ETP% and PH%, although the median levels are not within the normal range. Patients on SHL or EHL replacement therapy with or without emicizumab give the impression that their ETP% and PH% are approaching normal values.

Discussion/Conclusion: The TG-CAT assay may be used to monitor emicizumab and/or FVIII replacement treatment in SHA patients. Since one reliable uniform test is clinically needed, future applicability for this assay in monitoring SHA patients has to be studied in larger cohorts. Furthermore, the relevance of ETP% and PH% has to be related to clinical outcomes as severity of bleeding.

Disclosure of Interest: None declared.

PO018 | Progression of haemophilia treatment in developing countries compared to developed countries, advocating a need for increased collaboration measures: A literature review

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Introduction: Haemophilia, an X linked inherited disorder, is underdiagnosed and untreated in around 70% of the global population according to World Federation of Haemophilia. However, this unfortunate representation is higher in the developing world as compared to developed countries. Patients diagnosed with haemophilia suffer joint bleeds and deformity that influence their quality of life and life expectancy. Several factors contribute to the continued prevalence of suboptimal care in the treatment of haemophilia. Low income, lack of resources, low awareness, missed early diagnosis, unavailability of

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factor concentrates, lack of proficient care, insufficient pain relief, inhibitor development, focus on other predominant health conditions over haemophilia are some of the challenges faced by developing countries even to this date. In contrast to this, a haemophiliac in a developed country could almost have a very close life expectancy to that of a normal individual. This review attempts to highlight the advancement of Haemophilia treatment in both developing and developed countries, the current challenges in developing countries and the need for an increased collaboration to support developing countries in better management of haemophilia care. Various collective measures like the Twinning programme by the World Federation of Haemophilia and the humanitarian aid have proved beneficial in this respect. It is imporrant to identify and diagnose haemophilia at an early stage. Early treatment can let the patients have a better quality of life while they develop.

Methods: Literature available on PubMed, Google Scholar, Haemophilia journal over the last decade and other scientific resources was searched with terms like haemophilia, challenges in management of haemophilia, haemophilia in developed countries, haemophilia in developing countries to identify published research articles considering this review.

Results: Results and conclusion will be further discussed.

Discussion/Conclusion: Results and conclusion will be further discussed.

Disclosure of Interest: None declared.

PO019 | Identification and characterisation of a large insertion responsible for severe haemophilia B

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Introduction: Haemophilia B (HB) is caused by molecular defects in *F9*. Routine molecular diagnostic techniques, based on next generation sequencing (NGS) gene panel, allow the identification of pathogenic variants in *F9*. However, there are patients with severe HB in whom no variants are detected. Structural variants (SVs) have been documented as contributing to approximately 5% of mutations in patients with HB. Therefore, they should be considered when diagnosing patients with severe HB for whom conventional diagnostic methods resulted ineffective. The aim of this work was to investigate the molecular mechanism underlying severe HB (FIX:C = 0.5%) in a paediatric patient for whom a customised 23-gene panel related with congenital coagulopathies did not reveal any variant and could not amplify the exon 6, suggesting the presence of an SV.

Methods: The exon 6 was amplified separately and sequenced by Sanger method. Moreover, the obtained amplicon was fragmented using NGSgo Library Full kit (GenDx) and sequenced by NGS in a MiSeq instrument (Illumina). Both results were analysed using CLC Genomics Workbench software (Qiagen). Additional softwares such as Blast (https://blast.ncbi.nlm.nih.gov/Blast.cgi) were used to identify the insertion.

Results: The amplification of exon 6 of *F9* yielded an 800 bp fragment, corresponding to twice the expected size (407 bp). Sanger sequencing and NGS of the obtained amplicon allowed the identification of a large insertion in exon 6 at position c.20403_20404. Specifically, NGS enabled the characterisation of the insertion which corresponds to a sequence of poly-T followed by a 281 pb sequence of an *AluY* repetitive element. In addition, the 17 bp in *F9*, situated just before the breakpoint, were duplicated in an inverted orientation at the 3′ of the SV c.20403_20404ins[T[?];NC_000008.11:g.87450696_87450976; inv20387_20403]. Segregation studies confirmed that the patient's mother is a carrier of the mutation.

Discussion/Conclusion: This study demonstrates the value of NGS in the characterisation of large insertions in *F9*, overcoming the limitations and complementing the results obtained by conventional genetic approaches. To date, only four large insertions have been described in the in *Factor IX Gene (F9) Variant Database* (https://f9-db.eahad.org), of which one has been characterised. Our findings contribute to the expansion of our understanding of the molecular mechanisms underlying HB.

Disclosure of Interest: None declared.

PO020 | The possible role of OPG/RANKL system as biomarker in the progression of haemophilic arthropathy (HA)

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Introduction: In PWH recurrent joint bleeds eventually cause progressive HA. The Pettersson Score (PS) is widely applied to classify osteochondral changes of HA. There are studies that demonstrate the influence of OPG/RANKL in HA. The aim of our study is to compare OPG/RANKL in PWH and correlate it with PS, haemophilia type, severity and age.

Methods: From November 2021 to July 2022, 160 samples were collected for OPG/RANKL measurement from 65 PWH and 36 healthy controls.

X-rays of 149 target joints of the above patients were assessed (30 elbows, 70 knees and 49 ankles). The range of PS was 0–13/joint. OPG/RANKL were measured by ELISA. Statistical analysis was done with SPSS.

Results: Among the PWH mean age was 38 years (IQR18—83), whereas among the control group mean age was 43 years (IQR 22—73).

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A statistically significant difference in OPG and RANKL was found between controls and PWH ($p < .05$).

OPG is not associated with haemophilia type whereas RANKL is lower in PWHA compared to PWHB ($p < .05$): 2663.06 pg/mL (IQR 0–15,584.93) versus 4825.10 pg/mL (IQR 0–14,260.87), respectively.

Statistically significant differences were noted between patients with severe ($N = 55$) and moderate/mild ($N = 10$) haemophilia for both biomarkers: for OPG, mean values in severe haemophilia were 934.09 pg/mL (113.02–8302.30) versus 1785.36 pg/mL (66.21–5728.48) in moderate/mild ($p < .001$). For RANKL, mean values were 2881.84 pg/mL (0–15,584.93) versus 3469.37 pg/mL (1118.03–9515.81) respectively ($p < .001$).

Although no direct correlation was found between OPG and PS, we demonstrated a significant decrease in OPG between patients < 30 years old (primary prophylaxis) (mean 953.82 pg/mL) and >30 years old (late prophylaxis) (mean 805.57 pg/mL) and a significant increase in the PS_{joint} mean 3.23 (0–9) versus 8.89 (0–13), respectively. No statistically significant correlation of RANKL with the PS was found ($p > .05$).

The correlation between PS_{joint}, the age of PWH ($p < .01$) and the severity of haemophilia ($p < .05$) was statistically significant.

Discussion/Conclusion: Based on our preliminary results, PWH have lower OPG and RANKL levels than the general population. The higher OPG levels were associated with lower score of PS suggesting that the early prophylaxis in our younger patients contributes to healthier joints and that the OPG/RANKL system appears to play a role in the progression of HA.

Disclosure of Interest: None declared.

PO021 | Investigation of the suitability of the ROTEM assay to measure coagulation potential in blood from patients on concizumab prophylaxis

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Introduction: Concizumab is an anti-tissue factor pathway inhibitor (TFPI) monoclonal antibody in development as subcutaneous prophylactic treatment for haemophilia of all subtypes. It prevents inhibition of factor (F) Xa and enhances initiation of coagulation. In explorer7 and 8 (NCT04083781, NCT04082429; phase 3), patients with haemophilia A/B with/without inhibitors were treated once daily with concizumab. Coagulation potential of patients treated with concizumab may be measured using TF-dependent global coagulation assays. We evaluated use of a modified rotational thromboelastometry (ROTEM) assay with diluted TF reagent.

Methods: ROTEM was performed (see Augustsson et al. Haemophilia 2021;27 [suppl 2]:6-181) using blood from 12 patients in explorer7/8 treated with concizumab at four study sites (A–D). TF reagent (r ex-tem®) was manually diluted 1:50,000-fold relative to total sample volume. After study completion, diluted TF reagent was batch-analysed for TF content in a chromogenic FX activation assay. Quality control samples included Rotrol N plasma with diluted TF reagent. ROTEM parameters on patient samples were compared with concizumab plasma levels (exposure), free TFPI and thrombin generation (TG) parameters (peak height, endogenous thrombin potential [ETP] and velocity index) by Spearman's correlation coefficients.

Results: ROTEM clot time (CT) was stable for individual patients ($n = 6$) over the observation period at sites A–C. At site D ($n = 6$), CT values were low and more variable. Rotrol N control CT had a coefficient of variation (CV) of ≤12.4% at sites A–C. The corresponding CV was 35.4% at site D, and TF content varied greatly (CV = 85.9%). For data obtained at sites A–C, correlations between ROTEM CT and exposure, free TFPI or TG were weak (numerically < 0.6), and the direction of correlations between ROTEM CT and exposure or TFPI was not as expected. The correlations for ROTEM CT and the TG assay were in the direction expected (−0.238 for thrombin peak, −0.166 for velocity index, −0.508 for ETP; $n = 46$ each). The magnitude of correlation coefficient was similar for other ROTEM parameters.

Discussion/Conclusion: Based on this study, only experienced and trained laboratories can perform the modified ROTEM assay reliably. With the current data and assay setup, we cannot recommend this assay for general monitoring of coagulation potential for patients on concizumab prophylaxis.

Disclosure of Interest: H. Eichler Grant/Research support from: Bayer, CSL Behring, Pfizer, Consultant for: Bayer, BioMarin, CSL Behring, Novo Nordisk, Pfizer, Speaker Bureau of: Bayer, BioMarin, CSL Behring, Novo Nordisk, Pfizer, N. Butta Grant/Research support from: Novo Nordisk, Grifols, Takeda, Paid Instructor at: Novo Nordisk, Novartis, Octapharma, Roche, A. Riddell: None declared, C. Augustsson Grant/Research support from: Novo Nordisk, M. Kjalke Shareholder of: Novo Nordisk, Employee of: Novo Nordisk, A. Florencio Employee of: Novo Nordisk, J. Astermark Grant/Research support from: Shire, Sobi/Biogen, Bayer, Octapharma, CSL Behring, Consultant for: Takeda, Sobi, Pfizer, Bayer, Novo Nordisk, CSL Behring, Sanofi, Roche, Octapharma, BioMarin, Speaker Bureau of: Takeda, Sobi, Pfizer, Bayer, Novo Nordisk, CSL Behring, Sanofi, Roche, Octapharma, BioMarin, V. Jiménez Yuste Grant/Research support from: Pfizer, Shire, Novo Nordisk, Sobi, Octapharma, Grifols, Consultant for: CSL Behring, Sobi, Octapharma, Grifols, Pfizer, Shire, Novo Nordisk, Roche, Biomarin, Sanofi, P. Chowdary Grant/Research support from: Bayer, CSL Behring, Freeline, Novo Nordisk, Pfizer, SOBI and Takeda, Consultant for: Apcintex, Bayer, Boehringer Ingelheim, CSL Behring, Chugai, Freeline, Novo Nordisk, Pfizer, Roche, Sanofi, Spark, Sobiand Takeda.

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PO022 | Cross-reactivity of human anti-FVIII antibodies to porcine rFVIII: french field study to validate the modified Nijmegen method

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Introduction: Before initiating treatment with Susoctocog alfa, a recombinant porcine FVIII (rpFVIII), it is recommended to assess the cross-reactivity of anti-hFVIII with rpFVIII. Patient plasma should be incubated with rpFVIII instead of normal human plasma, and the samples should be diluted in human FVIII-deficient plasma (hFVIII DP) instead of imidazole buffer. The aims of this study were to validate the use of imidazole buffer for the titration of anti-rpFVIII inhibitors, and the modified Nijmegen method in a field study.

Methods: Ten laboratories took part in this study. Takeda supplied the rpFVIII. To validate the use of an imidazole buffer instead of hFVIII DP, the stability of rPFVIII diluted in the buffer or in hFVIII DP was studied. Two mixtures (M) were prepared: M1: rpVIII (100%) + hFVIII DP; M2: rpVIII (100%) + imidazole buffer. The FVIII activity of the mixtures was measured immediately and after incubation (2 h/37°C) using reagents commonly used in laboratories. To validate the use of Imidazole buffer and different aPTT reagents for titration against rpFVIII, 38 samples from 26 AHA patients (mean 33 BU, ranges 1–204) and 12 samples from seven haemophilia A patients with inhibitors (mean 10 BU, ranges 1–57) were tested. Two different centres systematically tested the same 10 samples.

Results: After 2 h incubation, the mean FVIII activity in M1 was equal to 49% and 47% in M2, demonstrating the stability of FVIIIrp in both media. Of the 50 samples tested, no cross-reactivity against rpFVIII was detected on 25 samples in either laboratory. The mean anti-hFVIII antibody of these 25 samples was 14.4 BU. Cross-reactivity with rpFVIII was detected by both laboratories on 20 samples with a mean titre of 8.1 BU (mean anti-hFVIII: 37 BU). Discrepant results were obtained on five samples with a mean anti-rpFVIII titre equal to 0.9 BU. Interestingly, only 10 of 38 samples from AHA patients (26%) showed a definite cross-reaction with rpFVIII, compared with 9 of 12 samples (75%) from HA patients with inhibitors. In addition, rpFVIII titre above 20 BU was detected in only one sample.

Discussion/Conclusion: This field study demonstrates the feasibility of performing the modified Nijmegen method to detect cross-reactivity of anti-hFVIII with rpFVIII. In addition, we validate the use of imidazole buffer in place of FVIII-deficient plasma, thereby reducing the cost of the assay.

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PO023 | Evaluation of one-stage and chromogenic assays for the measurement of FVIII:C post valoctocogene roxaparvovec infusion

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Introduction: Valoctocogene roxaparvovec (VR) is a factor (F)VIII gene therapy for severe haemophilia A which uses AAV-5 as a vector to implant B-domain-depleted-FVIII gene into hepatocytes so that individuals produce endogenous FVIII, with significant reduction in bleed rate.

A median ~1.65-fold difference between FVIII activity [FVIII:C] measured by one-stage [OS] and chromogenic substrate [CS] assays in a central laboratory was observed in the phase 3 study (range 1.29–2.01 in local laboratories). It has been suggested that OS/CS-conversion factor can be developed in laboratories that do not have access to a CS assay. However, with variation between different OS/CS for measuring many FVIII products, it may be erroneous to assume that data for one reagent can be applied to similar reagents.

Methods: We measured FVIII:C in 50 ex vivo samples from nine patients who have received VR, using commonly available reagents and standard protocols for OS (Hyphen Biomed Cephen and Cephen LS; Siemens Actin FSL, Actin FS, Actin and Pathromtin SL; Stago Cephascreen and CK Prest; Werfen SynthasIL and SynthaFAX) and CS (Hyphen Biomed (HB); Siemens; Precision Biologic) assays to see if the differences observed were the same across multiple reagents.

For all assays, results were expressed as a ratio in comparison to the HB FVIII CS assay.

Assays were defined as acceptable for use if medians were ±30% (median ratio 0.70–1.30) that of HB CS FVIII:C for samples with 10-30 IU/dL activity and within ±20% (median ratio 0.80–1.20) for samples with >30 IU/dL activity. Ratios were not calculated for FVIII:C < 10 IU/dL.

Results: Only three OS assays gave median results within 30% of the HB CS assay for samples with FVIII:C 10-30 IU/dL (Actin FSL median

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1.10 [interquartile range 0.84–1.26]; Actin FS 1.22 [1.10–1.49] and Cephen LS 1.06 [0.84–1.35]).

No OS assay gave median results within 20% of the HB CS assay for samples with FVIII:C > 30 IU/dL.

Both Siemens and Precision Biologic CS assays tested gave acceptable results.

Discussion/Conclusion: No OS assay tested met the criteria to be considered suitable for measuring VR in patient samples; all CS assays tested did meet those criteria.

An OS/CS-conversion factor should not be used to estimate VR activity, as there is wide variability of results, meaning that no single factor can be determined.

Those without access to CS assays should send samples to a laboratory with a CS assay available.

Disclosure of Interest: None declared.

PO024 | Investigating the role of factor VIII in endothelial cell function

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Introduction: Haemophilia A (HA) is a rare bleeding disorder caused by the absence or dysfunction of factor VIII (FVIII). Clinical manifestations are spontaneous bleedings that primarily consist of haemarthroses and intracranial haemorrhages. Attenuated microvascular endothelial functionality is observed in HA patients suggesting a dysfunction in endothelial cells (eCs). Current therapeutic practice consists of replacement therapy with recombinant FVIII (rFVIII). However, standard therapies are ineffective in preventing the bleeding episodes that can occur without any clear cause. Since new generations of rFVIII and replacement therapy are emerging, we aim to study the possible effects of several rFVIII products on the maintenance of EC functionality.

Methods: Blood outgrowth eCs (BOECs) were isolated from HA patients and healthy donors. HA BOECs were treated in vitro with B-domain deleted (BDD), Fc-fused, Pegylated or FL rFVIII. EC functionality was evaluated by tubulogenic, migration, permeability and proliferation assays. The impact of the BDD or FL forms of rFVIII were also evaluated in a permeability assay in vivo in NOD/SCID γ–Null HA (NSG-HA) mice.

Results: In vitro results demonstrated a weakening in tubulogenesis, migration potential, and permeability of HA eCs versus healthy eCs. A significant enhancing of tubule network formation was observed in HA BOECs treated with BDD-, FL- and pegylated-rFVIII, with a higher significance for BDD-rFVIII treated cells. Moreover, migration assays of HA BOECs treated with BDD-, FL- and pegylated-rFVIII showed an improvement in the migration ability of HA BOECs after treatment. In a permeability assay, we demonstrated that the HA BOEC monolayer was less permeable to FITC-dextran, when treated with BDD-, FL- and pegylated-rFVIII. However, in the migration and permeability assays, the treatment with BDD-rFVIII was more effective compared to the other rFVIII used. Finally, a vessel permeability assay in vivo demonstrated a significant reduction of dye extravasation in NSG-HA mice treated with rFVIII, with a greater effect in mice treated with BDD-rFVIII compared with FL-rFVIII.

Discussion/Conclusion: In conclusion, these results can provide new insights into unexplored roles of FVIII, and the knowledge of the possible effect of several rFVIII forms on EC functionality can lead to new therapeutic approaches resulting in a safer and more efficient treatment of HA.

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PO025 | expression of the human factor VIII transgene from dirloctocogene samoparvovec, a liver-specific recombinant adeno-associated virus gene therapy, for up to 72 weeks in adult mice

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Introduction: Liver-directed recombinant adeno-associated virus (rAAV) gene therapy is a promising method for treating genetic diseases such as haemophilia A. We explored long-term expression of a B-domain-deleted (BDD) human factor VIII (hFVIII) transgene delivered via our liver-directed AAV gene therapy platform in mice up to 72 weeks.

Methods: Adult male C57BL/6 mice were dosed with 3.5×10^{10} vector genomes/mouse of an AAV-Spark100 encapsidated rAAV with the same vector genome as investigational dirloctocogene samoparvovec (SPK-8011) and followed for up to 72 weeks, with terminal timepoints also at Weeks 5, 24 and 48. Circulating hFVIII was assessed via enzyme-linked immunosorbent assay, while vector genome copy number (VGCN) and transgene RNA levels in the liver were assessed via real-time quantitative polymerase chain reaction assays.

Results: BDD-hFVIII protein, VGCN and RNA were quantified at regular timepoints up to 72 weeks. BDD-hFVIII plasma protein expression varied but demonstrated mean ± standard deviation (SD) circulating levels of 81.5% ± 21.1% of normal (150 ng/mL = 100%) across measurements every 4 weeks. Mean ± SD hFVIII protein at Weeks 4, 24, 48 and 72 was 98.7% ± 39.9%, 114.7% ± 104.5%, 89.8% ± 61.7% and 94.4% ± 66.8% of normal, respectively. A linear mixed effects model was fit to hFVIII levels to evaluate protein over time after the initial incline, revealing a slope of −0.5% of normal protein per week (95% confidence interval: −1.2–0.1), which was not significantly

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less than zero (p = .082). Liver BDD-hFVIII VGCN and RNA were preserved up to Week 72. At Weeks 5, 24, 48 and 72, mean ± SD BDD-hFVIII VGCN was $3.2 \times 10^5 \pm 1.8 \times 10^5$; $1.8 \times 10^5 \pm 5.9 \times 10^4$; $2.2 \times 10^5 \pm 8.8 \times 10^4$ and $1.4 \times 10^5 \pm 1.1 \times 10^5$ CN/μg DNA, respectively, and mean ± SD RNA was $3.0 \times 10^5 \pm 1.5 \times 10^5$; $1.0 \times 10^5 \pm 9.1 \times 10^4$; $1.9 \times 10^5 \pm 8.4 \times 10^4$ and $1.6 \times 10^5 \pm 8.2 \times 10^4$ CN/μg RNA, respectively.

Discussion/Conclusion: Long-term expression from a rAAV-delivered BDD-hFVIII transgene was observed in adult male mice. Liver BDD-hFVIII VGCN and RNA were preserved at 72 weeks, and circulating BDD-hFVIII protein expression demonstrated no sign of a decline over the 72-week time course. Importantly, these data support the potential for FVIII-encoding gene therapies, such as dirloctocogene samoparvovec, to achieve durable FVIII levels.

Disclosure of Interest: E. Blanchard Shareholder of: F. Hoffmann-La Roche Ltd., Employee of: Spark Therapeutics, T. Antrilli Shareholder of: F. Hoffmann-La Roche Ltd., Employee of: Spark Therapeutics, G. Jones Employee of: Spark Therapeutics, D. Peterson Shareholder of: F. Hoffmann-La Roche Ltd., Employee of: Spark Therapeutics, G. Rivera-Pena Shareholder of: F. Hoffmann-La Roche Ltd., Employee of: Spark Therapeutics, J. Silverberg Employee of: Spark Therapeutics, E. Heinzel Employee of: J&J Consumer Health (Current), Spark Therapeutics (Previous), S. Smith Employee of: Spark Therapeutics (Previous), G. Atkins Shareholder of: F. Hoffmann-La Roche Ltd., Employee of: Spark Therapeutics, J. Frick Employee of: Century Therapeutics (Current), Spark Therapeutics (Previous), C. Li Shareholder of: F. Hoffmann-La Roche Ltd., Employee of: Spark Therapeutics, H. Beck Employee of: Spark Therapeutics, H. Hanby Shareholder of: F. Hoffmann-La Roche Ltd., Employee of: Spark Therapeutics, J. Alexander Shareholder of: F. Hoffmann-La Roche Ltd., Employee of: Spark Therapeutics, C. Riling Shareholder of: F. Hoffmann-La Roche Ltd., Employee of: Spark Therapeutics.

PO026 | Sonorheometry for assessment of haemostatic status—results of preclinical verification

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Introduction: The Quantra analyser is a novel point-of-care diagnostic device that uses an ultrasound-based technology, sonic estimation of elasticity via resonance (SEER) sonorheometry, to measure changes in viscoelasticity of a whole blood sample during coagulation.

The aim of this study was to compare SEER sonorheometry (Quantra) results to corresponding parameters of another viscoelastic testing device [rotational thromboelastometry (ROTEM)] and standard laboratory tests in selected individuals.

Methods: A total of 15 persons were enrolled in this prospective preclinical study: five healthy individuals, two patients with severe haemophilia A, one with thrombocytopenia, one with hypofibrinogenaemia, one with sepsis induced coagulopathy (SIC) and five heparinised patients.

Each case was assessed concurrently for laboratory tests [PT, APTT, fibrinogen, low-molecular weight heparin (LMWH, antiXa), VWF:Ag, VWF:Act, platelet count], ROTEM (EXTEM, INTEM, FIBTEM and HEPTEM), and Quantra [clot time (CT), heparinase clot time (CTH), clot stiffness (CS), fibrinogen contribution to CS (FCS), platelet contribution to CS (PCF)]. Correlation between Quantra and corresponding ROTEM parameters and standard lab tests was assessed with linear regression analysis/Spearman's correlation coefficient.

Results: Quantra parameters showed a strong correlation with corresponding ROTEM parameters: $r = 0.787$ for CT versus INTEM CT, $r = 0.651$ for CTH versus HEPTEM CT, $r = 0.678$ for CS versus EXTEM MCF and $r = 0.968$ for FCS versus ROTEM FIBTEM MCF. Quantra parameters also strongly correlated with corresponding lab tests: $r = 0.761$ for CT versus APTT, $r = 0.942$ for FCS versus Fibrinogen and $r = 0.556$ for PCS versus PLT. Quantra profiles were normal in healthy individuals. Quantra CT was prolonged in both haemophilia A patients. In the case with thrombocytopenia CS and PCS were decreased. No clot was detected in FCS, and low CS was identified in the case with hypofibrinogenaemia. Prolonged CT and normal CS were found in the SIC case with low PCS and high FCS. The effect of heparin was illustrated with a prolonged CT while CTH was normal.

Discussion/Conclusion: SEER sonorheometry results' were proportionate to comparators and identically interpreted in the clinical context, providing valuable information about the haemostatic status in real-time.

Disclosure of Interest: None declared.

PO027 | Impact of differential binding of recombinant factor VIII concentrates to platelets on platelet functionality

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Introduction: After vascular injury, platelets become activated and proaggregatory. A subpopulation undergoes a phenotype shift to a procoagulant state. These platelets bind factor VIII (FVIII). It is unclear if modifications in recombinant (r)FVIII products impact FVIII-platelet binding and intracellular signalling. We examined the binding of different rFVIIIs to platelets in vitro and their impact on platelet phenotype and signalling.

Methods: Activated platelets from healthy donors or haemophilia A donors were incubated with simoctocog alfa, efmoroctocog alfa, turoctocog alfa pegol or damoctocog alfa pegol. rFVIII-platelet binding was measured with static and dynamic assays, and quantified by flow cytometry. The extent of phosphatidylserine (PS) exposure on the platelet surface was used to quantify the shift to a procoagulant state and was detected with the molecular probe Annexin V-BV421. To

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assess the role of integrin αIIbβ3 signalling in response to FVIII-platelet binding, platelets were concurrently activated and incubated with the integrin αIIbβ3 inhibitory antibody 10E5.

Results: In the static assay, binding to platelets of healthy donors was significantly higher with simoctocog alfa than with the other rFVIIIs. Dynamic platelet-binding assays with the two rFVIIIs exhibiting the strongest binding in the static assay (simoctocog alfa and efmoroctocog alfa) confirmed the static assay results. Incubation of platelets with simoctocog alfa or efmoroctocog alfa resulted in increased PS exposure, with a greater effect observed with simoctocog alfa. Immunostaining showed co-localisation of simoctocog alfa and integrin αIIbβ3 in proaggregatory platelets. Inhibition of integrin αIIbβ3 decreased binding of simoctocog alfa to platelets in a dose-dependent manner. In platelets from haemophilia A donors, similar trends were observed for the analysis of both platelet binding and phenotype shift.

Discussion/Conclusion: Simoctocog alfa showed higher binding to activated platelets compared with other rFVIIIs. The increased binding was associated with a phenotype shift in platelets, which was blocked with inhibition of integrin αIIbβ3, suggesting a role of integrin αIIbβ3 signalling following FVIII-platelet binding. Variation in platelet binding and signalling between different rFVIIIs might impact their efficacy for bleed prevention in people with haemophilia A.

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PO028 | Adults with haemophilia B and history of chronic HCV/HBV infection receiving etranacogene dezaparvovec gene therapy in the HOPE-B clinical trial demonstrate long-term bleeding protection and sustained fix activity 3 years after administration

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Introduction: Etranacogene dezaparvovec (formerly AMT-061) has recently become a therapeutic option for patients (pts) with haemophilia B (HB) and comorbid chronic hepatitis C virus (HCV) and hepatitis B virus (HBV). The pivotal phase 3 HOPE-B trial (NCT03489291) evaluated etranacogene dezaparvovec in pts with severe or moderately severe HB; here we evaluate the efficacy and safety in the subset of pts with a history of chronic HCV and/or HBV over 3 years post treatment.

Methods: Adult males with haemophilia B (factor IX [FIX] ≤2%), were infused with a single dose of etranacogene dezaparvovec (2×10^{13} gc/kg; an adeno-associated virus serotype 5 (AAV5) vector containing FIX Padua R338L transgene under the control of the liver-specific promoter LP-1), following a ≥6-month lead-in period of FIX prophylaxis. Exclusion criteria included baseline liver chemistries > 2× upper limit of normal; active HCV/HBV or uncontrolled HIV infection; or advanced liver fibrosis (FibroScan score ≥9 kPa).

Results: Of 54 pts in the HOPE-B trial, 31 (57.4%) had comorbid chronic HCV without active disease. Of these, seven had a history of chronic HBV infection without active disease. Two were HCV/HIV co-infected. Two pts were HBV+/HCV−/HIV−. The mean age in HCV/HBV pts ($n = 33$) was 50.0 years (range, 31–75). Mean ± SD FIX activity was 46.5 ± 23.0, 40.2 ± 20.8 and 44.5 ± 19.0 at Years 1, 2 and 3 in HCV/HBV pts and 34.0 ± 17.8, 31.3 ± 14.6 and 31.0 ± 13.1 at Years 1, 2 and 3 in HCV−/HBV− pts ($n = 21$). Mean FibroScan score for HCV/HBV pts was 5.2 kPa (range 2.8–8.0). Excluding 1 pt with AAV5 neutralising antibody (NAb) titre of 1:3212, HCV/HBV pts ($n = 32$) demonstrated ABR ratio of 0.31 (95% CI, 0.13, 0.72), indicating 69% reduction in all bleeding, sustained from months 7–36 posttreatment.

In the HCV/HBV subgroup, 5/33 (15.2%) had ALT elevations, of which 4/33 (12.1%) were treated with corticosteroids versus 11/54 (20.4%) and 9/54 (16.7%) in the whole HOPE-B population, respectively. As reported previously HCV/HBV pt developed a hepatocellular carcinoma (HCC) deemed unrelated to treatment.

Discussion/Conclusion: Patients in the HOPE-B trial with HCV and/or HBV infection show comparable efficacy and safety to the rest of the study population.

Disclosure of Interest: A. von Drygalski Consultant for: Biomarin, Sanofi Genzyme, Novo Nordisk, Pfizer, uniQure, Hematherix, N. O'Connell Consultant for: CSL Behring, F. Hoffman-La Roche, Novo Nordisk, Sanofi, Speaker Bureau of: Takeda, P. Verhamme Consultant for: CSL Behring, Roche, CAP-DCF, Bayer HealthCare, LeoPharma, Boehringer Ingelheim, Daiichi Sankyo, Pfizer, Sanofi-Aventis, ThromboGenics, K. Meijer Consultant for: UniQure, Octapharma USA Inc., Bayer, Speaker Bureau of: Alexion pharmaceuticals Bayer, CSL Behring, P. van der Valk Consultant for: Bayer, R. Kazmi Consultant for: BioMarin Pharmaceuticals, CSL Behring, P. Raheja: None declared, N. Galante Employee of: CSL Behring, S. Le Quellec Employee of: CSL Behring, R. Church Employee of: CSL Behring, S. Lucas Employee of: CSL Behring, G. Castaman Grant/Research support from: CSL Behring, Pfizer, Sobi, Speaker Bureau of: Bayer, Biomarin, Roche, Sobi, Grifols, LFB, Novo Nordisk, Werfen, Kedrion, uniQure, P. Monahan Employee of: CSL Behring.

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PO029 | Effect of yoga on joint health in person with haemophilia

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Introduction: Though haemophilia is a bleeding disorder, with primary pathology in the blood, it is the joints and the muscles that are most commonly affected. Exercise and physiotherapy are known to strengthen the musculoskeletal system and also improve the quality of life in persons with haemophilia. We studied the role of Surya Namaskar Yoga in improvement in quality of life in person with haemophilia (PwH).

Methods: All PwH attending the haemophilia treatment centre who were willing to participate in this study were included in the study. Those with major bleeds and hospitalised due to any reason were excluded. PwH were randomly assigned to attend Yoga class twice a week, where they were taught Suryanamaskar Yoga under the supervision of physiotherapist, nurse and physician. Haemophilia Joint Health Score (HJHS) was calculated at the baseline and repeated after 1 year of Yoga practice.

Results: Eighty-seven PwH consented to participate, out of which only 31 could complete the study. Sixteen PwH underwent active Yoga practice more than three times in a week and 15 PwH continued prophylaxis therapy conservatively, without active yoga practice. The mean HJHS score improved from 26.25($\pm$15.29) to 8.63(+11.05) ($p < .001$) in PwH who underwent active Yoga intervention and 21.87 (+11.05) to 14.87(+8.42) ($p = .061$) in those with conservative treatment. There was 67% improvement (mean change in HJHS 17.62) in those with Yoga where as 32% improvement (mean change in HJHS 7.00) in those with conservative treatment.

Discussion/Conclusion: Yoga significantly improves the Joint Health in PwH.

Disclosure of Interest: None declared.

PO030 | Surgery in haemophilia with inhibitors under emicizumab prophylaxis

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Introduction: Surgery in people with haemophilia and factor VIII (FVIII) inhibitors is typically managed with perioperative administration of haemostatic agents. Both aPCC and rFVIIa have demonstrated haemostatic efficacy for the treatment of patients with inhibitors who are undergoing surgery. In recent years after emicizumab, clinical experience of surgery in patients with inhibitors who are receiving emicizumab is growing; however, there are still no standardised guidelines to the concomitant administration of haemostatic agents. Here, we report surgeries in PwH with inhibitor who are under emicizumab prophylaxis.

Methods: Six surgical interventions (two major, four minor) were performed in 4 PwH with inhibitor. All surgeries were arranged to coincide with patient's regularly scheduled emicuzumab maintenance dose of 1.5 mg/kg, which was administered the day of surgery. All patients received 40 mg/kg/day tranexamic acid before 12 h the surgery and continued for 10 days.

Results: Two major surgeries were performed. First one was femoral osteotomy in 17 years old PwH who had left distal femoral valgus deformity and multiple hereditary exostoses and the second one was total knee arthroplasty in 29 years old PwH. Both of them received decreasing doses rFVIIa. No adverse events (thrombosis, bleeding) were recorded. Two minor surgeries were circumcisions in PwH who were 10 and 8 years old. Both patients did not receive factor replacement and no adverse events were recorded in two procedures. Another two were dental procedures. In one procedure prolonged bleeding was recorded and rFVIIa was used to stop bleeding.

Discussion/Conclusion: In the current knowledge surgery can be successfully performed in patients with inhibitors who are receiving emicizumab and bypassing agents can be used concomitantly. In our patients, who had major surgeries received rFVIIa without any complications. Additionally, minor surgeries can be performed without factor replacement. Although clinical experiences were increasing, prospective studies are required to further recommendations for haemostatic management of surgery in patients receiving emicizumab.

Disclosure of Interest: None declared.

PO031 | Cardiovascular safety and brain protective effect of emicizumab in patients with haemophila older than 40

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Introduction: Frequent concerns have arisen regarding the cardiovascular safety and thrombosis risk in older patients with haemophilia, particularly those who have pre-existing cardiovascular risk factors (CRVF) on emicizumab. However, these concerns are predominantly grounded in limited real-world data.

Methods: To bridge this knowledge gap, we aimed to assess our proactive approach in adopting emicizumab across all our patients with severe haemophilia A, including older individuals with multiple comorbidities and CVRF.

Results: Out of the 117 patients with severe to moderately severe haemophilia A followed at the Saint-Luc university Hospital in Brussels, 52 are aged 40 or older. In the past three years, 44 (84%) patients opted to transition to emicizumab, while 8 (16%) chose to continue their prophylactic treatment with FVIII concentrate (standard half-life [3] and extended half-life FVIII [5]). Prior to switching to emicizumab, 34 patients were receiving FVIII prophylaxis, and 10 were on an

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on-demand treatment regimen. A majority of patients (42) now receive emicizumab every 4 weeks. Among them, 16 were observed to have an equivalent FVIII activity at a steady state, measured by chromogenic assay, exceeding 20%. Five patients did not have any known CVRF, while 19 had at least two CVRF, distributed as follows: hypertension (22), diabetes (5), high cholesterol (12), HIV treatment (7), obesity (7) and active smoking (15). One patient had atrial fibrillation (AF), and another had ischemic heart disease with a cardiac stent requiring platelet inhibition with clopidogrel at the initiation of emicizumab. Notably, during the follow-up period after the commencement of emicizumab, no cardiovascular events were observed, even in a patient aged 82 with AF and FV Leiden, who required hospitalisation for severe COVID-19 infection. In contrast, two patients on FVIII prophylaxis experienced intracranial bleeding due to uncontrolled hypertension, which was fatal in one case.

Discussion/Conclusion: Our experience, characterised by a lack of selection bias, does not substantiate the assumption that emicizumab is linked to an increased incidence of thrombotic events in older patients with multiple CVRF. Instead, our series suggests that emicizumab may have a significant protective effect against the incidence of intracranial bleeding, although confirmation in larger-scale studies is warranted.

Disclosure of Interest: C. Hermans Consultant for: Roche, Speaker Bureau of: Roche, E. Krumb: None declared, M.-A. Van Dievoet: None declared, C. Lambert: None declared.

PO032 | A novel gene editing lexicon strategy for the haemophilia community

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Introduction: Advances in gene editing technologies such as the CRISPR/Cas9 system show great potential to address the unmet needs of the haemophilia community. Despite the breakthrough in treatment with gene editing platforms, language used to explain and discuss gene editing is not aligned across lived experience experts (including people living with haemophilia and their families and loved ones), health care professionals, advocacy groups, regulatory agencies and payors. Here, we present the objective and rationale for developing a clear and consistent globally-aligned gene editing lexicon for the haemophilia community.

Methods: Effectively communicating gene editing concepts among the haemophilia community requires clear, consistent language. To this end, our main goal is to develop a lexicon by collaborating with leading organisations and societies across the haemophilia community. The goal of this lexicon is to be inclusive, scientifically accurate and reassuring while avoiding overpromising or highly technical terminology. In an innovative and iterative process, representatives from major organisations in the haemophilia community helped develop and refine written language concepts for testing. Then, approximately eighty participants ($N = 66–88$) across three countries (US, UK, Germany) will participate in in-depth virtual group listening sessions to provide their input on the language concepts and influence the development of the lexicon. Research participants include representatives from major stakeholders in the haemophilia community: lived experience experts and haematologists.

Results: Initial feedback from representatives across the academic and scientific haemophilia community have laid the groundwork for clear, consistent language around genetic treatment approaches in haemophilia with a special focus on gene editing that would allow development of valid informed consent and shared decision-making.

Discussion/Conclusion: Results so far provide important building blocks for the development of a clear and consistent gene editing lexicon. The next phase will involve the development of novel language (i.e., a diverse set of articulations explaining key elements of gene editing) and visual aid based on the analysis of insights from members of haemophilia community. These stimuli will be tested with lived experience experts and haematologists to understand what resonates most across audiences and to help shape the final lexicon.

Disclosure of Interest: C. Hermans Consultant for: Biomarin, CSL Behring, Pfizer, Spark, Regeneron, C. Thornburg Grant/Research support from: Biomarin Pharmaceuticals and NovoNordisk, Consultant for: CSL Behring, Genentech, Pfizer, Sanofi, Spark Therapeutics and Regeneron, C. Unzu: None declared, M. Kay Grant/Research support from: Catalyst Biosciences, Consultant for: LogicBio Therapeutics, Voyager Therapeutics, and Regeneron, Employee of: Cofounder of LogicBio Therapeutics. Scientific founder of Voyager Therapeutics, K. Starcevic Consultant for: Regeneron, M. Pillai Consultant for: Regeneron, M. Jones Shareholder of: Regeneron, Employee of: Regeneron, M. Chiao Shareholder of: Regeneron, Employee of: Regeneron, I. Antonino Shareholder of: Intellia, Employee of: Intellia, C. Kessler Grant/Research support from: Biomarin, Sangamo, Regeneron, Consultant for: Biomarin, Sangamo, Regeneron, CSL Behring, Pfizer, Spark.

PO033 | Value of MRI in early detection and evaluation of haemophilic arthropathy; correlation with clinical evaluation

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Introduction: Haemophilic arthropathy is the most common complication in patients with haemophilia. If not properly treated and controlled in the beginning, it could develop into a crippling condition that eventually necessitates extensive surgery, such as total joint

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arthroplasty. Objective imaging diagnosis rather than subjective evaluation is crucial, preventing over- or under-treatment.

The aim of the work is to evaluate the value of MRI in evaluation and early detection of joint affection in haemophilic patients in correlation with their clinical presentation. And to assess the role of T1 3D FFE MRI sequence in haemosiderin deposition and cartilage degeneration in haemophilic joints.

Methods: This prospective retrospective cohort study enrolled 70 haemophilic patients with age range (2–18 years) with or more target joint affection under either prophylactic or on demand therapy protocols. All patients were subjected to proper history, assessment of musculoskeletal function of the joints using HJHS scoring system version 2.1 which was assessed in all patients by both a haematologist and a physiotherapist. Assessment of the MRI score of the examined joints was performed in all patients using IPSG MRI scale. US and X-ray were done to evaluate joints in some patients.

Results: There was a strong positive correlation between haemophilic joint score and IPSG MRI score in symptomatic joints ($p < .001$) while There was no significant correlation between HJHS and IPSG MRI score among asymptomatic joints. The T13D FFE sequence was better for detection of haemosiderin and cartilage degeneration in asymptomatic joints than in symptomatic group.

Discussion/Conclusion: Pathological abnormalities in asymptomatic joints that seem normal on clinical evaluation can be found with MRI. As arthropathy progresses, the role of clinical examination increases to assess the disease severity. The 3DT1FFE MRI sequence is needed for detection of early arthropathic changes and its efficiency in asymptomatic joints rather than in cases of advanced arthropathy.

Disclosure of Interest: None declared.

PO034 | Interim results from a prospective, non-interventional study on the use of rVIII-SingleChain in patients with haemophilia A

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Introduction: Haemophilia A (HA), a rare X-linked bleeding disorder caused by factor VIII (FVIII) deficiency, can lead to severe bleeds. rVIII-SingleChain is a recombinant FVIII indicated for the treatment of HA. To confirm clinical trial outcomes in the real world, the efficacy of rVIII-SingleChain during routine clinical practice is being assessed across six European countries (22 centres). Following the results from the first data-cut, we are committed to reporting data from the second data-cut.

Methods: In a non-interventional, multicentre study, patients with HA received rVIII-SingleChain in routine patient care. Patients will be followed up, during routine clinical visits, for up to 3 years. Primary endpoints include annualised bleeding rate (ABR), annualised spontaneous bleeding rate (AsBR), infusion frequency, dosage and haemostatic efficacy. Patients with < 12 weeks of treatment were excluded from analyses.

Results: Seventy-two patients (45 severe HA), with a mean (SD) age of 31.2 (16.05) years were enrolled in the study. Patients were enrolled from: Austria ($n = 9$), Belgium ($n = 4$), Germany ($n = 43$), Greece ($n = 12$), Czech Republic ($n = 2$) and Hungary ($n = 2$). At the time of the data-cut, patients had been followed up for a mean (SD) period of 22.6 (7.96) months. Twelve patients discontinued (none due to lack of efficacy or safety concerns of rVIII-SingleChain). In total, 68/72 patients were on a prophylaxis (PPX) regimen, with a mean (SD) interval of 2.78 days (1.25). The mean ABR and AsBR ($n = 58$ and $n = 57$) for patients on PPX were 1.20 and 0.83, respectively. For those on an on-demand (OD) regimen, ABR and AsBR (both $n = 10$) were 2.36 and 0.24, respectively. Most bleeding episodes reported across both groups were mild ($n = 62$ and $n = 22$); eight severe bleeds were reported in the PPX group. The majority of bleeds occurred within the joints ($n = 81$ and $n = 13$ for the PPX and OD groups, respectively). For patients with at least one assessment of a bleeding episode, overall haemostatic effectiveness was excellent (42.0%) or good (39.5%). Adverse events ($n = 23$) were reported in 13 patients; none included inhibitor formation or were related to rVIII-SingleChain.

Discussion/Conclusion: Real-world data support the clinical trial data; this second interim analysis demonstrates the efficacy and favourable safety profile of rVIII-SingleChain when used for PPX and OD treatment in routine clinical practice.

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PO035 | Validity and reliability of thai version of the paediatric haemophilia activities list (PedHAL)

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Introduction: Objectives: To evaluate validity and reliability of Thai version of the Paediatric Haemophilia Activities List (PedHAL).

Study design: Descriptive study.

Setting: Department of Rehabilitation Medicine and Pediatric Department, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand.

Subjects: Haemophilia patients attending Department of Rehabilitation Medicine and Paediatric Department during June 2021–September 2022.

Methods: The owner of PedHAL and researchers translated PedHAL into Thai language by forward–backward method and measured content validity. Then, we used the form to evaluated construct validity by correlated with Functional Independence Score for Haemophilia (FISH) and Haemophilia Joint Health Score (HJHS). Finally, we measured reliability by calculated internal consistency and test-retest reliability.

Results: Thai version of PedHAL has acceptable content validity (CVI = 0.99; ≥0.90), good construct validity by strong correlation with FISH (r = 0.703; 0.70–0.89) and moderate negative correlation with HJHS (r = −0.475; 0.40–0.69), excellent test–retest reliability (ICC = 0.955; ≥0.90) and excellent internal consistency (Cronbach's alpha = 0.944; ≥0.9).

Discussion/Conclusion: Thai version of PedHAL has good content validity and good construct validity. We found good correlation with FISH and moderate correlation with HJHS. For reliability, this study found excellent test–retest reliability and internal consistency. Thai version also has good correlation with FISH that also be recommended as an assessment tool for activity domain. In contrast, FISH which is a performance test has more time consuming and has to be assessed by physician or therapist. FISH also requires more equipment and prepared vacancy. For this reason, assessing activity domain by Thai version of PedHAL could be more time-cost effective and done by patient and/or their parent while waiting to see the physician at that visit and health care provider can use the data immediately after they complete the form.

Thai version of The Paediatric Haemophilia Activities List has good validity and reliability as a self-measurement tool for assessment of limitation in activity in Thai children with haemophilia disease. In additional, it could be served as a tool in assessing patients in other research purposes.

Disclosure of Interest: None declared.

PO036 | A case of acquired factor XI deficiency and retroperitoneal bleed associated with Streptococcus pyogenes cellulitis

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Introduction: Acquired factor XI (FXI) deficiency is a rare autoimmune-associated bleeding disorder, described with for example systemic lupus erythematosus. We report the clinical phenotype and management of the first acquired FXI deficiency case in Finland.

Methods: Activated partial thromboplastin time (APTT) and FXI activity were measured in a BCS XP Analyser (Siemens, Germany). A mixing study using normal pooled plasma for FXI inhibitor detection was performed.

Results: A 77-year-old healthy man presented at the ER with severe upper extremity cellulitis originating from a wound of the thumb. The cellulitis was caused by *Streptococcus pyogenes* and required surgical revision. The initial coagulation lab work-up showed normal APTT. A few days later transfusion-dependent persistent anaemia developed. Large hematomas in the upper arm, iliopsoas and iliacus muscles, and some blood in the abdominal cavity appeared. Next, prolonged APTT (51 s, 1.5 x normal) was found to be explained by FXI deficit (18%). Without prior bleeding and with previous normal coagulation tests, inherited FXI deficiency was unlikely. However, the mixing study corrected APTT, not supporting acquired factor inhibitor, while multiple plasma infusions were ineffective in ceasing the bleeds or raising FXI levels. Phospholipid antibodies were absent and platelet function (PFA200) was normal. Both FXIII and FXII were low (30%–40%), and FXIII replacement was given. Immunosuppression with immunoglobulin (IvIg) 1 mg/kg/day and corticosteroids was started. Three days later an extensive retroperitoneal bleed was diagnoses and urgent angioembolisation was performed twice. rFVIIa (90 mcg/kg) failed to stop the leakage, and activated prothrombin complex concentrate (APCC) was administered daily at 50 IU/kg, and increased to 200 IU/kg/d. During APCC, extensive thrombosis in the upper limb developed. However, thrombosis

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resolved in 5 days with low molecular weight heparin. Haemostasis was finally controlled, and the follow-up immunosuppression comprised IVIg 0.5 g/kg for 5 days and rituximab 375 mg/m^2/week for 3 weeks with steroid tapering. FXI levels gradually improved (>30%), and the patient was transferred to rehabilitation care without further bleeds.

Discussion/Conclusion: Immunosuppressive therapy resolved bleeding and FXI levels improved. We postulate that the severe infection triggered the immune reaction and in vivo consumption of FXI.

Disclosure of Interest: None declared.

PO037 | French real-word data on rIX-FP prophylaxis use in paediatric patients with haemophilia B

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Introduction: The OrPHEe study is an ambispective, observational study (NCT05086575) describing real-world efficacy and safety data on the use of rIX-FP prophylaxis (PPX) in patients with haemophilia B (HB) in France.

Methods: This interim analysis included data collected from October 2021–August 2023. Dosing frequency, weekly consumption and bleeds before and after switching to rIX-FP were recorded. Annualised (spontaneous) bleeding rates (A[s]BR) were calculated only in patients on PPX with a follow-up period of ≥6 months. Results are presented as median (IQR). Wilcoxon matched-pairs signed rank tests were used to compare data pre- and post-switch to rIX-FP.

Results: Among 134 patients included, 97 were treated with rIX-FP PPX. This analysis focused on 25 patients <12 years old, including 23 (92%) severe HB patients. 20/25 (80%) were previously treated with PPX (16 with rFIXFc, four with rFIX). After switching to rIX-FP, patients were treated every 7 (7−14) days, including 10 patients treated every 10 days or more. Weekly consumption was 47 (38−54) IU/kg (n = 24, data missing [DM] for one patient). ABR and AsBR were 0 (0−3) and 0 (0−0), respectively (n = 22 for both; DM for three patients), with a follow-up period of 16.5 (14−20) months. 21/22 (95%) of investigators evaluated the efficacy of rIX-FP PPX as 'Excellent', and 21/21 evaluated the safety as 'Good' (DM for three and four patients, respectively). Three adverse events were reported, including one related to rIX-FP (one spontaneous haemarthrosis). Patients previously treated with rFIXFc reduced their infusion frequency from every 7 (7−7) days to every 7 (7−14) days with rIX-FP (n = 15; DM for one patient; $p < .05$). Weekly consumption was slightly reduced with rIX-FP from 62.5 (50−83) to 51 (42.5−55) IU/kg. Despite these reductions, patients treated with rIX-FP PPX maintained good protection against bleeds (ABR: from 1 [0−2] to 0 [0−2]; AsBR: from 0 [0−1] to 0 [0−0]; n = 13 for both; DM for three patients) during a follow-up period of 17 (16−20) months.

Discussion/Conclusion: To date, the OrPHEe study is the largest cohort of patients with HB treated with rIX-FP and confirms the good efficacy and safety observed during clinical development in paediatric patients (<12 years old). Data also showed that some paediatric patients who switched to rIX-FP were able to reduce their injection frequency and FIX consumption whilst maintaining a good level of protection against bleeds.

Disclosure of Interest: Y. Huguenin Consultant for: has participated to clinical trials, advisory board and symposia for CSL Behring, Roche, Sobi, LFB, Takeda, Sanofi, A. Harroche Consultant for: has participated to clinical trials, advisory board and symposia for CSL Behring, Roche, Sobi, LFB, Bayer, Takeda, Octapharma, Novo Nordisk, Sanofi, Y. Dargaud Grant/Research support from: has received grants/research support from Bayer, Baxter, Baxalta, Novo Nordisk, CSL Behring, LFB, Pfizer, LEO Pharma, Octapharma and Stago; an educational grant from Takeda and honoraria from Bayer, Baxter, Novo Nordisk, CSL Behring, Sobi and Octapharma, Consultant for: has received grants/research support from Bayer, Baxter, Baxalta, Novo Nordisk, CSL Behring, LFB, Pfizer, LEO Pharma, Octapharma and Stago; an educational grant from Takeda and honoraria from Bayer, Baxter, Novo Nordisk, CSL Behring, Sobi and Octapharma, A. Fournel: None declared, A. Rauch Grant/Research support from: has received research support for his institution from CSL Behring and Roche/ Chugai, has participated to clinical trials, advisory board and symposia for Biomarin, CSL Behring, LFB, Novo Nordisk, Octapharma, Roche-Chugai and Sobi, Consultant for: has received research support for his institution from CSL Behring and Roche/ Chugai, has participated to clinical trials, advisory board and symposia for Biomarin, CSL Behring, LFB, Novo Nordisk, Octapharma, Roche-Chugai and Sobi, C. Berger Consultant for: declares COI for Sobi and Octapharma, F. Volot Consultant for: declares COI from Sobi, Roche, Pfizer, Takeda and CSL Behring, B. Frotscher Consultant for: declares COI from Sobi, CSL Behring and Novo Nordisk, C. Oudot-Challard: None declared, M. Pondrom: None declared, H. Catovic Employee of: CSL Behring, C. Martin Employee of: CSL Behring, A. Hassoun Consultant for: has been a consultant for Bayer, CSL Behring and Sobi.

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PO038 | Stable and durable factor IX levels over 4 years after etranacogene dezaparvovec gene therapy administration in a Phase 2b trial in patients with haemophilia B

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Introduction: Etranacogene dezaparvovec is an approved gene therapy for haemophilia B (HB) comprising a recombinant adeno-associated virus serotype 5 (AAV5) vector and a codon-optimised FIX Padua variant transgene under the control of a liver-specific promoter. It is the successor to AMT-060; both are identical except for a two-nucleotide change to the wild-type FIX sequence in AMT-060 to encode the FIX Padua (R338L) variant. Sustained and stable FIX activity post-etranacogene dezaparvovec administration has been reported up to 3 years, allowing patients to discontinue prophylaxis; here we report the 4-year follow-up data.

Methods: The Phase 2b, open-label, multi-centre trial in adults with HB ($n = 3$) aimed to confirm FIX levels following the use of the Padua variant in the cassette (NCT03489291). Patients received a single intravenous dose of etranacogene dezaparvovec (2×10^{13} gc/kg) and will be initially followed for 5 years and then moved to an extension study. The primary endpoint was FIX activity at Week 6. Secondary endpoints included laboratory parameters, bleeding rates and adverse events (AEs).

Results: Patients had FIX levels ≤2%, required routine prophylaxis and had neutralising antibodies (NAbs) to AAV5 at mean titre of 25 at dosing. Post-etranacogene dezaparvovec administration, mean (SD) FIX activity increased to 31% (7.0) at Week 6, using the one-stage aPTT assay. Mean (SD) FIX activity ($n = 3$) remained stable at Year 1 (40.7% [9.45]), Year 2 (44.2% [7.66]), Year 3 ($n = 2$, (36.9% [6.51]) and Year 4 (45% [2.76]). No bleeding episodes were reported between Year 3 and 4, and consequently no FIX was infused outside of invasive procedures. ABR for the cumulative follow-up period decreased from 0.22 at Year 3 to 0.17 at Year 4. During 4 years of follow-up, no patients returned to continuous prophylaxis, no clinically significant liver enzyme elevations related to treatment occurred and no patient required steroids. As reported previously, one patient experienced two mild AEs possibly related to treatment shortly after dosing and one patient underwent hip surgery. No patients developed FIX inhibitors and no thrombosis events occurred.

Discussion/Conclusion: Sustained and stable FIX activity post-etranacogene dezaparvovec administration was observed over 4 years, enabling discontinuation of routine prophylaxis, irrespective of anti-AAV5 NAbs at baseline.

Disclosure of Interest: None declared.

PO039 | Real-world effectiveness and safety of damoctocog alfa pegol in previously treated patients with haemophilia a in italy: HEM-POWR study subgroup analysis

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Introduction: Damoctocog alfa pegol (BAY 94-9027, Jivi®) is an extended half-life factor VIII (FVIII) product approved in Italy for previously treated patients (PTPs) aged ≥12 years with haemophilia A. HEM-POWR is an ongoing Phase 4 study (NCT03932201) evaluating effectiveness and safety of damoctocog alfa pegol in PTPs with severe and non-severe haemophilia A. Here, we present the fourth interim analysis for a subgroup of patients from Italian study sites.

Methods: The primary endpoint was annualised bleeding rate (ABR) assessed in the full analysis set (FAS), which includes eligible patients with a documented first dose of study drug and ≥1 documented infusion in the patient diary. Safety, a secondary outcome, was evaluated in the safety analysis set (SAF) comprising PTPs with ≥1 study dose.

Results: At data cut-off (1 August 2023), 16 Italian PTPs were included in the FAS and 55 in the SAF. In the FAS, 68.8% of patients (11/16) were aged ≥18–< 65 years and 93.8% (15/16; missing 1/16) had severe haemophilia. Most patients received prophylactic treatment before enrolment (15/16); every 2 days (6/16) and every 3–4 days (4/16) were the most common regimens with previous FVIII product (missing 5/16). Every 3–4 days was the most common regimen with damoctocog alfa pegol at baseline (11/16) and follow-up windows 1 (11/16) and 2 (13/16). The mean (standard deviation [SD]) observation period was 638.5 (172.4) days. The total median (mean, SD) ABR was 0.0 (0.9, 1.9) within 12 months prior to initiation of damoctocog alfa pegol and 0.0 (0.7, 1.5) during the observation period; the total mean (SD) change in ABR was −0.3 (2.4). The median (mean, SD) ABR for joint bleeds was 0.0 (0.8, 1.9) prior to initiation and 0.0 (0.4, 0.7) during observation period. In the SAF, 4/55 (7.3%) patients had treatment-emergent adverse effects (TEAEs), 3 (5.5%) led to a change in treatment regimen; 2/55 (3.6%) had serious TEAEs during observation period, 1 (1.8%) led to a change of regimen. No TEAEs were study drug-related, and there were no inhibitor developments or deaths.

Discussion/Conclusion: The findings contribute to understanding real-world clinical practice in Italy and add to evidence of favourable effectiveness and safety of damoctocog alfa pegol in PTPs with haemophilia A.

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Disclosure of Interest: A. Coppola Consultant for: Acted as a paid consultant or speaker for Bayer, Kedrion, Novo Nordisk, Roche, and Werfen, C. Santoro Consultant for: Received honoraria for consulting or lecturing from Amgen, Bayer, CSL Behring, Novartis, Novo Nordisk, Pfizer, Roche, Sobi and Takeda, Speaker Bureau of: Speaker's fees

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PO040 | French real-word data on rIX-FP use for surgery in patients with haemophilia B

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Introduction: rIX-FP is a long-acting recombinant human coagulation factor IX (FIX) fused to recombinant human albumin. In clinical trials, rIX-FP has demonstrated excellent or good efficacy and a favourable safety profile in surgical use. The OrPHEe study is an ambispective, observational study (NCT05086575) describing real-world efficacy and safety data on the use of rIX-FP in patients with haemophilia B (HB) in France.

Methods: This interim analysis included data collected from October 2021 to August 2023, focusing on surgeries performed with rIX-FP. Dosing frequency, consumption and FIX activity data were collected. Data are presented as median (IQR).

Results: A total of 134 patients were included in the OrPHEe study. Of these patients, 24 (18%) underwent surgery, and their median age (range) was 44 (5—78) years, including one child. Twelve (50%) patients had a mild HB, 7/24 (29%) had a moderate HB and 5/24 (21%) had a severe HB. A total of 34 surgeries were performed with rIX-FP, of which 21 (62%) were minor surgeries (i.e., minor haemorrhagic risk) and 13 (38%) were major surgeries (i.e., major haemorrhagic risk). Minor surgeries were mainly orthopaedic (33%) and dental procedures (29%). The median pre-operative FIX level was 20 (6—35) IU/dL. The median pre-operative rIX-FP dose was 60 (48—69) IU/kg, giving a median peak FIX level of 92 (86—116) IU/dL [$n = 8$, data missing (DM) for 13 surgeries]. The median rIX-FP cumulative consumption was 60 (51—77) IU/kg/patient, administered in 1 (1—1) injection. 11/21 (55%) minor surgeries were performed on an outpatient basis. Major surgeries were mainly orthopaedic (46%) and digestive procedures (15%). The median pre-operative FIX level was 18.5 (4—42) IU/dL. The median pre-operative rIX-FP dose was 70 (61—95) IU/kg, giving a median peak FIX level of 100 (85—116) IU/dL ($n = 7$, DM for six surgeries). The median rIX-FP cumulative consumption was 160 (111—333) IU/kg/patient, spread over 3 (2—5) injections. 28/29 (95%) of investigators evaluated the efficacy of rIX-FP prophylaxis as 'Excellent' or 'Good' (DM for five surgeries). Safety was assessed as 'Good' in 100% of cases (DM for two surgeries). No adverse events were reported.

Discussion/Conclusion: Supporting data from clinical development, this interim analysis confirms in a real-world setting the efficacy and good safety profile of rIX-FP in preventing surgical bleeding in minor- or major-risk surgery in patients with HB.

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PO041 | Personalised prophylaxis with simoctocog alfa versus standard prophylaxis with efanesoctocog alfa in haemophilia A, a matching-adjusted indirect comparison

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Introduction: Matching-adjusted indirect comparison (MAIC) is a statistical method to compare outcomes from separate clinical studies when direct comparisons are not possible, such as in rare diseases like haemophilia A. MAIC was used to compare a pharmacokinetics (PK)-guided personalised prophylaxis regimen with simoctocog alfa (Nuwiq®; a 4th-generation recombinant FVIII [rFVIII] concentrate with no chemical modifications or fusion proteins) against prophylaxis with efanesoctocog alfa (Altuviiio®; an Fc-fusion rFVIII concentrate with XTEN polypeptides and von Willebrand factor fragments), in previously treated patients with severe haemophilia A.

Methods: After matching study populations, individual patient-level data (IPD) from 65 patients treated with simoctocog alfa (NuPreviq study) were compared against aggregate data from the once-weekly efanesoctocog alfa arm of the XTEND-1 study ($N = 133$). All patients were male, except for one female in XTEND-1. Baseline age and body weight were used to re-weight the simoctocog alfa IPD to match the aggregate data reported from XTEND-1. Unanchored indirect treatment comparisons were performed for outcomes using the re-weighted data for simoctocog alfa and efanesoctocog alfa. The endpoints analysed were annualised bleeding rates (ABRs), percentage of patients with zero bleeds and weekly consumption of FVIII, including treated and untreated bleeds.

Results: After matching, the effective sample size for simoctocog alfa was 35.3. The percentage of patients with zero bleeds was not statistically different for simoctocog alfa versus efanesoctocog alfa (64.1% vs. 55.5%; $p = .291$). The mean total ABRs were also similar: 1.5 for simoctocog alfa and 1.1 for efanesoctocog alfa ($p = .342$). The mean weekly dose was significantly higher in patients treated with simoctocog alfa versus efanesoctocog alfa (98.3 vs. 52.2 IU/kg; $p < .001$).

Discussion/Conclusion: PK-guided, personalised prophylaxis with simoctocog alfa resulted in zero bleed rates and ABRs that are not statistically different from those with efanesoctocog alfa. The higher weekly dose with simoctocog alfa is to be expected based on the dosing recommendations. This MAIC analysis provides comparative efficacy and utilisation data, which can help guide patients and physicians in making decisions regarding product choice for prophylaxis regimens.

Disclosure of Interest: None declared.

PO042 | Personalised prophylaxis with simoctocog alfa versus standard emicizumab prophylaxis in haemophilia A, a matching-adjusted indirect comparison

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Introduction: Matching-adjusted indirect comparison (MAIC) is a statistical method to compare outcomes from clinical studies when direct comparisons are not possible, such as in rare diseases like haemophilia A. MAIC was used to compare a pharmacokinetics (PK)-guided personalised prophylaxis regimen with a recombinant, fourth generation, factor VIII (FVIII) concentrate, simoctocog alfa (Nuwiq®), against prophylaxis with the bispecific monoclonal antibody emicizumab (Hemlibra®) in patients with haemophilia A.

Methods: After matching study populations, individual patient-level data (IPD) from 65 patients treated with simoctocog alfa (NuPreviq study) were compared against aggregate data for emicizumab administered once weekly (Q1W, pooled Group A [$N = 36$] and Group D [$N = 63$]), every 2 weeks (Q2W, $N = 35$), or every 4 weeks (Q4W, $N = 41$) (HAVEN 3 and 4 studies). Baseline age and body weight were used to re-weight the simoctocog alfa IPD to match the aggregate data reported for the emicizumab studies. Unanchored indirect treatment comparisons were performed for outcomes using the re-weighted and aggregate data. The endpoints analysed were annualised bleeding rates (ABRs) and percentage of patients with zero bleeds, including treated and untreated bleeds.

Results: After matching, the effective sample size for simoctocog alfa was 33.1, 39.8 and 29.1 for the emicizumab Q1W, Q2W and Q4W comparisons, respectively. The percentage of patients with zero bleeds was significantly higher with simoctocog alfa across all three comparisons: simoctocog alfa versus Q1W (74.3% vs. 46.5%; $p < .001$), versus Q2W (70.3% vs. 40.0%; $p = .003$) and versus Q4W (81.9% vs. 29.3%; $p < .001$). There was no difference in the percentage of patients with 0–3 bleeds across all three comparisons. The total ABRs were significantly lower with simoctocog alfa versus Q1W (1.5 vs. 2.9; $p = .035$) and Q4W (1.4 vs. 4.5; $p < .001$). When comparing simoctocog alfa versus Q2W, the difference was not statistically significant (1.3 vs. 2.6; $p = .083$).

Discussion/Conclusion: PK-guided, personalised prophylaxis with simoctocog alfa can lead to significantly higher zero bleed rates and decreased ABRs compared with standard emicizumab prophylaxis. This MAIC provides important comparative efficacy data which can help guide patients and physicians in making decisions regarding product choice for prophylaxis.

Disclosure of Interest: None declared.

PO043 | Interim analysis of real-world effectiveness and usage of recombinant factor IX Fc for surgical haemostasis from the 24-month prospective, non-interventional B-MORE Study

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Introduction: Extended half-life recombinant factor IX Fc fusion protein (rFIXFc; Alprolix®) has an established safety and efficacy profile in patients with haemophilia B (PwHB) but more real-world surgery data are needed.

Methods: B-MORE (NCT03901755) is an ongoing, 24-month prospective, non-interventional, international study evaluating the real-world effectiveness and usage of rFIXFc in PwHB. This descriptive interim analysis included PwHB who had ≥1 surgery whilst on rFIXFc (no other FIX) during retrospective/prospective periods.

Major surgery was any procedure involving general anaesthesia and/or respiratory assistance in which a major body cavity was penetrated/exposed. All other invasive surgeries were minor. Perioperative period was prior to, during and post-surgery until return to usual treatment.

Results: B-MORE enrolled 151 PwHB (data cut-off: 6 Oct 2022); 28 PwHB with 49 surgeries were included in this analysis [20 severe, 5 moderate, 3 mild haemophilia; median (range) age: 20.1 (1–81) years; no inhibitor history].

Nine surgeries were major ($n = 8$ PwHB; 7 severe, 1 moderate). Haemostatic efficacy was rated excellent/good for all eight major surgeries with available data. Median (range) total perioperative rFIXFc consumption was 182.9 (70–524) IU/kg with 4.0 (1–13) injections ($n = 9$ surgeries). Median (range) hospitalisation duration was 5.0 (2–10) days ($n = 8$ surgeries). Median (range) estimated blood loss during the intra-/postoperative period was 0.0 (0–750) mL ($n = 7$ surgeries). A total knee arthroplasty required one red blood cell unit transfusion.

Forty surgeries were minor ($n = 22$ PwHB; 14 severe, 5 moderate, 3 mild). Haemostatic efficacy was excellent/good for all 34 minor surgeries with available data. Median (range) rFIXFc consumption was 89.3 (12–452) IU/kg with 1.0 (1–8) injection ($n = 36$ surgeries). Median (range) hospitalisation duration was 2.0 (1–6) days ($n = 31$ surgeries). No blood loss was reported in 23 minor surgeries with available data.

Thromboprophylaxis was given for one major and one minor surgery. Concomitant anti-fibrinolytic therapy was used in five major and 23 minor surgeries. No inhibitor development or surgery-related adverse events (serious/leading to treatment discontinuation) were reported.

Discussion/Conclusion: Interim real-world data indicates perioperative rFIXFc is efficacious and well tolerated in PwHB.

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Disclosure of Interest: H. Glosli Grant/Research support from: Principal investigator for studies by Baxalta (Takeda), Bayer, Novo Nordisk, Octapharma, Roche and Sobi, F. Peyvandi Consultant for: Biomarin, Roche, Sanofi, Sobi and Takeda, Speaker Bureau of: Speaker/honoraria from Grifols, Roche, Sanofi, Sobi and Takeda, D. Allsup Grant/Research support from: Fee to attend conference from Bayer, CSL Behring and Gilead; Investigator in clinical trial sponsored by AstraZeneca and LOXO; research grants from Roche, O. Katsarou Speaker Bureau of: Speaker/honoraria from Bayer, CSL Behring, Novo Nordisk, Pfizer, Roche and Sobi; research grants from CSL Behring and Sobi, R. Berrueco Grant/Research support from: Reimbursement for attending symposia/congresses and/or honoraria for speaking and/or honoraria for consulting and/or funds for research from Bayer, Boehringer Ingelheim, CSL Behring, Novo Nordisk, Pfizer, Roche, Sobi and Takeda, E. Bednar Shareholder of: May hold shares and/or stock in Sobi, Employee of: Sobi, S. Lauer Consultant for: AbbVie, Boehringer Ingelheim and Sobi, E. Gresko Employee of: Former employee of Sobi, E. Santagostino Shareholder of: May hold shares and/or stock in Sobi, Employee of: Sobi.

PO044 | International data integration program of the WFH world bleeding disorders registry: bringing europe data to the global stage

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Introduction: Patient representativeness is key for data collection in the area of rare diseases such as bleeding disorders. The World Federation of Haemophilia (WFH) implemented the International Data Integration Program (IDIP) of the Word Bleeding Disorders Registry (WBDR) to ensure patients from established national registries are represented at the global level.

Methods: Data mapping processes are conducted to identify fields in common between the WBDR dataset and that of the national registry. For Model 1 using de-identified patient-level data: We developed a Data Exchange Protocol where each variable is assigned a code. Using a data import wizard, custom import files completed by the national registry are used to integrate the data in the WBDR database. Data quality checks are performed before the final integration in the database. Model 2 using aggregated data: WFH provide summary tables template where the national registry adds their aggregated data according to WBDR data analysis standards. Using various statistical methods, the aggregated data is combined with the rest of the WBDR global data for annual reporting.

Results: Data integration was done following two different models. The first model was conducted in collaboration with the Czech National Haemophilia Programme Registry (CNHPR). Data from 2018, 2019, 2020 and 2021 data from the CNHPR on over 870 PWH have been collected and annually updated. Data was used in comparative analysis based on regional and economic distribution of patients, with patients from Czechia providing the picture from a high-income country in Europe. In 2023, the WFH and the Norwegian People with Haemophilia

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Registry started a data linkage collaboration using a second model that integrates aggregated data from a national registry in the WBDR global data.

Discussion/Conclusion: The two data linkage models used in the WBDR IDIP provide established national registries with options to share data in compliance with their local data privacy and protection laws. Data from these registries complement those collected by the WBDR sites and are essential in the WFH mission of improving patient care across the world.

The WBDR is supported by Visionary Partners: Sobi, Takeda; and Collaborating Partners: Grifols, Pfizer, Roche, Sanofi.

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PO045 | Evaluation of adherence to prophylaxis treatment in haemophilia: Are we achieving our goal?

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Introduction: With the prophylaxis in the treatment of haemophilia, there has been a significant change in preventing bleeding, avoiding musculoskeletal complications and improving the quality of life of people with haemophilia. However, adherence to prophylaxis can be influenced by clinical and psychosocial factors, such as a family history of bleeding and a lack of social support. The aim of this paper is to provide an overview of the importance of adherence to prophylaxis in the management of haemophilia, highlighting the clinical and psychosocial factors that can affect adherence and the need for a multi-professional approach.

Methods: Clinical, laboratory and factor dispensing data were collected retrospectively through the records provided by the pharmacy and the Webcoagulopathies system.

Results: A total of 95 patients with haemophilia A and B were analysed, 62 had severe haemophilia, while 33 had moderate haemophilia. Among these individuals, 77 (92.5%) were on secondary/tertiary prophylaxis regimens, while 18 (57.89%) were primary prophylaxis. In the secondary/tertiary prophylaxis, only 23 patients adhered to regular prophylaxis, while 54 an irregular pattern. Among patients on primary prophylaxis, 12 maintained a regular regimen and 6 had irregular adherence. Adherence to prophylaxis is a critical factor in the management of haemophilia. The study highlights that a significant proportion of patients on secondary/tertiary prophylaxis (54 out of 77) were following an irregular treatment pattern. This is worrying since irregular adherence can increase the risk of bleeding and musculoskeletal complications. On the other hand, of the patients on primary prophylaxis, the majority (12 out of 18) were following regular prophylaxis, which is a positive sign.

Discussion/Conclusion: Non-adherence to prophylactic treatment has significant implications for the development of arthropathies and mortality in people with haemophilia. The individualisation of treatment is a factor to be considered to meet the specific needs of each case, considering factors such as unmet needs, the quality of venous access, the frequency of infusions, patients life routines, associated costs and the potential development of arthropathies, even when following a prophylactic treatment regimen. It is therefore essential to devise treatment approach strategies that make it possible to improve adherence, to preserve joint health and a better quality of life.

Disclosure of Interest: None declared.

PO046 | Challenges in managing mucosal bleeding in a PWH with high titre of inhibitors under prophylaxis with emicizumab: A case report

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Introduction: Bleeding from a bitten tongue in children with severe haemophilia with high titre of inhibitors can become life threatening due to the risk of significant blood loss or airway obstruction caused by tongue swelling.

Methods: We present the case of a 4-year-old boy known with severe haemophilia A with high titre of inhibitors who has been receiving prophylactic treatment with emicizumab q4w regimen. He also has cheilognathopalatoschisis (partially corrected through cheiloplasty and septoplasty at 10 months old).

Results: It should be noted that prior to the presentation in our clinic, he was admitted to a children's hospital for 12 days for bleeding control immediately after biting his tongue, where he received treatment with bypassing agent (eptacog alfa activated). Furthermore, a procedure was performed to evacuate the intramuscular hematoma, resulting in no improvement of the patient's condition.

The treatment consisted of oral cavity care, haemostatic treatment with eptacog alfa (activated), with an initial dosage of 140 μg/kg x 2 administrations every 5 h, followed by 107 μg/kg/dose at varying intervals of 3–4–5–6–8–12–24 h for the next 12 days, tranexamic acid 10 mg/kg every 8 h for 7 days, then every 12 h for 2 days, anti-inflammatory treatment with acetaminophen and local haemostatic management using haemostatic sponges.

The patient's response to the treatment was notably swift and positive. The bleeding stopped approximately 1 h after the treatment was

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initiated. There was minimal intermittent bleeding around the clot 48 h after admission, but it quickly subsided. The size of blood clot regressed rapidly, including the suture threads. This was completely detached 54 h after admission. The lingual mucosa, upon clot detachment, was found to be clean with discreet scarring at the suture site. Subsequently, there was no further bleeding, and the lingual mucosa had fully healed by the time of discharge.

Knowing that in patients under prophylaxis with emicizumab the results of coagulation assays cannot provide us with an estimation of efficacy, we used TGA for this purpose.

Discussion/Conclusion: We draw attention to challenges in managing mucosal bleeding in haemophilia patients under prophylactic treatment with emicizumab, which require adequate and prompt haemostasis; TGA proves to be a useful method for monitoring haemostatic status and adjusting doses in such cases.

Disclosure of Interest: None declared.

PO047 | Treatment-related humanistic unmet needs in haemophilia B without inhibitors

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Introduction: Despite improved haemophilia treatment options, patients with haemophilia B (HB) still experience treatment and disease burden. We present patient-reported data from a non-interventional study in US patients with HB without inhibitors.

Methods: Patients were recruited to the PicnicHealth research platform, which collects and abstracts medical records and invites patients to participate in surveys.

Data were collected via two validated questionnaires, Haemophilia Treatment Experience Measure (Hemo-TEM) and Patient-Reported Outcomes Measurement Information System (PROMIS)−29 2.0. Patients also reported concerns around bleeding protection of their prophylactic treatment. Informed consent wasx obtained.

Hemo-TEM domain scores were transformed onto a 0- to 100-point scale where higher scores indicate greater burden. Except for pain intensity, PROMIS-29 domain scores were transformed into T-scores, based on a reference sample (mean: 50; standard deviation: 10). The meaning of higher PROMIS-29 scores varied per domain.

Results: Sixty-six patients with HB without inhibitors (55 male; median age: 30.4 years; IQR: 21.0−40.2) responded to ≥1 survey; 27%, 20% and 53% with mild, moderate and severe HB, respectively. 64% of patients reported prophylactic (PPX) treatment use with standard half-life (26%) or extended half-life factor products (74%).

Treatment burden was observed via Hemo-TEM across subgroups of disease severity treated with PPX, with high scores (median [IQR] for mild, moderate and severe, respectively) in physical impact (38 [27−42], 19 [7−33] and 25 [17−33]), emotional impact (25 [12−29], 23 [18−28] and 25 [18−33]) and treatment bother (18 [11−25], 20 [12−41] and 21 [11−39]).

Similarly, PROMIS-29 scores demonstrated disease burden across subgroups treated with PPX, with burden in anxiety (58 [52−61], 60 [60−63] and 55 [48−61]), depression (56 [41−62], 55 [50−59] and 54 [41−59]) and pain interference domains (57 [42−59], 53 [50−54] and 55 [42−58]). Pain intensity was 5 [2−5], 2 [1−4] and 3/10 [1−5].

Patients reported feeling 'at least sometimes' anxious (33%) and/or worried (36%) that their current prophylactic treatment does not adequately protect them from bleeding episodes.

Discussion/Conclusion: Unmet needs remain for patients with HB, who continue to experience burdens associated with disease and treatment, both on their physical and mental health. Protection from bleeds remains a frequent concern for many patients.

Disclosure of Interest: A. Shapiro Consultant for: Novo Nordisk, Kedrion Biopharma, Pfizer, Genentech/Roche, Sanofi-Genzyme/Bioverativ, HEMA Biologics, Speaker Bureau of: Genetech/Roche, Kedrion Biopharma, Sanofi-Genzyme/Biovertativ, C. Percier Shareholder of: Novo Nordisk Health Care AG, Employee of: Novo Nordisk Health Care AG, T. Porstmann Shareholder of: Novo Nordisk Health Care AG, Employee of: Novo Nordisk Health Care AG, J. Dusendang Shareholder of: PicnicHealth, Employee of: PicnicHealth, A. Wheeler Consultant for: Novo Nordisk, HEMA Biologics, Takeda, Pfizer, Octapharma, CSL Behring, Bayer, Sanofi, and Genentech.

PO048 | Emicizumab improves thrombin generation and quality of life compared to previous FVIII prophylaxis in haemophilia a patients

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Introduction: Prophylaxis is the gold standard for haemophilia management. Emicizumab is approved for prophylaxis in severe haemophilia A and in mild/moderate haemophilia A with bleeding phenotype. There are scarce data in the literature regarding the thrombin generation (TG) profile in patients with haemophilia A (PWHA) receiving emicizumab.

Methods: Objectives: (1) To compare TG in PWHA in prophylaxis with factor VIII (FVIII) versus emicizumab; (2) to analyse TG profile and emicizumab levels in PWHA with emicizumab; (3) to assess changes in quality of life in PWHA with emicizumab.

Material and methods: This is a descriptive and cross-sectional study including PWHA in prophylaxis with emicizumab of all ages in our institution. TG was carried out by an automated method (Genesia®, Stago, Paris, France). Emicizumab levels were determined with a modified aPTT (Stago, Paris, France). Quantitative parameters were described as median (±standard deviation). $p < .05$ reached the statistical significance.

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Results: Thirteen patients were included. Median age at inclusion was 10 (7–16) and eight patients had previously received prophylaxis with FVIII. Eleven patients had severe haemophilia A while two patients had moderate haemophilia A with persistent bleeding phenotype despite prophylaxis with recombinant FVIII. In this setting, those patients changed to emicizumab.

The endogenous thrombin potential was 77.8% (±22.9) and maximum thrombin peak was 51% (±12.9), compared to a reference plasma. All patients were in normal emicizumab range: 49.9 (±8.51) μg/mL. The annual bleeding rate (ABR) was 0.27 and 7 treated bleeds (three joint traumatic and four non-joint traumatic bleeds) were registered. When comparing with patients previously receiving FVIII, the TG profile improved considerably, reaching $p < .05$ in all the parameters. The ABR with recombinant FVIII was 0.79 and 53 bleeds were described, 45 of them required treatment. When assessing quality of life, most of the patients reported an improvement: 77% had less pain and required fewer painkillers, 85% had fewer work or school absenteeism, while the rest remained similarly.

Discussion/Conclusion: Emicizumab maintains a low ABR in patients with haemophilia A. An improvement in TG and a better quality of life were described in patients with emicizumab compared to prophylaxis with FVIII.

Disclosure of Interest: None declared.

PO049 | Fragility fracture risk and bone mineral density predictive role in patients with haemophilia: A single centre retrospective study

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Introduction: Haemophilia is a rare bleeding disorder characterised by the partial or complete deficiency of clotting factor VIII or IX. Patients with haemophilia are burdened by many complications, the most common of which is joint bleeding.

Bone mineral density (BMD), measured by dual-energy X-ray absorptiometry (DXA), is a standard-of-care screening tool used to assess the risk of fragility fractures.

According to two meta-analyses, a reduction in BMD is observed since young age in patients with haemophilia. Alongside common risk factors, this finding may also be related to physical inactivity due to the presence of haemophilic arthropathy or to a biological role of factor VIII beyond coagulation. However, the role of BMD in patients with haemophilia is still debated.

This retrospective study aims to investigate the incidence of fragility fractures and to assess the role of BMD in predicting fracture risk in a cohort of patients with haemophilia.

Methods: We enrolled 91 adult patients with haemophilia A or B, followed at the Angelo Bianchi Bonomi Hemophilia and Thrombosis center and undergoing a DXA between July 2013 and August 2021. Exclusion criteria included history of fractures, cancer, endocrine conditions or other diseases that affect bone health, or use of medications that could affect bone remodelling.

Results: Median age of our study population was 42.5 years (IQR, 37.25–49.75). Seventy (81.4%) patients were affected by haemophilia A, 16 by haemophilia B, and a total of 72 (83.7%) had a severe disease. Among the whole cohort, 62 (68%) showed a certain degree of BMD loss, defined as a T-score ≤1 (osteopenia) or ≤2.5 (osteoporosis), with a median T-score of −1.4 [IQR, −2.2; −0.6]. Five patients experienced a fragility fracture during the observation period, of whom four had osteopenia. We found an incidence rate of fracture of 0.015 (95% CI: 0.008–0.025) fractures/year. The receiver operator characteristic (ROC) curve model showed an area under the curve (AUC) of 0.53.

Discussion/Conclusion: Compared with the Italian general population, patients with haemophilia have a higher incidence of fragility fractures and at a younger age. BMD does not seem to be a reliable parameter to identify patients with haemophilia at higher risk of fracture. Our findings pave the way for prospective studies aimed at explaining the contribution of all major haemophilia-related risk factors for bone fractures.

Disclosure of Interest: None declared.

PO050 | Clinical overview of perioperative outcomes from the XTEND-Kids study

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Introduction: Efanesoctocog alfa prophylaxis provided high sustained factor VIII (FVIII) activity and effective bleed prevention in previously treated children (<12 years) with severe haemophilia A in XTEND-Kids (Phase 3, NCT04759131). Here, we report the efficacy and safety of efanesoctocog alfa for perioperative management of children in this study.

Methods: Patients were to receive once-weekly efanesoctocog alfa 50 IU/kg for 52 weeks for routine prophylaxis. Patients undergoing surgery (major and minor) were to receive a preoperative loading dose of 50 IU/kg, followed by additional doses of 30 or 50 IU/kg every 2–3 days as needed for major surgeries. Perioperative period analyses included dose, number of injections, haemostatic response, factor consumption, blood loss, blood transfusions, FVIII inhibitor development and treatment-emergent adverse events (TEAEs).

Results: Major surgery: two patients had major surgery (tooth extraction, circumcision) during XTEND-Kids. Both had 1 preoperative loading dose and subsequently resumed once-weekly prophylactic efanesoctocog alfa 50 IU/kg dosing perioperatively. Blood loss during surgery was 0 mL with tooth extraction and 50 mL with circumcision. Haemostatic response was reported as excellent in both cases.

Minor surgery: Eight patients underwent nine minor surgeries. Haemostatic response was rated excellent for all assessed (8/8). A single preoperative loading dose of efanesoctocog alfa [median (range): 53.5 (38–59) IU/kg] was sufficient to maintain haemostasis during surgery. Median (range) duration of surgery and time from surgery to next prophylaxis dose was 0.6 (<0.05–1.8) h and 7.0 (6.0–11.0) days, respectively. Median (range) blood loss during surgery was 0 (0–15) mL and postoperatively was 0 (0–5) mL.

No patients required blood transfusions or experienced postoperative bleeding episodes/treatment-related TEAEs for major and minor surgeries. No FVIII inhibitors were detected at the end of the postoperative period.

Discussion/Conclusion: Efanesoctocog alfa was effective and well tolerated for perioperative management of children with severe haemophilia A. A single preoperative loading dose maintained haemostasis during surgery, all responses were rated excellent, and no FVIII inhibitors were detected.

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Disclosure of Interest: A. Chan Consultant for: Bayer, Novo Nordisk, Pfizer, Sanofi (clinical trials); Bayer, Novo Nordisk, Octapharma, Sanofi and Takeda (advisory board member), S. Meunier Consultant for: CSL Behring, Novo Nordisk, Octapharma, Roche, Sanofi, Takeda (clinical trials); LFB, Sanofi and Novo Nordisk (the institution of S. Meunier recieved honoraria for consulting/advisory board participation); Sanofi and Takeda (personal consultancy fees for consulting/advisory board participation), K. Fijnvandraat Grant/Research support from: CSL Behring, Sobi and Novo Nordisk (the institution of K. Fijnvandraat received unrestricted research grants), Consultant for: Sobi, Sanofi, Takeda, Novo Nordisk and Roche (received consultancy fees), M. T. Alvarez Roman Consultant for: Bayer, Sobi, Roche, LFB, CSL Behring, BioMarin, Pfizer, Takeda, Novo Nordisk, Amgen and Novartis (received honoraria for speaking/participating in advisory boards), A. Kupesiz Consultant for: Bayer, Novo Nordisk, Pfizer, Sanofi and Roche (clinical trials); Novo Nordisk, Roche, Pfizer, Sobi and Takeda (advisory board member), J. Motwani Speaker Bureau of: Sobi, Roche and CSL Behring (received honoraria, speaker fees, educational support), L. Malec Consultant for: Bayer, CSL Behring, Genentech, Novo Nordisk, Sanofi Genzyme, Sobi and Takeda (received honoraria for consulting/advisory board participation), Speaker Bureau of: CSL Behring and Sanofi Genzyme (received consulting fees for speakers bureau), T. Wynn Consultant for: Spark, Takeda, Sobi, AMAG and Sanofi (clinical trials), Employee of: T. Wynn's wife was an employee of Takeda, A. L. Dunn Consultant for: BioMarin, Hema Biologics, Regeneron and CSL Behring; Boards: National Bleeding Disorder Foundation-MASAC Chair, World Federation of Hemophilia–USA, Cascade; Research Foundation: Novo Nordisk, Sanofi/Sobi, BioMarin, Genentech, Pfizer, Spark, ATHN, Regeneron and Takeda, L.-S. Fetita Employee of: Sanofi; may hold shares and/or stock options in the company, L. Abad-Franch Employee of: Sobi; may hold shares and/or stock options in the company, J. Dumont Employee of: Sanofi; may hold shares and/or stock options in the company, L. Bystrická Employee of: Sobi; may hold shares and/or stock options in the company, B. Fuh: None declared.

PO051 | A rare case of acquired haemophilia a in a female

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Introduction: Haemophilia A is an autosomal X linked inherited disorder run in family and females are usually the carrier and asymptomatic. Acquired haemophilia are very rare and the incidence is 0.2–1.0 per million. Here we report a case of acquired haemophilia of autoimmune origin in a 37 year old female patient presented in the postpartum period.

Methods: A 37 year old female G5P4L4A1 was referred with complains of right lower limb swelling and ecchymotic patches of 3 weeks duration with uncontrolled bleeding. She gives history of COVID 19 seven months back with uneventful recovery. No family history of any bleeding diathesis and no history of menorrhagia or systemic illness in the past.

Investigations showed anaemia Hb –10.6 g/dL, Platelets 365 lakhs, PT –13.2 s, INR –0.98 and aPTT – 63 s. MRI lower limb showed bilateral hematoma in gluteal region.

Results: In view of the condition, patient was evaluated in detail to exclude common condition of bleeding diathesis and connective tissue disorder. The classical Bethesda assay of factor VIII (FVIII) inhibitor was found elevated 8 Bu (<1) and FVIII levels was only 2%. Isolated elevation of aPTT with positive aPTT mixing studies showed significant and is the hallmark of such condition. Further evaluation showed that patient has haemophilia A and we excluded other possibilities. In view of lack of a definite family history or no similar manifestation in the previous gestational and post-partum period, possibility of new onset

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acquired haemophilia is considered. She was treated with steroids and supportive measures and had an uneventful recovery.

Discussion/Conclusion: Acquired haemophilia A due to autoimmune aetiology in a female is very rare condition. If the usual cause for a bleeding diathesis is not detected, acquired haemophilia A has to be considered as it could be life-saving.

Disclosure of Interest: None declared.

PO052 | Real-world data of prophylaxis with emicizumab in children and adolescents with severe haemophilia: A single centre experience

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Introduction: Real-word data with emicizumab as prophylactic treatment in patients with haemophilia A (HA), with or without inhibitors against factor VIII (FVIII-Inh), are still limited in paediatric population. In this study we aimed to evaluate the safety and efficacy of prophylaxis with emicizumab in children, and especially the changes in annualised bleeding rate (ABR) and annualised joint bleeding rate (AJBR) post-emicizumab transition, based on data from a single paediatric haemophilia centre.

Methods: All children with HA treated with emicizumab in a single haemophilia Greek centre were included. Correletions were done with *t*-test.

Results: Seventeen children, all with severe HA, were included in the study. Four patients had FVIII-Inh in the past, successfully treated with immune tolerance induction (ITI) and three patients had high-titre FVIII-Inh at the time of transition, with one of them being on parallel ITI. The rest of the patients had negative inhibitor history. Median age of the patients at initiation of emicizumab was 8 (1.5–16.5) years, with three of them being younger than 2 years. Median treatment period was 9 (1–52) months. Concerning dose and frequency of emicizumab after the 4-week loading dose period with 3 mg/kg weekly, 11 patients continued with 1.5 mg/kg weekly, five patients with 3 mg/kg Q2W and one patient with 6 mg/kg Q4W. After transition to emicizumab, significantly reduced ABR [0.39 (0—2) vs. 3.0 (1—10) before transition, $p < .01$] and AJBR [0.2 (0—2) vs. 2.7 (0—10), $p < .01$], were observed. In 7/17 of patients with target joints historically, no bleeding in these joints occurred after transition. Five patients developed skin reaction at the injection site during first doses and two patients experienced headache after the first injection. No thrombotic episode occurred. Orthopaedic surgery was successfully performed in one patient with high-titre inhibitor, receiving rFVIIa intraoperatively and surgical dental extractions were performed in one patient without inhibitor, who received extra doses of rFVIII for three days.

Discussion/Conclusion: Therapy with emicizumab in our study proved to be effective in reducing total bleeds, as well as joint bleeds in paediatric patients with/without FVIII-Inh and eliminating target joints. Further observation is necessary to evaluate the effect of long-term administration of emicizumab in overall joint health.

Disclosure of Interest: None declared.

PO053 | Paediatric cases of previously untreated patients with severe haemophilia A and B on extended half life products: A single centre experience

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Introduction: The standard of care for patients with haemophilia A and B is the prevention of bleeds through prophylaxis with factor VIII (FVIII) and FIX products. extended half life (EHL) recombinant products were developed to reduce the treatment burden by allowing for less frequent infusions and/or to enable more optimal protection by maintaining higher factor levels.

Methods: A retrospective review of medical records of previously untreated patients (PUPS) with haemophilia A and B on therapy with EHL products was conducted. The presence of inhibitor was defined by at least two consecutive positive samples at least 4 weeks apart.

Results: There are 7 children with severe haemophilia A on EHL products, all on Fc fusion FVIII. Mean age at evaluation is 7 months (range: 0.25–21 months). There is one patient with inhibitor (14%), classified as low-titre. Mean ED of follow-up is 35 (range: 11–100 ED). In the inhibitor patients the inhibitor manifestation occurred at 22th ED at the age of 16.5 months. Only four out of seven patients are on prophylaxis. Mean age at first treatment is 10 months (range: 0.25–21 months) and at start of prophylaxis 15.5 months. Intensive treatment for at least 5 days at initial FVIII exposure occurred in 3/6 non-inhibitor and in the inhibitor patient. The overall median ABR is 1 and ABJR 0. None patients experienced treatment related adverse events. Finally, there was a successful immune tolerance induction in the inhibitor patient lasted 5 months.

As for haemophilia B, there are three PUPS with severe haemophilia on EHL products, two on albumin-fusion and one on Fc fusion FIX. EDs of patients are 10–63. All children are on prophylaxis. There is none inhibitor patient. Mean age at first treatment is 25 months. Intensive treatment for at least 5 days at initial FIX exposure occurred in 1/3 patients. The overall median ABR is 1 and ABJR 0. None patients experienced treatment related adverse events.

Discussion/Conclusion: Based on the results obtained from our experience, it can be concluded that therapy with EHL products in PUPS with haemophilia is effective and well tolerated.

Disclosure of Interest: None declared.

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PO054 | Women diagnosed with postpartum haemophilia, more than an anecdotal fact: Retrospective analysis in a single centre

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Introduction: It is currently documented that haemophilia carriers present greater bleeding manifestations than average; however, the path to diagnosis is sometimes tortuous, with a significant delay (especially when there is no direct family history). The objective of this work is to document the experience of a group of women who were diagnosed postpartum as carriers of haemophilia (after the diagnosis of their children) and their haemorrhagic manifestations prior to diagnosis.

Methods: Analytical, retrospective and descriptive study that documents haemorrhagic manifestations prior to diagnosis in women who coincidentally are labelled as carriers of haemophilia (A–B) after childbirth (when their children are diagnosed) in a rural hospital in Spain. Clinical and epidemiological variables were collected.

Results: Five women with haemophilia (four with haemophilia A and one with haemophilia B) met the inclusion criteria. None of them documented immediate family members diagnosed with haemophilia. The median age was 30 years. The median age at diagnosis after delivery was 11 months, all of them after the clinical debut of their children. None had significant haemorrhagic complications during delivery. The median factor VIIIc (FVIIIc) was 30.5% in the four haemophilia A carriers and 35.0% in the haemophilia B carrier. Upon re-examination, 80% of the sample presented pathological scores on the ISTH-BAT scale (with prevalence of excessive menstrual bleeding, which in one case developed secondary anaemia) without requesting prior haematological evaluation.

Discussion/Conclusion: The diagnosis of haemophilia carriers after childbirth is not an anecdotal fact and, although no obstetric complications occurred in our sample, the risk of suffering from them can compromise their quality of life. Although a high percentage of the sample presented haemorrhagic manifestations, the absence of a close family history of haemophilia delayed early diagnosis.

Disclosure of Interest: None declared.

PO055 | Satisfaction with the treatment received and adherence in haemophilic patients in a rural area of spain

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Introduction: The effective treatment of congenital coagulopathies in rural areas is a medical and logistical challenge, a fact that deepened during the COVID-19 pandemic, when the 'home delivery' system was implemented in our hospital, with positive results maintaining adhesion. The objective of this work is to quantify the degree of satisfaction with the treatment received by haemophiliac patients in a regional hospital in a rural Spanish area.

Methods: Individual interviews were carried out with patients and family members (if they were minors) to collect satisfaction with the treatment received, the percentage of adherence to it and the usefulness of 'home delivery' in those patients who requested it, in addition of patient inclusion in clinical trials to date. Sociodemographic and clinical data were collected.

Results: Ten patients with haemophilia were included in the study, four children (with a median age of 4.4 years) and six adults (with a median age of 26.7 years). 90% of the sample were haemophiliacs A. 20% of the sample were severe patients, 10% moderate and 70% mild. 30% of the sample (moderate and severe) received prophylaxis. The median distance between the patients' home and the hospital centre was 34 km. All moderate and severe patients were or are included in a clinical trial. Both patients and parents were very satisfied with the treatment provided, without decreasing adherence after the implementation of 'home delivery'. The entire sample highlighted that avoiding hospital trips is a fact that positively affects their quality of life.

Discussion/Conclusion: Home treatment strategies in rural areas are essential to reduce travel in haemophiliac patients, and this translates into an improvement in their quality of life and their environment.

Disclosure of Interest: None declared.

PO056 | Pharmacoeconomy and clinical well-being in haemophilia (FARBENE): An interim analysis

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Introduction: The Piedmont Region determination of 13 September 2021 approved the Congenital Haemorrhagic Disease's PDTA, a document describing the care pathway, organisation and laboratory requirements of each Expert Centre (EC) and a protocol for the governance of pharmaceutical spending according to cost-benefit criteria. The process of therapy individualisation, if effective, carries with it a message of solidarity among patients (pts) and between pts and health care providers for the common goal of saving resources and improving pts' quality of life. The objective of this study is to evaluate clinical indicator for pharmaceutical expenditure governance according to PDTA for each pts with severe haemophilia A (HA) or B (HB), follow at the EC of City of Health and Science (CHS).

Methods: A retrospective-prospective, observational and nonprofit was carried out. The population was composed of 70 pts, 60 with severe HA and 10 moderate-severe HB, affering to the EC between January 2020 and December 2022. The study was approved from

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CHS Ethical Committee. An interim analysis of pts who undergoes therapeutic switch to emicizumab was done.

Results: Eleven pts (15%) switched to emicizumab, three of them had anti factor VIII (FVIII) inhibitors while the other eight pts did not. For the latter group, the indications for switching were maintenance of compliance and exhaustion of peripheral venous accesses. For these pts the cost increment went from 18% to 160%, for those who switched from recombinant FVIII, and to 220% for those who switched from plasmatic FVIII. The switch led to a reduction of NRS in 50% of pts and achievement of ABR zero in one out of eight pts. Among pts with inhibitors, one started emicizumab in 2019 with a savings of 68% and the other two started emicizumab in 2020 (as part of clinical trial) with net average savings of 800,000 euros annually over the 3-year period 2018–2020. Clinically there was reduction of ABR and NRS to zero.

Discussion/Conclusion: This data suggest that it will be important to balance the economic benefit (seemingly in favour of replacement therapy) with the well-being of pts and their quality of life. A simple mathematical calculation of costs fails to value these latter elements. It is therefore necessary to find assessment tools of pts welfare that can be included in the economic calculation for better quantification of expenditure.

Disclosure of Interest: None declared.

PO057 | One-stage assay analysis demonstrates that gene therapy-derived factor VIII (FVIII) from dirloctocogene samoparvovec reduced clot times compared with endogenous FVIII at comparable FVIII levels

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Spark Therapeutics, Inc., Philadelphia, Pennsylvania, USA

Introduction: Previously, we reported increased measures in the thrombin generation assay (TGA)—a global coagulation assay—in a subset of study participants who received dirloctocogene samoparvovec (SPK-8011), compared with pooled plasma from healthy individuals containing comparable levels of factor (F)VIII antigen. Here, we expand on that report by evaluating clotting times of samples containing gene therapy-derived and endogenous FVIII using the one-stage clotting assay (OSA).

Methods: FVIII antigen and activity were determined in pooled plasma from healthy individuals (factor assay control plasma [FACT]) and in plasma from a subset of Phase 1/2 study (NCT03003533/NCT03432520) participants with haemophilia A (HA) who received dirloctocogene samoparvovec. FVIII antigen levels were determined by a human (h)FVIII immunoassay (MSD technology using Green Mountain Antibodies, GMA8023/GMA8024). Circulating hFVIII activity in plasma samples was measured by OSA, using TCoag TriniCLOT aPTT reagent.

Results: Plasma samples from study participants who received dirloctocogene samoparvovec yielded shorter clotting times in the OSA compared with endogenous FVIII at similar levels of FVIII antigen. Using a linear model fit to FACT sample clot times, gene therapy-treated samples demonstrated, on average, a 35% reduction in clot times (mean ± SD of 34.7% ± 11.7%) compared with predicted times from healthy individual plasma samples. These differences varied across the range of FVIII levels interrogated, with lower FVIII antigen levels correlating with larger discrepancies between the two sample sets, suggesting that FVIII levels may be an important factor in this effect.

Discussion/Conclusion: Plasma from people with HA who received dirloctocogene samoparvovec consistently results in shorter clot times compared with pooled plasma from healthy donors containing similar FVIII antigen levels. These findings corroborate our previous observation that dirloctocogene samoparvovec-derived FVIII may have enhanced activity compared with endogenous FVIII in a global coagulation assay (TGA) and emphasise the importance of characterising gene therapy-derived FVIII to understand its functional benefit to patients.

Disclosure of Interest: C. Rizzo Shareholder of: F. Hoffmann-La Roche Ltd., Employee of: Spark Therapeutics, I. Rojas Shareholder of: F. Hoffmann-La Roche Ltd., Employee of: Spark Therapeutics, E. Blanchard Shareholder of: F. Hoffmann-La Roche Ltd., Employee of: Spark Therapeutics, D. Lupo Shareholder of: F. Hoffmann-La Roche Ltd., Employee of: Spark Therapeutics, T. Chang Shareholder of: F. Hoffmann-La Roche Ltd., Employee of: Spark Therapeutics, J. Coleman Shareholder of: F. Hoffmann-La Roche Ltd., Employee of: Spark Therapeutics, V. Howard Shareholder of: F. Hoffmann-La Roche Ltd., Employee of: Spark Therapeutics, L. Peed Shareholder of: F. Hoffmann-La Roche Ltd., Employee of: Spark Therapeutics, R. Straub Shareholder of: F. Hoffmann-La Roche Ltd., Employee of: Spark Therapeutics, H. Hanby Shareholder of: F. Hoffmann-La Roche Ltd., Employee of: Spark Therapeutics, J. Alexander Shareholder of: F. Hoffmann-La Roche Ltd., Employee of: Spark Therapeutics, C. Riling Shareholder of: F. Hoffmann-La Roche Ltd., Employee of: Spark Therapeutics.

PO058 | One-stage bilateral HIP arthroplasty in a patient with severe haemophilia B

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Introduction: Femoral neck fractures are common in the elderly population frequently confronted with osteoporosis, but rarely can also occur, mainly unilaterally, in younger individuals following a

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high-energy trauma. Only a few articles describe bilateral simultaneous femoral neck fractures as an injury result of seizures, not reported in patients with haemophilia (PwH).

Methods: We report a case of a bilateral femoral neck fracture in a 50-year-old male, with severe haemophilia B (SHB), following a generalised convulsion.

Results: Case Presentation. The patient was addressed to the emergency department following a generalised tonic-clonic seizure episode, known and treated for epilepsy; he is in evidence with SHB and haemophilic arthropathies, without a history of trauma or any comorbidities. On examination, both the lower limbs were externally rotated; there were no distal neurovascular deficits, no open wounds or trauma evidence. The radiography revealed a bilateral femoral neck fracture. Under rigorous haemostatic control, the orthopaedic surgeon team decided to intervene in one stage, and bilateral simultaneous hip arthroplasty was performed. The right hip joint was complicated with pertrochanteric fracture and needed additional osteosynthesis with screws. Postoperatively bedside hip range of motion exercises were started within days 2–3 after surgery, continuing with an enhanced rehabilitation program. The patient had a favourable outcome, without any post-operative complications. Overall cost analysis highlighted the fact that costs for hospitalisation days and investigations were 3.400€, and the factor concentrate accounted for 95% of expenditures (recombinant FIX, 64.800€). However, these two simultaneous major interventions had a decisive favourable effect on the costs and rehabilitation of the patient.

Discussion/Conclusion: Due to a forceful contraction of muscles during an episode of generalised tonic-clonic seizures, a fracture or dislocation may develop. A bilateral hip-neck fracture is a rare occurrence, especially in PwH; a comprehensive approach and one-stage surgery intervention are solutions for these disabling conditions, claiming a fastidious and expensive therapy. The high costs of orthopaedic surgery can be avoided in the condition of appropriate and timely management.

Disclosure of Interest: None declared.

PO059 | Haemophilia surgery with extended half life products

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Introduction: Haemophilia A and haemophilia B are X-linked coagulation factor diseases characterised by varied severe bleeding. Patients appear with acute bleeding symptoms that require prompt treatment, and patients undergoing surgery or invasive treatments must plan ahead of time.

Methods: In this study, it is shared surgical experiences with different extended half-life factor VIII (FVIII) products. Case report-1: 2 years 8 months ages haemophilia A patient. He has prophylaxis once a week. He had circumcision and bilateral hernia surgery: −1 day (presurgery) he had hospitalised and begun tranexamic acid. Surgery day: efmoroctocog alfa 50 UI/kg/first dosage, see normalisation of coagulation, trenexamic acid. FVIII 50 UI/kg dosage (second dosage 12 h). No bleeding. +1. dayefmoroctocog alfa 2x 50 UI/kg/dosage. +2,+3. efmoroctocog alfa 1x 50 UI/kg prophylaxis efmoroctocog alfa once a week. Case report-2: 10 years old ages, haemophilia A. Dental extraction and filling surgery-1 day (predental surgery) tranexamic acid. Dental procedure day: N8-GP 50 UI/kg/dosage normalisation of coagulation, tranexamic acid. Second dosage at 12 h. +1+2. Day: N8-GP 1x 50 UI/kg tranexamic acid. Circumcision N8-GP-1 day, hospitalisation, tranexamic acid O. Day N8-GP 50 UI/kg normalisation of coagulation, tranexamic acid. FVIII 50 UI/kg at 12 h. +1. Day N8-GP 2x 50 UI/kg/dosage tranexamic acid, +2, +3 day N8-GP 1x 50 UI/kg prophylaxis with N8-GP twice a week.

Results: Recombinant FVIII with prolonged half-life products are well tolerated for the management of perioperative haemostasis across a wide spectrum of major and minor surgeries in haemophilia.

Discussion/Conclusion: All extended half-life factor products have a good option in preventing bleeding by ensuring that safe factor levels are maintained for a longer period of time with less frequent applications in prophylaxis and effective enough to prevent bleeding, reducing the number of annual bleedings to less than 4–5, and 90% of bleedings can be successfully treated with a single dose.

Disclosure of Interest: None declared.

PO060 | The rheumatologic journey of factor X deficiency

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Introduction: In patients with active bleeding symptoms at various sites of the body, without a history of bleeding tendencies, prolonged PT and/or APTT tests, and no complete correction in mixing tests, suspicion of the presence of an inhibitor related to acquired haemophilia should be considered. In this case, we will present a rare condition of secondary factor X deficiency associated with a rheumatologic disease.

Methods: A 60-year-old female patient was referred to the haematology clinic due to coagulation tests revealed an INR of 4.58 and PTZ of 54.9 s. In the past month, she had undergone five dental treatments without experiencing any abnormal bleeding. Her other test results were as follows: WBC: 7.03 * 1000/μL, HGB: 12.1 g/dL, PLT: 306 * 1000/μL, erythrocyte sedimentation rate: 74 mm/h, albumin: 4.7 g/dL, total protein: 8.68 g/dL, CRP: 16.6 ng/dL, creatinine: 1.04 mg/dL, fibrinogen: 373 mg/dL, D-dimer: 4 mg/L. She had no liver disease. There was no paraprotein detected in serum protein electrophoresis. The factor X level measured as 3%. FV level measured as 67%. When she sought help from the eye clinic due to detergent splashing into her eye, xerophthalmia was observed. In addition, she experienced bilateral ankle pain. During the rheumatologic examination, the following results were obtained: anti-nuclear antibody, fine speckled strong positive; anti-SS-A, strong positive; anti-SS-B, strong positive. The presence of sicca symptoms and the positivity of Ro/La antibodies in the patient suggested secondary FX deficiency due to Sjögren's syndrome.

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Results: When encountering a patient with abnormal coagulation, it is important to consider the possibility of 'acquired haemophilia'. Initially, the mixing test is performed to determine whether the issue is related to a deficiency problem or the presence of an inhibitor. In cases of acquired haemophilia, it is crucial to investigate whether there is an underlying cause. At the same time, the necessary treatments should be initiated for patients with bleeding issues.

Discussion/Conclusion: Our patient, who had not experienced any bleeding in previous surgeries and had no family history of bleeding, was initially considered to have acquired factor X deficiency. The absence of a mixing test for the patient and the inability to determine the inhibitor are limiting and debatable factors. However, living without bleeding in such a severe factor deficiency is another interesting aspect.

Disclosure of Interest: None declared.

PO061 | Varna expert centre of coagulopathies and rare anaemias – 10 years experience

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Introduction: The aim of this review is to present the 10-year experience of Varna Expert Centre of coagulopathies and rare anaemias in treating congenital coagulation disorders and rare anaemias.

Methods: For the period 2013—2023 in the Varna Expert Centre are treated 196 patients with congenital coagulation disorders and rare anaemias from the age of 6 months to 75 years. For all the patients are analysed the following indexes: diagnosis, gender, familial history, age of diagnosis, initial clinical manifestation, severity of disease and treatment regimens.

Results: From the studied 196 patients, 136 are with coagulation disorders and 60 are with rare anaemias.

According to the type of coagulopathy the patients are as follows: haemophilia A 75(70%), haemophilia B 11(10%), von Willebrand's disease 11(10%), congenital afibrinogenaemia 4 (4%), factor II deficiency 1 (1%), factor VII deficiency 3(3%) and X deficiency 2 (2%) patients. There are also 23 known and genetically proven carriers registered in the centre. 29% of the patients are children < 18 years and 71% are adults. Seventy-eight of the patients are with severe coagulopathy, 13 patients are with moderate disease and 18 with mild. In 2023 most of the patients are on a prophylactic regimen, five are still small and have never been treated with factor replacement. All the inhibitor patients of the centre (3) are on non-factor therapy.

At the moment the patients with transfusion dependent anaemias are 57 with beta thalassemia major, two patients with congenital dyserythropoietic anaemia and one with hexokinase deficiency. According to age at the moment are treated and followed 18 children and 39 adults. From them 45 % are females and 55% males. During follow-up we succeeded to improve the compliance of the patients to the chelating therapy. Only six patients have not started chelation therapy because of age.

Both groups of patients are regularly monitored from a multidisciplinary team including haematologist, endocrinologist, gastroenterologist, cardiologist and other specialists.

Discussion/Conclusion: The presented results characterise the nosological structure and clinical status of patients with congenital coagulopathies and rare anaemias, who have been treated in Varna Expert centre of coagulopathies and rare anaemias in the period 2013–2023. The ambition of the authors is to improve the quality of care for the patients and implement the modern guidelines and therapies for these rare disorders.

Disclosure of Interest: None declared.

PO062 | Promoting gender equity in haemophilia care through proactive and systematic screening of haemophilia carriers: Results of the PROCARRIERS1 study

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Introduction: Despite multiple awareness-raising initiatives, a considerable number of carriers and female persons with haemophilia (PwH) still go undiagnosed. We present findings from a proactive and extensive haemophilia carrier screening project.

Methods: From May 2021 until April 2023, potential and obligate carriers of haemophilia A (HA) and B (HB) were identified by updating pedigrees of all PwH followed at the Cliniques Universitaires Saint-Luc. Retrospective data on previously screened females were collected from medical records, including bleeding history, coagulation factor assays and testing for the index patient's genetic variant. Female individuals who had not been previously screened or with missing data were provided with a total of 125 invitation letters by related index haemophilia patients.

Results: All 287 male PwH (226 HA, 61 HB) from 228 families (180 HA, 48 HB) were included in the analysis. Seven female PwH (3 HA, 4 HB) were considered as index cases in their families. Based on the family trees, there were 900 females, among which 454 were obligate and/or genetically proven carriers of haemophilia, and 118 were found to be non-carriers. Genetic testing was conducted in 133 obligate, 237 potential and 4 sporadic carriers, and remains to be performed in 190 obligate and 328 potential carriers. Eight females were obligate non-carriers. Among carriers with known coagulation factor levels (261/454), 42 (23.0%) and 23 (29.5%) carriers of HA and HB, respectively, had a factor level below 40 IU/dL. The proportion of carriers with a factor level below 40 IU/dL did not significantly differ between families with severe, moderate and mild haemophilia (22.6%, 34.7% and 22.7%, respectively, $p = .213$). Carriers with a coagulation factor deficiency were screened earlier than other female

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individuals (mean age at diagnosis 25.8 and 31.8 years, respectively, $p = .034$).

Discussion/Conclusion: This study represents the first reported attempt to systematically identify all (potential) haemophilia carriers within families of PwH followed at a single haemophilia treatment centre and reflects the major challenges in providing appropriate screening to all women genetically linked to one or more PwH. Such carrier screening efforts are a critical step towards providing equal access to haemophilia diagnosis and care for all potentially affected individuals, regardless of gender.

Disclosure of Interest: E. Krumb Grant/Research support from: CSL Behring, Swedish Orphan Biovitrum (Sobi), C. Lambert: None declared, A. Van Damme: None declared, C. Hermans: None declared.

PO063 | Unraveling muscle tension: A study on lower extremity muscle stiffness in haemophilia in dependence of joint status

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Introduction: Haemophilic arthropathy results in muscular atrophy, pain, impaired mobility and hence, in altered biomechanical muscle properties, as observed, for example, in electromyography studies. As these changes are linked to musculoskeletal disorders, it is crucial to understand these properties in PwH, as they present a risk factor for impaired muscle functionality. Therefore, this study aims to evaluate biomechanical properties [i.e., tone (MT) and stiffness (MS)] of the leg musculature of PwH in dependence on joint arthropathy.

Methods: Forty-one PwH and 14 age- and BMI-matched healthy controls (CON) were included in this study. MT [Hz] and MS [Nm^{-1}] of the main lower extremity muscles (tibialis anterior, rectus femoris, vastus medialis and lateralis, gastrocnemius medialis and lateralis, biceps femoris, semitendinosus) were evaluated using the validated MyotonPRO. Clinical [HJHS (score)] and ultrasound [HEAD-US (score)] joint examinations were performed. Each lower limb was separately analysed, resulting in a total of 82 PwH limbs and 28 CON limbs. PwH limbs were distributed according to the limb HJHS score (mean of HJHS of ankle and knee joint) into minorly (HJHS of the limbs ≤5, $n = 40$; MINOR) and majorly affected limbs (HJHS of the leg > 5; $n = 42$; MAJOR) and compared to CON limbs ($n = 28$).

Results: MS and MT were higher ($p < .01$) in MAJOR than in MINOR and CON, respectively, at the rectus femoris, vastus lateralis and medialis, and gastrocnemius lateralis and medialis with highest differences observed at the vastus lateralis (MT: MAJOR = 18.4[16.2,22.5], MINOR = 13.4[12.5,15.8], CON = 13.2[12.2, 14.0]; MS: MAJOR = 344[294,466], MINOR = 254[197, 298], CON = 226[206,253]; all Median[IQ1,IQ3]). HEAD-US scores revealed no difference in mean limb activity, but higher ($p < .001$) structural mean limb damage in MAJOR than in MINOR (3[2,4] vs. 0.5[0,1]; all Median[IQ1,IQ3]).

Discussion/Conclusion: Majorly affected PwH limbs exhibit increased MS and MT compared to healthy and minorly affected limbs at the quadriceps and gastrocnemius muscles, with no difference at the hamstring and tibialis anterior muscles. Higher MS and MT is accompanied by larger clinical and sonographic abnormalities. Clinical implications include that PwH should engage in lower limb strength training, while incorporating MS and MT reducing methods, for example, massage and stretching, as increased MS and MT can result in altered muscle-joint functionality.

Disclosure of Interest: None declared.

PO064 | Surgical procedures and haemostatic outcome in patients with haemophilia receiving concizumab prophylaxis during the phase 3 explorer7 and explorer8 trials

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Introduction: Concizumab is an anti-tissue factor pathway inhibitor monoclonal antibody antibody in development as once-daily subcutaneous prophylactic treatment for haemophilia of all subtypes. The phase 3 explorer7 (NCT04083781) and explorer8 (NCT04082429) trials investigated the efficacy and safety of concizumab prophylaxis (PPX) in patients with haemophilia A or B with (HAwI/HBwI) or without (HA/HB) inhibitors. Minor surgical procedures performed at the 56-week cut-off are summarised.

Methods: Patients in explorer7 and explorer8 trials were exposed to no PPX (arm1) or concizumab PPX (arms2–4) based on their treatment regimen before the trial. After the main part of the trial, all patients could continue in the extension part receiving concizumab for up to 136 weeks. Informed consent/ethics committee approval was obtained. Minor surgical procedures were permitted. Planned major surgery was not permitted, a concizumab pause was advised for acute major surgery. Surgical procedure data were collected at the 56-week cut-off. Local/topical use of anti-fibrinolytics was permitted during surgical procedures. Patients undergoing minor surgical procedures continued to receive concizumab PPX during the perioperative period with no change to dosage.

Results: In total, 278 patients received concizumab PPX, of these, 30 patients (six adolescents aged 12–17 years and 24 adults aged 18–64 years) underwent minor surgical procedures. Nine patients had HA (30.0%), 10 had HB (33.3%), seven had HAwI (23.3%) and four had HBwI (13.3%). Dental procedures were most frequent ($n = 24$), other procedures included port removal, colonoscopy, arthrodesis and urethral augmentation. In addition, seven cases of major surgery were

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reported in two patients with HA, two with HB, one with HAwI and two with HBwI.

Minor surgery-related bleeding episodes ($n = 15$) were reported for 14 of the 38 minor surgical procedures, and eight bleeding episodes were treated. Fourteen of the 15 bleeding episodes were classified as mild/moderate. The median duration of minor surgery-related bleeding was 2 days and the mean number of injections with factor products required to treat these bleeds was 1.5 (SD 0.8).

Discussion/Conclusion: Minor surgical procedures were undergone safely in patients with haemophilia on concizumab PPX during the phase 3 explorer7 and explorer8 trials. Except for one, all surgical-related bleeding episodes were mild or moderate.

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PO065 | Haemophilia A with low activity of factor VIII: A case well managed with homeopathy

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Introduction: Haemophilia is a genetic disorder that affects the blood's ability to clot. People with haemophilia have a deficiency or dysfunction of certain proteins in the blood called clotting factors, which are necessary for normal blood clotting. Haemophilia A, the most common type of haemophilia, is caused by a deficiency of clotting factor VIII (FVIII). Treatment for haemophilia A typically involves replacing the missing FVIII with injections of the protein. This can be done regularly to prevent bleeding episodes or as needed to treat bleeding that has already occurred. In some cases, gene therapy may also be an option for people with haemophilia A.

Methods: Case Presentation: An 8-year-old boy visited a homeopathic opd with a prediagnosed case of haemophilia A. He was diagnosed at a very early age when at age of a few months he fell down and bleeding started from his tongue due to cut. Which was continued for 5 days. Then he was diagnosed with FVIII deficiency. His coagulation profile showed an FVIII level of 2.6%. From that time to till the first visit to the homeopathic opd, he needed FFPS transfusions and injections of VIII, mostly 4–6 bags of plasma in a month. He presented with left knee and left elbow swelling due to internal bleeding. His father told that whenever he gets injured his bleeding does not stop until they go for a fresh frozen plasma transfusion. If the swelling and bleeding persist even after FFPs, he has to get an injection of FVIII.

Results: After detailed history taking he was given individualised homeopathic prescription plan. Gradually, with continued medicines, he started to respond to the treatment. Internal bleeding inside joints started to disappear without any sort of transfusions and after an injury, he no more required factor injections. His most recent factor report showed a factor activity level of 47%. Which shows a huge improvement in the coagulation profile. He is taking medicines for the past 2 years and doing well.

Discussion/Conclusion: The narrated case report shows a well-managed case of haemophilia with homeopathic medicines. The patient had a severe form of the disease which converted into a moderate type of haemophilia. According to the present situation of the patient, it can be assumed that his disease can be in a mild haemophiliac state in the future. Homeopathy works more gently on all living creatures. This case is evident to show the effectiveness of homeopathy.

Disclosure of Interest: None declared.

PO066 | Fc-fusion and glycopegylated rFVIII: Pharmacokinetic comparison case series

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Introduction: Haemophilia A is a rare congenital X-linked coagulation disorder caused by factor VIII (FVIII) deficiency. Prophylaxis (PPX) with replacement therapy is the mainstay of disease management in severe haemophilia, aiming to decrease both spontaneous bleeding and morbidity of chronic arthropathy. Recently, new recombinant factors with prolonged pharmacokinetic (PK) profiles (e.g., extended half-life, EHL) can reduce the frequency of administration and treatment burden and can maintain higher plasma factor concentrations. The aim of this work is to compare PK parameters of two different EHL recombinant FVIII (rFVIII): an Fc-fusion rFVIII (efmoroctocog alfa) and a glycopegylated rFVIII (turoctocog alfa pegol, N8-GP), to give the best treatment option to patients.

Methods: PK parameters were evaluated in five severe haemophilia patients, all treated with both rFVIII-EHL. All patients were in PPX treatment with Fc-fusion rFVIII as standard of care and, after at least 4 days of wash-out, a singled dose of N8-GP was administered at the same dosage. Blood samples were collected before drug administration and after, up to a maximum of 96 h. Residual FVIII activity was measured using chromogenic assay. Data analyses was performed by the WAPPS-Hemo.

Results: Patients (12–47 years old) were treated with a median dosage of 46.15 IU/kg of efmoroctocog alfa (IQR 7.60) and 46.15 IU/kg of N8-GP (IQR 10.70). N8-GP showed a longer half-life (15.50 h, IQR 2.00) compared with efmoroctocog alfa (14.50 h, IQR 4.50). Estimated time

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spent with FVIII levels above 5% when infusing every 4 days has given better results for N8-GP. In detail, PPX treatment with N8-GP allowed patients to spent 89.58% of the week with FVIII above 5% (3.27 days; IQR 0.51), while patients treated with efmoroctocog alfa spent only 70.77% of time above 5% (2.48 days; IQR 0.98).

Discussion/Conclusion: This paper shows for the first time a real-world head-to-head PK profile comparison between two EHL rFVIII within a subset of severe haemophilia A patients, including a 12-year-old young boy. Our real-world experience underlines improvement in PK parameters by treating severe Haemophilia A patients with glycopegylated rFVIII. These data were collected after a single infusion of N8-GP therefore it is presumable that continuous and regular PPX will lead to both improved PK parameters and clinical outcomes, due to steady state achievement of FVIII plasmatic levels.

Disclosure of Interest: None declared.

PO067 | Novel insights into factor VIII and FIX levels among paediatric haemophilia carriers

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Introduction: While traditionally assumed female haemophilia carriers (HCs) are asymptomatic, recent evidence of increased bleeding in HC challenges this. However bleeding phenotype is poorly understood, especially in children. New HC nomenclature by the ISTH SSC suggests five groups: mild/moderate/severe haemophilia, symptomatic and asymptomatic HC (FVIII/IX ≥0.40 IU/mL with/without bleeding). Whether these groups are appropriate in children is unknown.

Methods: A clinical HC dataset was established, bleeding phenotype and FVIII/FIX levels assessed. As genetic testing is not routine <16 years, females were classed as 'Obligate' HC with a paternal history of haemophilia, as having '50% Chance' of being a HC with a maternal carrier history or 'Possible' HC if factor deficiencies were found de novo.

Results: A total of 217 females (n = 62 FIX n = 155 FVIII, median age 9.6[IQR 7.3] years) were included; 47 (22%) obligate HC, 115 (54%) 50% chance and 53 (25%) possible HC. Median age at FVIII/FIX test: 2.3[IQR 5.4] years. Using age-specific reference ranges: 52% (113/217) normal, 47.5% (103/217) mild and 0.5% (1/217) moderate FVIII/FIX deficiency. Using <40 IU/mL to define deficiency: 78.3% (170/217) normal, 21.2% (46/217) mild and 0.5% (1/217) moderate FVIII/FIX deficiency. 17% received haemostatic therapy; 64% tranexamic acid (TXA) only, 18% TXA + DDAVP, 7% TXA + DDAVP + Elocta, 4% TXA + Elocta, 4% Alprolix only and 4% DDAVP only. Recipients were significantly older (mean 12 vs. 9.6 years, p = .01). There was no difference between FVIII and FIX HC regarding age, absolute levels or proportions with mild FVIII/FIX deficiency. Significantly more FVIII HC received haemostatic therapy than FIX (20% vs. 9% χ^2 4.1, p = .04). Commonest indications: mucosal bleeding; epistaxis and menorrhagia and surgical prophylaxis.

Discussion/Conclusion: Mild FVIII/FIX deficiency is common in HC. Complexities in evaluating paediatric HC include variations in reference ranges with age and fewer bleeding challenges faced by children than adults. Female adolescents/young adults experience greater haemostatic challenges than young children. Thus, we found haemostatic therapy recipients were older, likely attributable to menorrhagia. Interestingly, FIX HC received less haemostatic therapy than FVIII, consistent with studies suggesting FIX deficiency may confer a less severe bleeding phenotype. Overall, our novel data from a large paediatric HC cohort highlight significant bleeding phenotype and treatment burden in these children.

Disclosure of Interest: None declared.

PO068 | Real-world effectiveness and usage of recombinant factor IX Fc: Secondary paediatric analysis from the 24-month french, prospective, non-interventional B-SURE study

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Introduction: B-SURE (NCT03655340) evaluated the real-world outcomes of recombinant factor IX Fc (rFIXFc; Alprolix®) in patients with haemophilia B (PwHB).

Methods: Final B-SURE data for PwHB <18 years on rFIXFc prophylaxis (PPX) were analysed, including annualised bleeding rate (ABR), injection frequency (IF) and factor consumption (FC). For those with prior PPX, 6-month retrospective FIX data were collected for comparison.

Results: This analysis included 30 PwHB aged <12 (n = 16)/12–<18 (n = 14) years, with median (range) age of 8.4 (3.6–11.95)/14.8 (12.2–17.8) years, respectively. All but one patient 12–<18 years had severe disease.

In the 6 months prior to rFIXFc, 13 PwHB <12 years were on PPX, while one had on-demand treatment and two had both regimens; all

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PwHB 12–<18 years were on PPX. All but one patient 12–<18 years initiated rFIXFc before enrolment. rFIXFc PPX was most commonly initiated to reduce IF while maintaining bleed protection for PwHB < 12 (n = 9/16)/12– < 18 (n = 8/14) years.

Before rFIXFc initiation, median (IQR) ABR was 0.0 (0.0–2.0)/2.0 (0.0–2.0) for PwHB < 12 (n = 14)/12–<18 (n = 13) years, respectively; annualised IF and FC were 99.3 (56.2–104.4; n = 14)/86.0 (54.5–108.2; n = 11) injections and 2579.1 (2337.1–4390.0; n = 14)/2848.7 (2655.6–4013.7; n = 11) IU/kg. After rFIXFc initiation, median (IQR) ABR was 0.6 (0.3–2.2)/0.8 (0.0–2.3) for PwHB < 12 (n = 14)/12– < 18 (n = 13) years, respectively; annualised IF and FC were 53.7 (50.1–55.4; n = 14)/51.2 (36.1–57.0; n = 11) injections and 2631.5 (2422.6–3058.5; n = 14)/2538.0 (2315.8–3736.5; n = 11) IU/kg.

Change (pre- vs. post-switch) in median (IQR) ABR was +0.2 (−1.6 to +0.7)/0.0 (−1.5 to +0.3) for PwHB < 12 (n = 14)/12–<18 years (n = 13), respectively; change in annualised IF and FC were −46.0 (−49.8 to −1.7; n = 14)/−39.0 (−50.0 to −9.9; n = 11) injections and +50.1 (−1832.5 to +370.2; n = 14)/−171.6 (−1763.5 to +289.2; n = 11) IU/kg.

Most physicians (<12 years: n = 10/13; 12–<18 years: n = 12/14) and PwHB/caregivers (<12 years: n = 15/15; 12–<18 years: n = 10/12) were satisfied or highly satisfied with rFIXFc PPX at last assessment.

Reported adverse events were broadly consistent with what is expected for PwHB.

Discussion/Conclusion: Real-world data from B-SURE in paediatric PwHB showed that rFIXFc prophylaxis maintained effective bleed protection, while reducing injection frequency and reducing/maintaining factor consumption.

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PO069 | Registry of haemophilia carriers: A pilot study for the characterisation of the joint health and the bleeding phenotype

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Introduction: Little is known about the bleeding phenotype and prevalence of joint damage in haemophilia carriers (HC). Moreover, though HC have a decreased quality of life, many reject their clinical condition having inadequate medical follow-up. Objectives: We aimed to carry out a local registry of HC and explore their joint damage, bleeding phenotype and the global haemostatic capacity.

Methods: The registry was performed by searching information from available databases, we also received support from the Málaga Haemophilia Association and haemophilia patients. Once families were identified, some carriers were invited randomly to participate in an exploratory study. Joint health and bleeding tendency were evaluated by the HEAD-US and the ISTH-BAT scores, respectively. Global haemostatic capacity was evaluated in fresh by rotational thromboelastography (ROTEM®; naTEM® test). Data is reported using the median [25%–75%]. p-value < .05 was considered significant.

Results: A total of 66 families were identified and 15 patients were evaluated. Five patients were excluded: three due to concomitant von Willebrand disease (factor [F] VIII = 47.8 [39.8–53.7] IU/dL; plasma von Willebrand factor antigen = 47.5 [46.4–52.8]%; plasma von Willebrand factor activity = 39.5 [36.1–56.3]%; HEAD-US = 0.0 [0.0–0.0]; ISTH-BAT = 8.0 [5.0–9.0]; age = 47.8 [39.8–53.7] years old [YO]) and 2 other patients due to FVIII/FIX < 40 IU/dL (one patient with FVIII = 21.4 IU/dL; HEAD-US = 3; ISTH-BAT = 2; age = 30.9 YO and the other with FVIII = 27.1 IU/dL; HEAD-US = 3; ISTH-BAT = 7; age = 32.3 YO). In the remained 10 patients (true haemophilia carriers without other known coagulopathy), the median age was 45.8 [35.5–59.1] YO and basal FVIII/FIX = 55.7 [46.7–80.1] IU/dL. Slight joint damage (HEAD-US = 0.5 [0.0–3.0]) (minimum–maximum values = 0–5) and mild bleeding phenotype (ISTH-BAT = 3.5 [1.5–5.0]; minimum–maximum values = 1–9) were observed. ROTEM® of the HC were similar to the healthy controls (p < .05). No relationship between basal FVIII/FIX levels, joint damage or bleeding phenotype were found.

Discussion/Conclusion: This pilot study shows that HC may presented joint damage accompanied by a mild bleeding phenotype that did not show correspondence with the FVIII/FIX basal levels or the kinetic of clot formation. Larger studies are needed to further characterise the haemorrhagic phenotype and joint conditions in this group of patients.

Disclosure of Interest: None declared.

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PO070 | Ultrasound for the assessment of arthropathy in patients with moderate haemophilia A: A multi-centre cross-sectional study

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Introduction: The risk of developing haemophilic arthropathy (HA) in patients with moderate haemophilia A (moHemA) is highly variable. People with moHemA seem to be under-treated, and this may lead to joint damage and worsen quality of life. The aims of the present study were: (i) to evaluate the added value of ultrasound (US) compared to clinical examination in identifying moderate HA patients at high risk of developing HA; (ii) to investigate the potential of the HEAD-US in driving treatment modifications in these patients.

Methods: We performed a multicentre cross-sectional study. Consecutive patients with moHemA receiving on-demand replacement treatment underwent a clinical assessment of joint status for all the six major synovial joints according to HJHS protocol. On the same day, all patients underwent an US examination performed according to the HEAD-US protocol.

Results: A total of 51 subjects were included and 306 joints were evaluated by clinical and US examination.

The median HJHS value was 2.0 (IQR: 0–3), with a score ranging from 0 to 1 found in 25 patients (49.0%) and a score >4 in 6 (11.8%). The HEAD-US median value was 2.0 (IQR: 1–7) and a statistically significant correlation between HJHS and HEAD-US was found (rho = 0.732, $p < .001$). HEAD-US was concordant with HJHS in the identification of the six patients with arthropathy, but it also detected pathological joint changes in 8% of patients with a HJHS ranging from 0 to 1. Overall, a pathologic HEAD-US was found in 16 patients with moderate haemophilia (31.4%).

Discussion/Conclusion: Our study suggests that the prevalence of HA in patients with moHemA receiving on-demand treatment is not negligible (≈30%) and that US able to detect clinically overt as well as sub-clinical changes in this clinical setting.

Disclosure of Interest: None declared.

PO071 | Prospective ultrasound assessment of the joint status in 61 haemophilia patients in a single paediatric centre: 7-year follow-up results

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Introduction: Progressive arthropathy is the main cause of morbidity in haemophilia. The ultrasound detection of early joint damage may contribute to optimise treatment of haemophilia patients.

Methods: Starting from January 2016, we prospectively performed the ultrasound examination of the elbows, the knees and the ankles in a series of 61 consecutive haemophilia patients. Forty-six of them are affected by haemophilia A (HA) (31 severe, eight moderate and seven mild HA) and 15 by haemophilia B (HB) (seven severe, one moderate and seven mild HB). Forty-six are on prophylaxis (11 with SHL products, 20 with EHL products and 15 with Emicizumab) while 17 are on demand therapy. Median age is 16 years (range 4–24). Ultrasound assessments are routinely performed during the annual follow-up visit by means of the Haemophilia Early Arthropathy Detection with Ultrasound (HEAD-US) system. In case of synovial hypertrophy detection, an additional ultrasound study is planned within the next 6 months. Patients who switched to emicizumab are monitored every 3 months during the first year of therapy.

Results: A total of 225 ultrasound examinations (1350 joints) using the HEAD-US protocol were performed with a median number of evaluations/patient of 3 (range 1–9). Median follow-up is 31 months (range 8–82). Overall, the median HEAD-US score at baseline is 0 (range 0–24). The same has been found in patients on demand (range 0–2) while patients on prophylaxis have a median HEAD-US score of 1 (range 0–24). Only two patients (3%) have overt joint disease while 44 patients (56%) did not present any signs of arthropathy at the first examination. Among this group,18 patients (30% of the entire cohort) maintained HEAD-US 0 during follow-up. For patients with joint damage, the most frequently involved joints were ankles, mostly affected of synovitis. No significant differences have been observed between patients on sostitutive prophylaxis and those with non-sostitutive therapy.

Discussion/Conclusion: Ultrasound performed with the HEAD-US protocol is feasible and suitable to monitor synovial hypertrophy and osteochondral damage in haemophilia patients in order to optimise therapy. In this cohort of young haemophilia patients, a significant percentage of cases presents healthy joints. This observation suggests that primary prophylaxis may contribute to avoid joint damage in childhood.

Disclosure of Interest: None declared.

PO072 | Joint status follow-up in haemophilia patients on prophylaxis with Efmoroctocog alfa using the haemophilia early arthropathy detection with ultrasound (HEAD-US) score: A single centre experience

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Introduction: Progressive arthropathy due to recurrent joint bleeds is the main cause of morbidity in patients with severe haemophilia.

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Prophylaxis significantly reduces acute bleedings but subclinical disease and progression of arthropathy may occur despite treatment. In clinical practice, the introduction of EHL products has allowed clinicians to personalise doses and regimens in order to minimise risk of bleeding and maximise patients' compliance. Aim of this study is to assess the status of joints in severe haemophilia patients during prophylaxis with efmoroctocog alfa.

Methods: We prospectively evaluated the elbows, the knees and the ankles by means of the Haemophilia Early Arthropathy Detection with Ultrasound (HEAD-US) system in a series of 13 patients with severe haemophilia A who switched to efmoroctocog alfa. Patients' median age at the time of the switch was 14 years (range 4–37 years). US joint evaluation was assessed at the time of the switch and then every year afterwards during routine follow-up check. An additional evaluation was performed at 6 months in patients who showed synovial hypertrophy in one or more joints at baseline.

Results: Forty-eight US exams (288 joints) were performed. At baseline, three patients under primary prophylaxis had HEAD-US score 0, seven patients with clinically asymptomatic joints exhibited signs of active disease and three patients with clinical severe arthropathy presented HEAD-US score >10. Overall, the median HEAD-US score at baseline was 3 (range 0–22). Notably, no correlations with ABR (median 0, range 0–2) and HJHS (median 0, range 0–10) were found in patients with subclinical arthropathy (median HEAD-US score 3, range 2–7). Median follow-up was 29 months (range 12–74). During follow-up, HEAD-US score gradually decreased due to a progressive and persistent reduction of synovial proliferation (median HEAD-US synovial subscore decreased from 3 at baseline to 2 after 1 year and turned to persistent 0 after 2 years).

Discussion/Conclusion: Our data suggest positive results of long-term prophylaxis with efmoroctocog alfa in terms of joint status. Further studies on a larger patient population are needed to confirm this data. In this cohort of young haemophilia A patients, HEAD-US proved to be more effective and more sensitive than ABR and HJHS in monitoring haemophiliac arthropathy.

Disclosure of Interest: None declared.

PO073 | The costs and benefits of extended half-life clotting factors in patients with severe haemophilia A at a single institution

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Introduction: Proactive prophylaxis and management of bleeding events can improve the quality of life of patients with severe haemophilia A. Extended half-life (EHL) clotting factors have shown benefit with longer half-lives and less frequent injections than standard half-life (SHL) clotting factors. Here, we report the real-world experience to evaluate the costs and benefits of changing from SHL to EHL in MacKay Children's Hospital.

Methods: Patients with severe haemophilia A were enrolled in the retrospective study. The clotting factor was switched from SHL (Advate) to EHL (Adynovate) product since November 2019. The peak and trough level of factor VIII were obtained for PK study. The PK tools including WAPPS-Hemo and MyPKFiT were performed. Personalised APPs were introduced for treatment diary of patients. Adjustment of treatment was according to pharmacokinetics study and clinical conditions. The bleeding records including annual bleeding rate (ABR), annual joint bleeding rate (AJBR), annual spontaneous bleeding rate (ASBR), target joints and zero bleeding rate were reviewed.

Results: There were 20 patients with severe haemophilia A enrolled. The median age was 23 years old (4–33). Eighteen received prophylactic and two received on-demand (OD) anti-haemophilic treatment, respectively. The SHL dose was 15-25 IU/kg three times a week and the EHL dose was 40-50 IU/kg twice a week, respectively. The PK study was performed in 15 patients. The EHL/SHL half-life ratio increased by 1.3–1.8 times. From SHL to EHL, the mean annual dose and cost increased 2.5- and 2.3-fold, respectively. ABR, AJBR and ASBR decreased more than 50% after switching. Zero bleeding rates increased from 23.5% in SHL to 44.4% in 1-year EHL and 77.8% in 2-year EHL groups. Target joint resolved in 100% patients after 3-year EHL use.

Discussion/Conclusion: The annual doses and costs are increased in patients with EHL compared with SHL. However, patients are encouraged to switch from OD to prophylaxis to achieve better life quality and minimise the bleeding episodes according to the utilisation of EHL, PK tools and personalised APPs.

Disclosure of Interest: None declared.

PO074 | Joint health in participants with haemophilia A and haemophilia B without inhibitors treated with marstacimab from the phase 3 basis trial

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Introduction: Marstacimab is an investigational monoclonal antibody targeted to tissue factor pathway inhibitor to improve haemostasis. BASIS (NCT03938792) is an open-label, phase 3 marstacimab trial in participants (pts) with severe (FVIII < 1%) haemophilia A (HA) or moderately severe to severe (FIX ≤2%) haemophilia B (HB) with or without inhibitors. We report joint health data of pts without inhibitors.

Methods: Screened males aged 12–<75 years entered a 6 months observational phase (OP) and received on-demand (OD) or routine prophylaxis (RP) factor replacement. Pts in the 12 months active treatment phase (ATP) received a 300 mg subcutaneous marstacimab loading dose and subsequent 150 mg once/wk. Pts could then enrol in a long-term extension (LTE) study. Joint and target joint bleeds

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were monitored. Joint health was assessed using the Haemophilia Joint Health Score (HJHS; lower score indicates better joint health).

Results: A total of 128 pts (median age, 30 [range 13–66] years) entered the OP (*n*: OD: HA 29, HB 8; RP: HA 72, HB 19); 116 (*n*: OD 33, RP 83) entered the ATP and 87 were treated in the LTE (at time of data cut, *n*: OD 29, RP 58; duration: 34–483 days). At baseline (BL), 89 pts (69.5%; *n*: OD 36, RP 53) had ≥1 target joint. Compared with OD, marstacimab reduced the incidence of joint bleeds (32.9 vs. 2.8; $p < .0001$) and target joint bleeds (23.2 vs. 1.8; $p < .0001$), with numerical reductions in the LTE (1.9 and 0.9, respectively). HJHS decreased 2.8 points versus OD ($p = .3$) at 6 months and maintained to d180 of the LTE (mean [SD] change from LTE BL [CFB]; 1.1 [2.5]; $n = 19$). Mean (SD) number of target joints were lower versus OD (0.2 [0.7] vs. 1.7 [1.4]) and maintained over the LTE (0.07 [0.258]). Compared with RP, marstacimab reduced the incidence of joint bleeds (5.7 vs. 4.1, $p = .1680$) and target joint bleeds (3.4 vs. 2.5; $p = .2811$), with numerical reductions in the LTE (1.9 and 0.9, respectively). HJHS decreased 2.0 points versus RP ($p = .0835$) at 6 months and maintained to d180 of the LTE (mean [SD] CFB, −2.7 [14.3]; $n = 24$). Mean (SD) number of target joints were similar versus RP (0.3 [0.9] vs. 0.3 [0.7]) and maintained over the LTE (0.1 [0.4]).

Discussion/Conclusion: Marstacimab reduced joint bleeds, HJHS and number of target joints in pts with severe HA or moderately severe to severe HB without inhibitors and with high BL prevalence of target joints versus prior OD or RP. Efficacy of marstacimab was maintained up to 16 months in the LTE.

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PO075 | Epidemiological data and treatment strategies in haemophilia patients in a portuguese centre—differences between 2017 and 2023

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Introduction: In Portugal, extended half-life factor VIII (EHL FVIII) products and emicizumab, for inhibitor patients (pts), were approved in 2018, and EHL factor IX (FIX) products in 2019. Emicizumab for persons without inhibitors was finally reimbursed in 2023.

Our aim is to compare changes in epidemiology and clinical practice in pts with haemophilia registered at our Centre between 2017 and 2023.

Methods: Pts demographics, disease severity and treatment information were retrospectively collected in two selected time points (2017 and 2023) and analysed, to evaluate changes in the demographics and in the type and regimen of treatment. Women with factor levels below 40% were included in the mild haemophilia group.

Results: In 2017, 158 pts (141 males/17 females) were registered at our Centre, 145 with haemophilia (HA) and 13 with haemophilia B (HB), of which 60 had severe HA (SHA); 7 moderate HA (MdHA); 78 mild HA (MiHA); 6 SHB; 1 MdHB and 6 MiHB.

Comparing 2017–2023, a growth in number of pts (31.4%) becomes apparent and now there are 230 registered pts (199 males/31 females); 90 SHA; 8 MdHA; 104 MiHA; 10 SHB; 6 MdHB and 12 MiHB. This increase is especially evident in SH with 30 new SHA and 4 SHB patients.

In 2017, there was already a high rate of prophylaxis in severe pts (90% HA; 66% HB) but prophylaxis was less common in moderate pts and only 2/7 HA pts and none MdHB pt were on prophylaxis. In 2023, the number of pts in prophylaxis is higher, especially in moderate pts (SHA 97%, SHB 83%; MHA 37.5%; MHB 50%).

In 2017, pts with HA and HB were treated with standard recombinant half-life products. In 2023, all HA pts on prophylaxis with FVIII products and all HB pts are treated with EHL products. To note, 16/78 SHA pts without inhibitors (20.5%) are already on prophylaxis with emicizumab.

In 2017, only five pts with SHA and inhibitors were registered, and all were on prophylaxis with bypassing agents. In 2023, we have 12 inhibitor patients all on prophylaxis with emicizumab.

Discussion/Conclusion: Our Centre had a significant increase in registered pts, mainly due to immigration from other countries, but some new pts came from other Portuguese Centres in search of alternative therapeutic approaches. Changes in treatment strategy included a complete switch to EHL products and the introduction of prophylaxis with emicizumab for pts with and without inhibitors.

Disclosure of Interest: None declared.

PO076 | Artrial fibrillation—a challenge in patients with haemophilia A

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Introduction: With the aging population of haemophilic patients, cardiovascular diseases are also increasing among these patients. Atrial fibrillation is one of these increasing diseases. Despite the reduction in a clotting factor, these patients are at risk of a stroke. Permanent anticoagulation may be necessary despite bleeding tendency. In this case, we report a patient with mild haemophilia A and atrial fibrillation.

Methods: The therapeutic options in patients with atrial fibrillation were anticoagulation with, for example, apixaban 2 × 5 mg or 2 × 2.5 mg

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in a reduced dose. The second option would be pulmonary vein isolation with subsequent medium-term anticoagulation until the atrium has completely healed or cardioversion, as a third option, with short-term anticoagulation. If no thrombus can be detected in TEE after 4 weeks of anticoagulation, anticoagulation is stopped again. The final option would be an atrial occluder, which prevents a thrombus from forming. It is particularly suitable for patients where long-term anticoagulation is contraindicated. However, long-term secondary prophylaxis with aspirin is usually indicated.

Results: After unsuccessful rhythm control with medication, cardiologist decided to undergo cardioversion with amiodarone within 1 year of the onset of persistent atrial fibrillation. This results in an improvement in morbidity and a reduction in cardiovascular events. Mortality remains unaffected in this procedure.

For this purpose, the patient received recombinant factor VIII, which he had already received regularly in the past as on-demand therapy. After 1 week, anticoagulation with apixaban was reduced to 2 × 2.5 mg and continued for another 3 weeks. Factor therapy was also continued during this time (trough level 30%). A TEE check was carried out after 4 weeks. If there was no evidence of cardiac thrombi and sinus rhythm was present, anticoagulation therapy was stopped. So far the patient remains in sinus rhythm. Neither thromboembolic complications nor bleeding complications occurred during therapy or afterwards.

Discussion/Conclusion: Although patients with haemophilia have an increased risk of bleeding, diseases such as atrial fibrillation also have an increased risk of stroke. A lack of guidelines in this area leads to difficult therapy decisions, which are sometimes certainly wrong for the individual patient.

Disclosure of Interest: None declared.

PO077 | Mental health outcomes from the learning to live with non-severe haemophilia study: First report using coreHEM mental health outlook

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Introduction: Modern treatment for haemophilia modifies bleeding phenotype. The Learning to Live with Non-severe Haemophilia study sought to identify the ongoing support needs of those who transition to a milder bleeding phenotype. Quality of life (QoL) and mental health outlook (MHO) are outcomes important to people living with haemophilia (PWH). The Patient Reported Outcomes Burdens and Experiences (PROBE) Study is an established QoL tool for PWH. MHO was measured using coreHEM a recently developed, haemophilia-specific, content validated questionnaire. The relationship between scores on the two questionnaires is assessed for the first time.

Methods: This is a mixed methods study comprising both quantitative and qualitative components. The study was promoted via four haemophilia centres to men with mild, moderate or severe haemophilia, including those treated with gene therapy. The quantitative portion comprised of collection of demographic data, PROBE and coreHEM MHO. Both have scores which range from 0 to 1, in which a higher number indicates better QoL/MHO. The study was approved by HRA and Health and Care Research Wales in September 2022 (22/WM0205). Recruitment and data collection closed on 29 September 2023.

Results: The survey was sent to 1279 PWH (625 mild, 160 moderate and 494 severe). Between 9 March and 9 July 2023, 165 participants were enrolled (68 mild, 22 moderate, 70 severe, 5 unsure; RR 13%). Mean age at survey was 40.2 years (range 16–78 years). PROBE scores were calculated on 152 participants, and coreHEM scores were calculated on 135 participants. Compared with those with mild haemophilia, people with severe haemophilia had lower median PROBE scores (0.738118 vs. 0.859445; $p < .01$), and lower median coreHEM MHO scores (0.726667 vs. 0.84; $p < .01$).

Discussion/Conclusion: This is the first report of a field study using both PROBE and coreHEM MHO. Gene therapy offers a potential cure for severe/moderately severe haemophilia yet PWH live with long term physical and psychosocial impacts. coreHEM MHO scores followed a pattern established by PROBE: on both PROBE and coreHEM MHO, scores are lower in those with severe haemophilia despite effective treatment. Psychosocial support remains an important part of care for PWH regardless of access to treatment.

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PO078 | First report of lived experience from the learning to live with non-severe haemophilia study

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Introduction: Gene therapy for severe haemophilia converts the bleeding phenotype to mild or moderate. However, people with haemophilia (PWH) postgene therapy may require a greater degree of ongoing care and support than those with genetically mild or moderate haemophilia due to past bleeding. Assessing subjective experiences of PWH with genetically mild or moderate haemophilia versus those converted to a milder phenotype allows comparison of expectation across the spectrum of disease.

Methods: A mixed methods study collecting demographic and quantitative data, including the PROBE survey and an optional qualitative in-depth interview, analysed using thematic analysis and Nvivo software. Participants were recruited from four UK haemophilia centres and anonymised to study number. Ethical approval from HRA and Health and Care Research Wales (22/WM/0205). The qualitative data are presented here.

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Results: A total of 136 of 165 respondents were interested in being interviewed; 73 were approached; 45 consented. Forty-four PWH aged 19–72 years with haemophilia A (n = 31) or B (n = 13) (8 postgene therapy, 11 severe, 10 moderate and 15 mild) were interviewed. A total of 123 points were raised; these were coded into five main themes: (1) Acceptance versus rejection (includes positive attitude vs. anger/anxiety/denial), (2) Benefits versus burdens, (prioritised/improved treatment vs. bleeds and family disruption), (3) Control versus uncertainty (coping and self-treatment vs. inequity of treatment), (4) Freedom versus constraint (exercise and sport vs. risk aversion/protection) and (5) The future versus the past (new treatment and 'cure' vs. past journey and viral infection).

Discussion/Conclusion: Those with mild and moderate haemophilia reported similar impacts on quality of life (QoL) to those with severe haemophilia. When they bleed, they are less able to self-infuse and require hospital delivered care, but complain of mixed messaging: they are told to limit activity to reduce bleeds but when injured, to wait to see if it is a bleed. Treatment disparity needs to be addressed if the QoL of those with non-severe haemophilia (including those on phenotype altering treatments) is to improve. This includes facilitating self-infusion and home treatment for all as well as rapid access for bleed assessment and follow up regardless of primary diagnosis.

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PO079 | Patient preferences and usage patterns of mobile device applications for haemophilia A prophylaxis in eastern europe: results from a descriptive, observational, cross-sectional, survey-based study

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Introduction: Haemophilia A is a rare genetic bleeding disorder caused by insufficient clotting factor VIII (FVIII). Mobile device applications support personalised FVIII prophylaxis based on individual pharmacokinetic (PK) profiles. This study aimed to assess mobile application utilisation patterns and preferences among patients using PK-guided prophylaxis for the treatment of haemophilia A.

Methods: This observational cross-sectional study (May to September 2022) recruited patients (≥12 years old) with haemophilia A from Bulgaria, Czechia, Hungary, Lithuania and Romania. Patients completed a survey that collected information on patient demographics, documentation preferences (mobile application/written paper diary), application utilisation patterns, satisfaction (scale of 1—10) and suggestions for future use.

Results: In total, 84 patients with haemophilia A receiving PK-guided FVIII prophylaxis completed the survey. Almost all patients (98.8%) were male and most were aged 18—29 years (32.1%). The most commonly used FVIII therapeutic was efmoroctocog alfa (19.1%). Most patients used a written paper diary only (40.5%) or a mobile application only (40.5%). Among patients using a mobile application, Florio® HAEMO was the predominant mobile application (72.5%). Mobile application use was most common in Czechia (94.1%) and Romania (50.0%). Among patients using a mobile application, 77.5% used it to check FVIII levels less than once daily; 57.5% used FVIII levels calculated by the application to guide the timing of physical activity. No correlations were found between patient age and document management status or application type. Most patients (93.1%) reported high application satisfaction (score ≥8 out of 10). User suggestions included the incorporation of additional features to improve tracking of medication and FVIII levels, and smartwatch compatibility.

Discussion/Conclusion: Mobile device applications allow patients to monitor FVIII levels and document infusions, choose daily activities based on calculated FVIII levels and provide physicians with real-time access to symptoms and treatments. Overall, the findings from this study will facilitate the development of mobile device applications that support personalised FVIII prophylaxis for patients with haemophilia A.

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PO080 | Combined haemophilia A and C: A case report

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Introduction: Hereditary coagulation factor deficiencies are relatively rare disorders. Haemophilia C (or factor XI deficiency) is among the most common, but its combination with haemophilia A is very rare. This work reports the case of a patient with these two disorders.

Methods: A 58-year-old male patient was referred to coagulopathies consultation because of factor VIII (FVIII) deficiency revealed after a prolonged activated partial thromboplastin time (aPTT) of 41.7 s. The study was performed before an exploratory laparotomy to characterise and stage an abdominal mass. The patient had no history of previous surgical procedures and denied major bleeding events. Regarding other pathological antecedents, the patient reported tuberculosis diagnosed in 1980. Family history was irrelevant. Physical examination showed no signs of arthropathy or muscle oedema.

Results: The analytical study revealed FVIII values compatible with mild haemophilia A (32%); von Willebrand and IX factors' values were

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normal. The genetic study, performed by NGS, showed a mutation in Gene F8, exon 24, c.6622C > G, in hemizygosity, previously described and associated with mild haemophilia A. Surprisingly, another mutation was found in Gene F11, exon 5, c.442C > T, in heterozygosity, associated with FXI deficiency. Consequently, the FXI dosage was performed and revealed an FXI level of 27%.

Discussion/Conclusion: Familial multiple coagulation factor deficiencies (FMCFDs) are defined by more than one coagulation factor deficiency and is very rare. It represents a difficulty in diagnosis and treatment. In this patient, the discovery of the pathogenic variant of Gene F11 was unexpected and may have a cumulative effect on the haemorrhagic phenotype. In case of a haemorrhagic event, the treatment of the two haemophilias can be challenging considering the safety and limitations in availability of the products.

Disclosure of Interest: None declared.

PO081 | zero bleeds followed the administration of albutrepenonacog alfa, the rIX-FP with fewer frequency of administration in an argentinian cohort

J. Schmiedl[1] on behalf of M. S. Cruz; S. Borchichi; S. Gastaldo; M. E. Sánchez; G. Sciucatti; A. Torressi; P. Casais; L. Aversa[2,*]; D. Neme[3] on behalf of received research grants; honoraria for speaker activities, AB, participation in CT from CSL Behring, Novo Nordisk, Roche, Sanofi, Takeda

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Introduction: Based on the 2020 annual World Federation of Haemophilia (WFH) report, in Argentina (population: 45 million), there are 2814 people with haemophilia (PWH) registered, of which 386 have haemophilia B.[2] Approximately 80% of all patients with severe haemophilia, younger than 21 years old receive prophylactic treatment. This represents 27% of the population of PWH in Argentina. Frequent joint bleeds and impact on life expectancy are the major challenges for PWHB.[1–6]

Objective: The aim of this analysis was to determine real-world annualised bleeding rates (ABR), FIX dosing frequency and consumption in patients switching to prophylaxis with rIX-FP from previous factor IX replacement therapy.

Methods: We retrospectively collected data from ten individuals with severe haemophilia B, who were on rFIX-FP treatment between January and June 2023, from eight different haemophilia centres in Argentina.

Results: The mean age was 17.3 years (range 2–44). Two patients were on demand treatment and eight on prophylaxis prior to switching. Five patients received recombinant SHL FIX and five plasma derived products. The mean prophylactic treatment time with rIX-FP was 15.2 months. The median ABR; annualised spontaneous bleeding rate (AsBR) and annualised joint bleeding rate (AjBR) were 0 (0–4), 0 (0) and 0 (0–1), respectively. The median monthly dose of FIX prior and after switching to prophylaxis with rFIX-FP were 15,000 and 7,000 IU/kg, respectively. rIX-FP was administered once per week in five patients, once every 10 days in three and once every 15 days in two individuals. No inhibitor development, and adverse events were reported after switching to rIX-FP.

Discussion/Conclusion: This real-world analysis showed that switching to rIX-FP prophylaxis from prior FIX was associated with improved bleeding rates, increased zero bleedings, reduced frequency of administration and factor consumption.

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Disclosure of Interest: None declared.

PO082 | Emerging and exciting new treatments in haemophilia future

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Introduction: Haemophilia is a bleeding disorder clinically important due to its frequency and severity. The usual treatment, especially in severe and moderate types, is the administration of the deficient factor, which can trigger the appearance of antibodies that neutralise the function of the infused protein. Inhibitors render standard treatment ineffective, leading to haemorrhagic episodes more prolonged and difficult to control, increasing the risk of morbidity and mortality.

Methods: Based on the type of response, patients are classified as: low responding commonly managed with higher doses of factor to overcome the inhibitor titre; and high responding that need optimal management based on three strategies: prevention of bleeding, control of bleeding episodes and eradication of the inhibitor. The short half-life of FVIII and FIX means that frequent infusions are required to maintain a >1% and the burden from those infusions, cost and availability of concentrate are not ideal for continuous use as prophylaxis regimen.

Results: The search for treatments that overcome these limitations has been aimed at products with longer half-life, lower immunogenicity, subcutaneous administration and effectiveness in patients with or without inhibitors. Several pharmacological therapies developed for haemophilia aim to rebalance the clotting cascade and potentially circumvent challenges mentioned above. Emicizumab is a factor VIIIa (FVIIIa)-function mimetic bispecific antibody (BsAb) to FIXa and FX, has become an indispensable treatment for haemophilia A.

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Although potent, long-term outcomes suggest that a small proportion still bleeds. A new BsAb, named *NXT007*, resulted from further engineering of emicizumab. Nonclinical studies demonstrated maintained non-haemophilic range of coagulation potential, improved cofactor activity and more convenient dosing regimen. A phase 1/2 clinical study of NXT007 is on-going. Other alternative is concizumab, a humanised monoclonal Ab against tissue factor pathway inhibitor (TFPI), that binds to the Kunitz-2 domain and prevents its binding to activated factor. Developed for treatment of haemophilia A and B with and without inhibitors, recently approved in Canada for the treatment of adolescent and adult patients with haemophilia B who have FIX inhibitors and require routine prophylaxis to prevent or reduce the frequency of bleeding episodes.

Discussion/Conclusion: Novel haemophilia therapies offer an arsenal of treatment options and could revolutionise the future of haemophilia management.

Disclosure of Interest: None declared.

PO083 | Prophylaxis in patients with moderate–mild forms of haemophilia:experience in a single centre

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Introduction: According to the latest WFH guidelines, prophylaxis should be offered to patients with haemophilia A or B with a severe phenotype, and this would include some moderate patients with severe clinical phenotype, a practice supported by results reported from several real-life studies.

Methods: Report our experience with implementation of prophylaxis in a group of moderate and mild patients who agree to initiate this treatment modality and how this impacts on their quality of life both in terms of reduced bleeding and dependence on the centre. Collection of data from clinical history (see table) 12 months after and 12 months before starting prophylaxis.

Results: Of all patients with moderate haemophilia (F8/F9 2–5 IU/dL), previously on demand treatment, 75% started prophylaxis with factor concentrate: in five HA patients (mean F8:C 3.4 IU/dL) the mean factor consumption was 105 IU/kg/week for SHL-CF8 (3 times/week) and 90 IU/kg/week for EHL-CF8 (2 times/week) (one patient started prophylaxis with EHL-CF8 once a week but requested a change to 2/week, as he felt more confident). Prophylaxis adjusted for minimum trough level of 5 IU/dL. Reduction in total ABR was 96.78% (mean total ABR pre: 6.2; post 0.2) and non-attendance at Centre's ED after starting prophylaxis. One patient suffered a traumatic left ankle hemarthrosis requiring two doses more of EHL-CF8.

75% of moderate HB are already on prophylaxis: four patients (mean F9 level 3.3 IU/dL) and one mild patient (F9 6 IU/dL), all of them with established arthropathy at different levels. All patients, less 1, underwent prophylaxis with EHL-CF9, once a week, dose 60 IU/kg. Reduction in total ABR was 91.67% (mean total ABR pre: 3; post 0.25) and no attendance at Centre's ED. One patient had traumatic right knee hemarthrosis requiring three doses more of SHL-CF9 (prophylaxis with SHL-CF9 100 IU/kg/week).

Discussion/Conclusion: Different studies (e.g., MoHem) showed that patients with mild–moderate haemophilia also develop joint damage and are at risk of requiring orthopaedic surgeries so, according to current guidelines, it is important to identify and implement prophylaxis in these patients, especially those with more severe bleeding phenotypes. In our case, this strategy showed to be effective, reducing ABR and associated burden of disease, despite having to be infused more frequently. All in all, patients report satisfaction and improvement in their quality of life.

Disclosure of Interest: None declared.

PO084 | Iliac stent in mild ha and arterial peripheral disease: Experience from a single centre

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Introduction: Haemophilia patients are aging, with more patients at least 45 years old. Although haemophilia was considered to exert a protective effect against CVD, data seem to show that, compared to men without coagulopathy, haemophiliacs have similar frequency of CVD risk factors (CVRF).

Methods: Report management of haemophilia A (HA) male, 77 years, with peripheral arterial disease, according to algorithm proposed by Fogarty et al. (see image, from An algorithmic approach to peripheral artery disease in haemophilia: extrapolation of management principles from noncoagulopathic patients, *Blood Coagul Fibrinolysis* 2012;23:23-29).

Results: Mild HA (F8:C 22 IU/dL) without inhibitor. On demand treatment. F8 mutation: (NM_000132.3): c.1372 C > T, p. (Arg458Cys). Presents peripheral arterial ischemia of left leg, G IIb, double antiaggregate. Other CVRF: arterial hypertension, obesity. Total hip replacement (2019). He presented critical stenosis at distal portion of common iliac and occluded superficial femoral (AngioRMN January 2023) and we decided revascularisation with left leg AIE stent (Viabahn 8*5 cm). Before anaesthetic induction, we administered Elocta® (Lab. Sobi) (40–45 IU/kg) and bolus of UFH (1000 IU), by common femoral access. Surgery was uneventful. 12 h after, started Elocta® (20 IU/kg, day * 2), then 15 IU/kg (2 days) and antithrombotic prophylaxis (enoxaparin sodium 40 mg/day and mechanical methods), being discharged on 4th day, completing treatment out, every 48 h, two doses (total factor consumption: 12,000 IU). Simple antiplatelet therapy (ASA) was maintained at all times, suspending antithrombotic prophylaxis on day 7. No transfusion of red blood cells or other blood products was necessary.

Discussion/Conclusion: Atherosclerosis of iliac arteries and left leg vessels is marker of systemic atherosclerosis and ischemic risk and shares similar RF with other CVD, being fundamental the control of these in haemophiliacs. Revascularisation therapy is generally reserved, among others, for patients who present claudication, not

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respond to medical therapy and if it is isolated iliac disease, stenting may be the preferred method due to its durability, low restenosis and complication rates, In haemophiliacs, this technique seems safe if it is performed by expert team, with adequate replacement therapy, in our case we used Elocta® with excellent haemostatic efficacy and reduced consumption of units as well as infusions.

Disclosure of Interest: None declared.

PO085 | Real-world effectiveness and safety of a recombinant factor VIII Fc in patients with haemophilia A by age groups: pooled analysis (A-SURE/PREVENT)

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Introduction: Haemophilia A is a rare bleeding disorder caused by factor VIII (FVIII) deficiency. Standard of care is FVIII replacement therapy. Efmoroctocog alfa (Elocta®), a recombinant FVIII Fc fusion protein (herein rFVIIIFc), has an extended half-life allowing higher FVIII levels and a longer dosing interval than standard half-life products. This analysis evaluated real-world outcomes by age groups in patients with haemophilia A (PwHA) treated with FVIIIFc in two observational studies.

Methods: PwHA receiving prophylactic rFVIIIFc were pooled from the A-SURE (Europe, NCT02976753) and PREVENT (Germany, NCT03055611) phase four prospective observational studies. Only variables recorded in the same way for both studies were included. Patients were grouped by: <12 and ≥12 years. Annualised bleeding rate (ABR), annualised joint bleeding rate (AjBR), weekly injection frequency and factor consumption (prospective period) were assessed, as were serious adverse events (AEs) and AEs leading to treatment discontinuation (retrospective + prospective periods).

Results: In total, 336 patients were included, 88 < 12 years (44 from each study) and 248 ≥12 years (A-SURE $n = 142$; PREVENT $n = 106$). Mean (SD) age was 6.5 (3.4) years in the <12 years group and 33.6 (16.4) years in the ≥12 years group. Median (IQR) prospective follow-up was 20.5 (19.1; 22.2) and 21.1 (19.1; 24.0) months in the <12 and ≥12 years groups, respectively. Median (IQR) ABR/AjBR was 0 (0; 1.8)/0 (0; 0.6) in the <12 years group ($n = 87$) and 0.6 (0; 1.6)/0 (0; 1.0) in the ≥12 years group ($n = 246$). Median (IQR) weekly injection frequency was 2.2 (2.0; 3.0) in the <12 years group ($n = 87$) and 2.1 (2.0; 2.5) in the ≥12 years group ($n = 246$). Mean (SD) factor consumption was 108.2 (44.8) and 78.1 (30.4) IU/kg/week in the <12 years ($n = 87$) and ≥12 years groups ($n = 244$), respectively. Serious AEs were reported in 15 (17.0%) and 35 (14.1%) patients in the <12 years and ≥12 years groups, respectively; of these, one was considered treatment related (FVIII inhibition in a patient <12 years). Two AEs led to treatment discontinuation in the ≥12 years group (0.8%).

Discussion/Conclusion: These pooled real-world data from two large observational studies support the use of rFVIIIFc prophylaxis in PwHA of all ages. Across all age groups, low ABRs and AjBRs (<1.0) could be achieved with low injection frequencies and factor consumption rates.

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PO086 | Bleeding and clotting paradox: A child with haemophilia B and cTTP encounters anaphylaxis post-ITI and triumphs with the beutel protocol

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Introduction: Haemophilia B (HB) is a bleeding disorder caused by factor IX (FIX) deficiency. The occurrence of an anti-FIX inhibitor is currently the most serious complication, associated with an increase in the frequency and severity of bleeding, as well as with the occurrence of anaphylactic reactions. Congenital thrombotic thrombocytopenic purpura (cTTP) is an ultra-rare thrombomicroangiopathy caused by ADAMTS-13 gene mutations that result in reduced or absent ADAMTS-13 activity (<5%). The treatment of choice for cTTP is the administration of fresh frozen plasma.

Methods: This case report was formulated based on an in-depth review of the patient's medical documentation maintained at the University Clinical Hospital in Wrocław. The records were sourced from

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the Children's Hematology Department and the Specialised Clinic for Coagulation Disorders. The authors were the patient's physicians.

Results: A boy presented with severe haemophilia B symptoms, including mucosal bleeding, numerous bruises and joint swelling, at 9 months of age. Following 3 months of prophylactic FIX administration, the emergence of an FIX-inhibitor complicated his condition, leading to an attempted immune tolerance induction (ITI). However, an anaphylactic shock on the first day of ITI necessitated its discontinuation. Although the patient was considered for a clinical trial with concizumab, he was deemed ineligible. Subsequently, ITI was successfully administered as per the Beutel Protocol, achieving a negative inhibitor titre. Family genetic testing revealed heterozygosity for the ADAMTS13 gene in both the patient's mother and sister, who are haemophilia carriers. Despite this genetic predisposition, ADAMTS13 activity for these individuals, inclusive of our patient, was observed at around 50%, without any associated clinical manifestations.

Discussion/Conclusion: This unique case underscores the intricate challenges of managing a patient with severe haemophilia B complicated by the presence of an FIX-inhibitor and concurrent genetic predisposition to cTTP. The manifestation of anaphylactic shock during the first attempt at ITI highlights the unpredictability of individual immune responses, emphasising the importance of vigilant patient monitoring. Successful ITI application via the Beutel Protocol in a subsequent attempt demonstrates the adaptability of therapeutic strategies in such multifaceted cases.

Disclosure of Interest: None declared.

PO087 | The haemophilia B divergent path: When eggs deceive and diverticula reveal

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Introduction: Haemophilia B presents unique challenges within the realm of bleeding disorders. This case details a young boy with severe haemophilia B, whose initial manifestation was a massive gastrointestinal bleeding necessitating blood transfusion. Despite enhanced prophylaxis and treatment, subsequent episodes, often intensified by specific foods like chicken eggs, led to numerous repeated transfusions. These episodes, initially misattributed to severe food intolerance and a suspected egg allergy, were inconsistent with typical haemophilia presentations. Comprehensive investigations, suggestive of allergic colitis, were conducted. Yet, an inconclusive scintigraphic study ultimately prompted a laparoscopic intervention.

Methods: This case report was compiled from the patient's comprehensive medical records at the University Clinical Hospital in Wrocław, with the authors as the attending physicians.

Results: Despite various interventions, the severe bleeding episodes persisted. Scintigraphy failed to detect abnormalities. An exploratory laparoscopy, undertaken due to the persistent diagnostic puzzle, identified and facilitated the resection of Meckel's diverticulum. The boy remained on prophylaxis, and with a negative molecular allergy test, dietary recommendations were expanded, reintroducing eggs.

Discussion/Conclusion: This case highlights the diagnostic challenges faced when treating haemophilia B patients with recurrent gastrointestinal bleeding. While haemophiliacs are inherently prone to bleeding, it is vital to identify additional contributors. Even if initial imaging modalities remain inconclusive, thorough diagnostic approaches, including exploratory laparoscopy, can be both diagnostic and therapeutic. Clinicians must evaluate all potential bleeding sources in haemophiliacs and occasionally make bold diagnostic choices amidst consistent clinical uncertainties.

Disclosure of Interest: None declared.

PO088 | Trial in progress: Disease characteristics of haemophilia B in patients receiving standard-of-care prophylactic factor IX (FIX) replacement therapy

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Introduction: The severity of haemophilia B and related manifestations correlate with the degree of deficiency of factor IX (FIX) functional activity. The standard of care (SoC) for haemophilia B involves FIX clotting factor concentrates, with prophylaxis recommended in patients (pts) with severe and moderately severe disease. FIX prophylaxis is advantageous but presents a treatment and economic burden, and fails to eliminate the risk of all joint bleeding.

We are exploring CRISPR/Cas9-mediated insertion of the *Factor 9* gene into the albumin locus in hepatocytes to generate normal or near-normal FIX functional activity in plasma. We showed that the gene insertion platform generated durable, clinically relevant FIX expression after one-time intravenous administration in mice and non-human primates. FIX levels were durable and stable in multiple mouse models of rapid liver growth, suggesting potential applicability of the targeted gene insertion approach in the paediatric haemophilia B population. Thus, *Factor 9* gene insertion represents a novel potential therapeutic strategy for adult and paediatric pts with haemophilia B.

This study aims to estimate the annualised rate of bleeding events requiring treatment of breakthrough bleeding with FIX replacement therapy in haemophilia B pts receiving SoC prophylaxis.

Methods: This is a prospective, global, non-interventional study with a duration of 6–24 months for each patient. Up to ~120 male pts, aged 16–65 years with moderately severe to severe haemophilia B, will be enrolled. Pts will have a history of low FIX functional activity/FIX:C (≤2% or <0.02 IU/mL); stable FIX prophylaxis regimen for >2 months;

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and intention to use FIX replacement therapy throughout the study. Exclusion criteria include: history of FIX inhibitor or a positive test for FIX inhibitors during screening; pre-existing antibodies to AAV8; significant liver disease, or other disease/condition that could worsen during the study.

The primary endpoint is annualised rate of bleeds treated with FIX replacement therapy. Secondary endpoints include annualised utilisation of FIX, FIX activity levels and FIX replacement therapy associated clinical events and morbidities (including thromboembolic events). Quality of life (QoL) will be assessed using the Haemophilia QoL questionnaire, Haemophilia Activity List and EuroQol 5-Dimension 3-Level.

Results:

Discussion/Conclusion:

Disclosure of Interest: M. O'Brien Shareholder of: Regeneron, Employee of: Regeneron, S. Pipe Grant/Research support from: BioMarin Pharmaceutical Inc, Freeline, Genentech/Roche, Sanofi, uniQure, Consultant for: Apcintex, ASC Therapeutic, Bayer, BioMarin Pharmaceutical Inc, CSL Behring, HEMA Biologics, Freeline, Novo Nordisk, Pfizer, Roche/Genentech, Sanofi, Spark Therapeutics, Takeda, uniQure, G. Pierce Consultant for: BioMarin, Regeneron SAB for Be Bio, Decibel, Frontera, Metagenomi, Employee of: Boards of World Federation of Hemophilia and Voyager Therapeutics., L. Sabin Shareholder of: Regeneron, Employee of: Regeneron, D. Chalothorn Shareholder of: Regeneron, Employee of: Regeneron, K.-C. Chan Shareholder of: Regeneron, Employee of: Regeneron, K. Tuckwell Shareholder of: Regeneron, Employee of: Regeneron, K. Deshmukh Shareholder of: Regeneron, Employee of: Regeneron, R. Reinhardt Shareholder of: Intellia, Employee of: Intellia, A. Haagensen Shareholder of: Intellia, Alnylam, Beam, Vertex, Novo Nordisk, Employee of: Intellia, L. Walsh Shareholder of: Intellia, Employee of: Intellia, D. Gutstein Shareholder of: Regeneron, Employee of: Regeneron.

PO089 | Skeletal complications in patients with haemophilia

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Introduction: Arthropathy is a common complication in patients with haemophilia. We examined the prevalence of this skeletal complication in patients with haemophilia who were registered in a Comprehensive Hemophilia Center in Shiraz, Southern Iran.

Methods: In this cross-sectional study, 448 patients were visited by an orthopaedic specialist and screened for skeletal complications. The type of haemophilia, disease severity, treatment type, inhibitors' presence and skeletal complications were assessed.

Results: Ninety patients with haemophilia A with a mean age (SD) of 31.6 (14.4) years and 10 patients with haemophilia B with a mean age of 30.5 (20.6) years were evaluated. The most common joints involved were knee and ankle joints. In univariate analysis, patients with severe diseases were more likely to have synovitis, target joint and bone disease than patients with non-severe diseases. Besides, a history of treated or active hepatitis and annual bleeding rate had significant relationships with the target joint. In multivariable logistic regression analysis, disease severity (OR 14.43, 95% CI, 1.6-129.6) and higher age at diagnosis (OR 1.06, 95% CI, 1.00-1.13) increased the chance of osteoporosis. History of hepatitis (OR 3.67, 95% CI 1.28-10.48) was an independent risk factor of the target joint.

Discussion/Conclusion: Skeletal complications are frequently observed in haemophilia. Regular visits by orthopaedic specialists with emphasis on the control of bleeding and prevention of hepatitis are the key points to decreasing this debilitating complication.

Disclosure of Interest: None declared.

PO090 | Emicizumab as a primary and immediate standalone therapy for acquired haemophilia A: Shaping a novel therapeutic approach for a complex hematological condition

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Introduction: The validated treatment of acquired haemophilia A (AHA) involves rapid immunosuppression and treatment or prevention of bleeding complications with fast-acting and short half-life bypassing agents (rFVIIa and APCC). A bispecific antibody (emicizumab) mimicking and bypassing the action of FVIII has led to a reevaluation of AHA management.

Methods: We recently treated 14 consecutive patients with AHA, prioritising haemostatic control through the fastest possible administration of emicizumab.

Results: Over the last 3 years, 9 male and 5 female patients (median age 74 years) were referred for AHA, 6 with benign presentation and 8 with severe/life-threatening bleeding complications (deep muscular/internal bleeds/severe anaemia) either spontaneous (7) or provoked (7). Emicizumab was initiated on admission in 11/14. Four patients with a severe bleeding complication or candidates for invasive procedures required adjuvant haemostatic therapy [rFVIIa (3), FVIII (2)]. 13/14 patients received immunosuppression [steroids (9), rituximab (9), cyclophosphamide (2), mycophenolate mofetil (1)] within 1-month from emicizumab initiation (10) or after a delay of up to 4 months (3) required to control comorbid and/or infectious conditions contra-indicating IS. IS was not started in a single patient for logistic reasons. Inhibitor eradication was achieved in seven patients. Six patients are currently on prolonged uninterrupted emicizumab. No haemorrhagic or thrombotic complication occurred during emicizumab maintenance. There was no case of serious infectious complication or death.

Discussion/Conclusion: Prompt treatment of AHA with emicizumab reduces haemorrhagic complications, the need for bypassing agents,

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enables tailored IS based on patient's comorbidities but requires access to extended emicizumab prophylaxis for patients who have not yet achieved effective inhibitor eradication.

Disclosure of Interest: None declared.

PO091 | Outcomes of emicizumab–KXWH use in persons with haemophilia A at moi teaching and referral hospital

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Introduction: Haemophilia A is a rare inherited X-linked recessive bleeding disorder, characterised by a deficiency in factor VIII. Standard care for haemophilia A globally involves intravenous replacement therapy, with prophylaxis being the recommended approach to prevent bleeding and improve the quality of life. Unfortunately, prophylaxis is largely inaccessible in Kenya. The World Federation of Haemophilia (WFH) commenced the donation of emicizumab-kxwh, a bispecific humanised monoclonal antibody medication for haemophilia A, in March 2021, launching Kenya's first sustainable prophylaxis program. The objective of this study was to evaluate the outcomes of emicizumab-kxwh use in persons with haemophilia A (PWH-A) at MTRH.

Methods: A retrospective chart review study was conducted on a cohort of patients who received emicizumab-kxwh treatment starting March 2021 at the MTRH haematology clinic. Data was collected 12 months after emicizumab-kxwh use and compared with data 12 months before. The inclusion criteria encompassed patients with inhibitors, life-threatening bleeds, and high annualised bleeding rate (ABR). The study focused on reviewing the following parameters; ABR of these patients over the 12 months before and after use of emicizumab-kxwh, use of walking aid, missed school or work due to illness, hospitalisation, Eastern Cooperative Oncology Group (ECOG) performance index, coagulation factor concentrate (CFCs) infusion and specialised clinic referrals preceding the initiation of emicizumab-kxwh.

Results: Results of the study demonstrated a significant reduction in bleeding episodes and severity following the commencement of emicizumab-kxwh. A remarkable decrease in bleeding events from a mean score of 10.4 to 0.6, total bleeds reduced from 906 to 55, use of walking aid reduced from 34.5% to 20.7%, missed school or work due to illness reduced from 31% to 17.2%, the number of hospitalisation decreased from 31% to 13.8%, ECOG performance index improved from 72.4% to 86.2%, average monthly consumption of coagulation factor concentrates (CFCs) decreased from 1650 to 1125 IU and specialised clinic referrals significantly reduced compared to before initiation of emicizumab-kxwh treatment.

Discussion/Conclusion: The study findings strongly support the effectiveness of emicizumab-kxwh in improving the quality of life and well-being of PWH-A by offering preventative treatment and minimising bleeding episodes.

Disclosure of Interest: None declared.

PO092 | Future of haemophilia patient registries: A pioneering initiative in the UAE

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Introduction: Data-driven healthcare solutions and registries are integral in advancing patient care and optimising healthcare services. International and national haemophilia registries are well-established. However, global surveys cannot ensure data homogeneity across all these databases, which requires every country to establish its registry. Tawam Hospital is a pivotal institution, serving as a tertiary centre for all haematology cases. The commitment extends beyond haematology, supporting various healthcare services, including general paediatrics, paediatric surgery and other subspecialties. With unwavering dedication and a commitment to enhancing haemophilia patients' lives, we introduced the United Arab Emirates Haemophilia Patient Registry.

Methods: A structured process was built to collect, manage and analyse data for all haemophilia patients through accessing Tawam Hospital EMR and patients attending to haemophilia clinic. Currently, our efforts have successfully gathered data for all haemophilia patients under the age of 20 years.

Results: Fifty-one haemophilia patients were recruited. Male patients represent 100%. The age distribution revealed that 22% were under the age of 5, 31% were in the 5–10 years age group, 31% were between 11 and 15 years, and 16% were between 16 and 20 years old. 80% were diagnosed with haemophilia A, while 20% were haemophilia B.

For treatment, 72.5% were managed with long-acting factor replacement, while 7.8% received short-acting factor replacement therapy. 15.7% were treated with non-factor therapies, and 3.9% were under an on-demand therapy regimen. Notably, 29.4% had a history of inhibitor administration. Only 3.9% were currently undergoing inhibitor treatment. The majority, with 55% of cases experienced no joint bleeding, while 37% of patients had bleeding in one joint. A smaller subset of 6% reported bleeding in two joints. Only 2% of cases with an inhibitor history reported bleeding in five joints. Only 7.8% of the patients experienced intracranial haemorrhage.

Discussion/Conclusion: Establishing a National Haemophilia Registry in the UAE is a pivotal step in enhancing the quality of care for individuals living with haemophilia. We aspire to create a robust and comprehensive platform for tracking and managing haemophilia patients' vital

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information. Integrating the registry with critical services such as insurance and pharmacy procurement further demonstrates its potential to streamline and elevate patient care.

Disclosure of Interest: None declared.

PO093 | Circumcision in patients with haemophilia: Using the classic reduced dose regimen of factor concentrates

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Introduction: In Algeria, circumcision is a social obligation. In patients with haemophilia, it constitutes a medical and surgical challenge which requires multidisciplinary coordination.

Methods: A retrospective single-centre descriptive study of patients with haemophilia who have undergone circumcision was conducted between (January 2000 and June 2023) at the University Hospital Centre of Tlemcen. The replacement therapy adopted for circumcision is the classic reduced dose (CRD) regimen. By passing agents were used in haemophilia patients with inhibitors. Preventive treatment for erection was instituted in patients over twenty years of age.

Results: Of the 107 patients with haemophilia followed at the University Hospital Centre of Tlemcen, 80% had haemophilia A, (86 patients). Seventy-four patients had a severe form, including 10 patients with inhibitors. In our cohort, patients with mild haemophilia (six patients) were circumcised before the age of 2. The 27 patients with moderate haemophilia were circumcised before the age of 5. 2/3 of patients with severe haemophilia were circumcised before the age of 5, including 3% at birth. Only 5% benefited from circumcision after the age of 20 [25–36 years old]. The median weight is 24 kg (weight range, 5–85 kg), accordingly, the amount of factor concentrates used is <3000 U/day in more than 90% of patients. The length of hospital stay was 3 days (1–17 days). Post-circumcision haemorrhagic complications were observed in 18% of patients of a post-traumatic nature and two cases of wound dehiscence. Extra injection of factor concentrate was administrated to prevent bleeding on day 7.

Discussion/Conclusion: In our study, the optimal age for circumcision is between 2 and 5 years; in accordance with the legal texts. The incidence of haemorragic complications is 18%, dominated by post-traumatic causes probably linked to the young age of the patients. Circumcised patients benefited from the CRD regimen, thereby reducing the length of hospital stay, without increasing complications.

Disclosure of Interest: None declared.

PO094 | Safety, efficacy and laboratory profile of reduced emicizumab dosing in haemophilia A patients

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Introduction: Haemophilia A (HA) results from a deficiency or dysfunction of clotting factor VIII (FVIII). Emicizumab (Emi), a novel FVIII mimetic drug, is a chimeric bispecific humanised antibody, which has been approved for severe and recently moderate (FVIII levels 1%–2%) HA patients with and without inhibitors. The standard Emi dose is 3 mg/kg/week for loading, for 4 weeks, followed by a continuous 1.5 mg/kg weekly dose. Reduced dosing by 30%–50% has showed comparable efficacy but larger studies and randomised settings are missing. We aimed at assessing the safety of reduced Emi dosing by following the annualised bleeding rate (ABR) and laboratory parameters for a longer period in an observational study.

Methods: At Helsinki University Hospital, we did a retrospective observational chart review of 26 HA patients on Emi. We collected dosing, treatment period, clinical outcome and all relevant haemostatic laboratory data. Descriptive data analysis was performed.

Results: Total of 26 patients were included. Nine out of 11 inhibitor positive patients and 12 out of 15 inhibitor negative patients were receiving the reduced Emi dosing. The rest of the patients (5) received a full dose as they participated in a Phase VI Emi study. Altogether 21 patients have been receiving a reduced dose for a mean period of 26 months [range 7–60 months]. All these 21 patients had lower intrinsic FXI and FXII levels by 18% and 7%, respectively, compared with patients on full dose, according to APTT-based assays. In ROTEM-INTEM analysis typically the clotting time shortened and MCF increased. APTT tended to be short (23–24 s, ref. 28 s) and stable during entire follow-up, excluding noncompliance and antidrug antibodies. After exclusion of the non-bleeders, patients on reduced Emi dose had 96% reduction in ABR versus a 100% reduction in patients on full dose. One exceptional patient had an ABR of 3 instead of several ABRs before Emi.

Discussion/Conclusion: Since Emi is an expensive drug, it is not readily available in low-middle income countries. Our cohort with reduction of Emi dosing showed a stable bleeding phenotype over a follow up period of about 2 years, with an exception of one case. Our management strategy thus led to 30%–50% cost savings and this experience encourages shared decision making with the patient on tailored dosing of Emi.

Disclosure of Interest: None declared.

PO096 | Observational, pro study to evaluate quality of life for haemophilia patients on hemlibra, single study

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Introduction: Emicizumab (Hemlibra) is a novel molecule, and its widespread prophylactic use is expected to have dramatic impact on reducing the bleeding frequency in the community of haemophilia A (HA) patients, thereby significantly improving their clinical condition and, ultimately, their quality of life.

Objectives: To assess the quality of life for haemophilia patients before and after emicizumab usage in a real-world setting.

Methods: A prospective PRO study was planned on paediatric patients older than 4 years with HA with or without inhibitors who received

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emicziumab for at least 6 months at a Centre for Blood Disorders for Paediatric Patients, Alaziziyah Children Hospital. Validated Arabic versions of HAL, Heam-A-Qol, and EQ-5D-5L questionnaires were prepared. All patients were asked to mention their responses before and after Hemlibra usage.

Results: Among 23 children with HA who started emicizumab, the survey was done on 10 haemophilia patients who met the eligible criteria. All patients were males. As for mobility, the percentage of patients with no mobility problems before Hemlibra use was 10%, which was increased to 80%. Of them, 70% had no problems with self-care before use, which was increased to 100% after use. Patients with no problems in usual leisure and activities were 30%, which increased to 70% after use. One-fifth of patients (20%) had no pain and discomfort before use; this percentage increased to 90% after use. The overall positive emotional feelings were 29% before use compared to 78% after use. Positive feelings about self-perception also increased from 22% before use to 66% after use. Feelings about school/work improved from 13% before use to 83% after use, and feelings about treatment improved from 27% to 72% after use. The positive feelings of patients about the future before Hemlibra use was 45%, which increased to 92% after use.

Discussion/Conclusion: Patients' feelings, overall self-perception, daily activities and feelings towards haemophilia treatment improved after 6 months of using Hemlibra. Patients started living everyday lives and became less worried about their case worsening and could control their bleeding after Hemlibra usage. However, there is room for enhancement in the rest of the work/school activities.

Keywords: haemophilia, Hemlibra, life, observational, quality, single.

Disclosure of Interest: None declared.

PO097 | Using of emicizumab in paediatric haemophilia A patients: KSA single centre experience

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Introduction: Emicizumab, a bispecific monoclonal antibody, plays a crucial role in bleeding episode prophylaxis in patients with HA with or without factor F (FVIII) inhibitors, regardless of severity. This study aimed to report results from assessing the tolerability, efficacy and safety of emicizumab prophylaxis in paediatric patients with HA.

Methods: This study was a retrospective study conducted between April 2019 and July 2023 at a Center for Blood Disorders for Pediatric Patients, Jeddah, Saudi Arabia.

Eligible study participants were individuals <16 years of age, weighing over 3 kg, presenting severe or moderate congenital haemophilia A with or without FVIII inhibitors and those who were treated with emicizumab for at least 3 months at our centre.

Results: Twenty-three children with HA who started emicizumab was initially included. A total of six patients were excluded as they did not meet the eligible criteria. Ten patients with severe haemophilia (59%) and seven patients with moderate haemophilia (41%). Patient were followed for median duration range of 217 weeks (15–232 weeks). All study patients were males and median (range) age at enrollment was 8.0 (11 months to 16 years). All of them were treated previously with factor either on demand or as prophylaxis. Two patients presented with inhibitors, while the rest were the non-inhibitor type. The initial baseline ABRs median (range) was 48 (range 5–120). Compared to the ABRs after initiation of emicizumab which showed median of 2 (range 0–18), the ABR mean value decreased from 38.5 at baseline to 4.6 after emicizumab treatment.

All bleeding events were traumatic and resolved with less than 48 h. Eleven (64.7%) patients experienced zero bleeding.

We observed unusual side effect of asymptomatic persistent neutropenia was observed in 10 (58.8%) out of 17 patients. The absolute neutrophil count (ANC) ranged from 0.6 to 1.45 cells/μL in these cases. There was no other adverse event was observed.

Discussion/Conclusion: Our study demonstrates the effectiveness of emicizumab prophylaxis for treating patients with moderate to severe HA. The participants reported high adherence to the treatment, improved satisfaction rates and the concept of subcutaneous injections was well accepted. Although neutropenia is considered an unusual side effect of this treatment, the treatment progressed smoothly and favourable safety profile was observed.

Disclosure of Interest: None declared.

PO098 | A case of thrombosis in a patient with severe haemophilia B

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Introduction: It is believed that haemophilia patients are naturally protected from thrombosis due to a deficiency of one of the coagulation factors, so thrombotic complications are rare in them. The incidence of venous thrombosis is 1 in 27,000 in patients with haemophilia, while among men in the general population it is 1 in 1000–2000. The main condition under thrombotic complications are thrombophilia, redundant use of clotting factors concentrates (especially shunt medicine), surgical operations, etc.

Methods: Description of a clinical case.

Results: Patient M, 61 years old, has been observed for a severe form of haemophilia B since early childhood. The disease is manifested by hemarthrosis of almost all large joints. As a result of frequent haemorrages, deforming arthropathy of both knee and elbow joints developed. Repeated punctures of knee joints were performed with ultra-articular injection of hydrocortisone, also noted soft tissue hematomas, recurrent haematuria and gastrointestinal bleedings. Receives haemostatic therapy with factor IX (FIX) concentrates on demand.

In July 2022, he was hospitalised with ischemic intestinal disease, acute segmental venous thrombosis of mesenteric vessels, necrosis

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of section of the small intestine. Sectoral resection of small intestine was performed, which was complicated by the development of acute myocardial infarction.

Discussion/Conclusion: In most cases, haemophilia patients do not require pharmacological prophilaxis of thrombotic complications. Thus, the occurrence of thrombotic complications in haemophilia patients is possible.

Disclosure of Interest: None declared.

PO099 | Real-world effectiveness and safety of a recombinant factor VIII Fc in patients with haemophilia A by disease severity: Pooled analysis (A-SURE/PREVENT)

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Introduction: Haemophilia A is a rare bleeding disorder caused by deficiency of factor VIII (FVIII). Standard of care is FVIII replacement therapy. Efmoroctocog alfa (Elocta®), a recombinant FVIII Fc fusion protein (herein rFVIIIFc), has an extended half-life allowing higher FVIII levels and a longer dosing interval than standard half-life products. This study assessed whether treatment outcomes in patients (pts) with haemophilia A in a real-world setting are influenced by disease severity.

Methods: All pts receiving prophylactic rFVIIIFc from the A-SURE (Europe, NCT02976753) and PREVENT (Germany, NCT03055611) phase 4 prospective observational studies were pooled. Only variables recorded in the same way in both studies were included. Pts were grouped by non-severe (NSV; mild and moderate) or severe (SV) haemophilia A. Annualised bleeding (ABR) and joint bleeding (AjBR) rates, injection frequency and factor consumption (prospective period) were assessed, as were serious adverse events (AEs) and AEs leading to treatment discontinuation (retrospective + prospective periods).

Results: A total of 336 pts was included, 29 in the NSV group (A-SURE $n = 11$; PREVENT $n = 18$) and 307 in the SV group (A-SURE $n = 175$; PREVENT $n = 132$), with a mean (SD) age of 23.9 (19.3) and 26.7 (18.5) years, respectively. Median (IQR) prospective follow-up was: NSV group, 20.1 (19.2; 22.0) months; SV group, 21.0 (19.1; 24.0) months. Median (IQR) ABR/AjBR was 0 (0; 0.9)/0 (0; 0.2) in the NSV group ($n = 28$) and 0.6 (0; 1.7)/0 (0; 0.9) in the SV group ($n = 305$). Median (IQR) weekly injection frequency was 2.0 (1.8; 2.3) in the NSV group ($n = 28$) and 2.2 (2.0; 2.6) in the SV group ($n = 305$). Mean (SD) factor consumption was 76.1 (25.7) in the NSV group ($n = 28$) and 86.9 (38.0) IU/kg/week in the SV group ($n = 303$). Serious AEs were reported in 2.0 (6.9%) NSV and 48 (15.6%) SV pts; one of these was considered treatment related (FVIII inhibition in a pt with SV haemophilia). AEs led to treatment discontinuation in two (0.7%) SV pts.

Discussion/Conclusion: These pooled real-world data from two large observational studies support the use of rFVIIIFc prophylaxis in pts with haemophilia A across all severities, including pts with mild and moderate severity on regular prophylaxis. In both severity groups, mean ABRs and AjBRs of less than one were observed despite low injection frequencies and low factor consumptions.

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PO100 | The value-based healthcare approach to haemophilia: Development of outcome measures for the evaluation of care of people with haemophilia

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Introduction: Considering the advances in haemophilia management and treatment observed in the last decades, a new set of value-based outcome indicators is needed to assess the quality of care and the impact of these medical innovations. The Value-Based Healthcare in Haemophilia project aimed to define a set of clinical outcome indicators (COIs) and patient-reported outcome indicators (PROIs) to assess quality of care in haemophilia in high-income countries with a value-based approach to inform and guide the decision-making process.

Methods: A value-based healthcare approach based on the available literature, current guidelines, and the involvement of a multidisciplinary group of experts was applied to generate a set of indicators to assess the quality of care of haemophilia. The approach followed five phases including the identification of a set of indicators by a multidisciplinary working group composed of 17 Italian experts in the field of haemophilia, the validation by an international panel of experts, and the approval by the members of Italian Association of Haemophilia Centres (AICE) following a consensus process through a modified Delphi method. Finally, this project defined a composite outcome indicator for clinical outcomes and one for patient-reported outcomes combining single indicators previously validated and approved.

Results: A final list of three COIs and five PROIs was created and validated. The identified COIs focus on two domains: musculoskeletal health and function, and safety. The identified PROIs cover five domains: bleeding frequency, pain, mobility and physical activities, Health-Related Quality of Life, and satisfaction. Finally, two composite outcomes, one based on musculoskeletal health and function COIs, and one based on pain, mobility and physical activities PROIs, were proposed as synthetic outcome indicators of quality of care.

Discussion/Conclusion: The presented standard set of health outcome indicators provides the basis for harmonised longitudinal and cross-sectional monitoring and comparison. The implementation of this value-based approach would enable a more robust assessment of quality of care in haemophilia, within a framework of continuous treatment improvements with potential added value for patients. Moreover, proposed COIS and PROIS should be reviewed and updated routinely.

Disclosure of Interest: None declared.

PO101 | Follow-up of haemophiles and management of complications

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Introduction: Haemophilia is an X-linked recessive hereditary disease affecting males only. It involves a reduction or total deficiency of factor VIII (haemophilia A) or IX (haemophilia B), which leads to a coagulation disorder and consequently to repeated haemorrhages. Articular and muscular haemorrhages progressively lead to disabling arthropathies and muscular atrophies, followed by social, economic, professional and even psychological repercussions.

Methods: This was an exhaustive descriptive study of all haemophiliacs followed at the Farhat Hached Haematology Department in Sousse, Tunisia.

Results: A total of 130 haemophiliacs were followed in our department. Ninety-eight cases of haemophilia A (75%), 32 cases of haemophilia B (25%), mean age 24 years (range 1–58 years), including 28% children (36 cases) and 72% adults (94 cases), 20% (27 cases) were classified as severe haemophilia, 36% (47 cases) as moderate haemophilia and 43% (56 cases) as minor haemophilia. Ninety-seven cases were treated on demand, 13 with prophylaxis and 20 with intermittent prophylaxis. 70% (92 cases) were treated with plasma factors and 29% (38 cases) with recombinant factors. Four haemophiliacs presented a serious bleeding episode requiring hospitalisation, including two psoas hematomas, one digestive haemorrhage controlled by substitution therapy and tranexamic acid, and one case of lightning haemoptysis uncontrolled by substitution and resulting in the patient's death. Nineteen cases were complicated by arthropathy, including four children who all underwent synovectomy, and three young adults who had one total hip replacement (THR) and two total knee replacements (TKR). Six cases were complicated by inhibitors, four of them children, three of whom were able to neutralise the antibody by immune tolerance induction (ITI), and one case still had the inhibitor due to the impossibility of carrying out ITI for administrative reasons, and was on recombinant factor VII in case of haemorrhage. Three cases are complicated by hepatitis C, which is being followed up in gastroenterology, and one by HIV, which is being followed up in infectious diseases.

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Discussion/Conclusion: Improving the quality of life of haemophiliacs requires regular monitoring, prevention of complications, multidisciplinary management and early intervention.

Disclosure of Interest: None declared.

PO102 | Particularities of care for haemophilic children

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Introduction: Haemophilia is a recessively inherited genetic disorder linked to the X chromosome. Genes may be absent or damaged, leading to absence or deficiency of the coagulation factor. The disease causes difficulties in daily life, especially for children who do not yet fully understand or accept their difference.

Methods: This was an exhaustive descriptive study of all children with haemophilia followed at the Farhat Hached haematology department in Sousse, Tunisia.

Results: A total of 130 haemophiliacs of all ages are monitored in the department, 27% (36) of them were children. The average age is 7 years (extremes 1 and 17 years). 75% of cases (27) are hereditary, while 25% (9) are sporadic. A number of problems arise when caring for children with haemophilia, starting with the announcement of the diagnosis to the parents, particularly those with no history of haemophilia.

In our series, 75% (27) were haemophiliacs A and 25% (9) haemophiliacs B. In the majority of cases, that is 60% (17), the diagnosis was made in infancy, and in 71% (20) during a life-threatening haemorrhagic syndrome or during the evolution of the haemophilia. Hence, the need to increase public awareness of the need for systematic screening of boys with a family history of haemophilia, with a view to early diagnosis and prevention of haemorrhagic accidents. Currently, haemophilia continues to be diagnosed in 11% (4) of cases of post-circumcision haemorrhagic syndrome, including one case who developed an anti-FVIII inhibitor following massive exposure to FVIII to control the bleeding. All children were on plasma FVIII replacement therapy, in 67% (24) of cases, and recombinant FVIII in 33% (12). Prophylactic treatment was provided in only 36% (13) of cases, mainly due to the continuous unavailability of factor for children with poor social status, the difficulty of venous access for some, and parental refusal for others.

Discussion/Conclusion: To minimise the difficulties involved in caring for children with haemophilia, it's important to take a whole-family approach. Make sure the factor is available. Envisage a therapeutic project. Establish a therapeutic educational program. Organise awareness-raising campaigns in schools and recommend suitable sports activities to strengthen muscles and flexibility and avoid accidents.

Disclosure of Interest: None declared.

PO103 | Immune tolerance induction with a recombinant factor VIII Fc in haemophilia A: Final data from a chart review study

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Introduction: This non-interventional, retrospective/prospective immune tolerance induction (ITI) chart review study (NCT03951103) describes real-world use of efmoroctocog alfa [Elocta®; a recombinant factor VIII (FVIII) Fc; herein rFVIIIFc] for first-time/rescue ITI in patients with haemophilia A (PwHA).

Methods: We present final data on rFVIIIFc usage and short-/long-term ITI outcomes (as judged by the investigator) for PwHA (all ages) enrolled from Europe and the Middle East from November 2018 to September 2022.

Results: In 16 sites in 7 countries, 41 of 42 enrolled PwHA were analysed; 40/1 had severe/moderate disease, respectively. Initial rFVIIIFc ITI dose ranged from 100 to 1400 IU/kg/week and initial dosing frequency from twice weekly to twice daily.

First-time ITI with rFVIIIFc was used in 24 PwHA; median (range) age at initiation was 2.6 (0–32) years, with inhibitor titres of 32.5 (6–772) and 29.9 (1–734) BU/mL for historical peak and at ITI start, respectively. Fourteen (58.3%) out of 24 patients achieved a negative inhibitor titre in a median (range) of 115 (22–569) days. In 16 patients with ITI outcome, 13 (81.3%) had ITI success with a median (range) ITI duration of 346 (49–717) days, while three had failure. Eight had ongoing ITI at study end.

Rescue ITI with rFVIIIFc was used in 17 PwHA; median (range) age at initiation was 11 (2–53) years with median of 2 (1–8) ITI attempts prior to rFVIIIFc ITI in a total duration of 61.9 (9–289) months. Twelve (70.6%) out of 17 achieved a negative inhibitor titre in a median (range) of 88 (0–769) days. In 16 with ITI outcome, 6 (37.5%) had ITI success, two partial success, seven failure and one early withdrawal. One had ongoing ITI at study end. Median (range) ITI duration in PwHA with ITI success and partial success was 542 (33–1888) and 869.5 (500–1239) days, respectively. Relapse occurred in one patient after 656 days.

Most first-time ITI PwHA (70.8%, $n = 17$) used < 300 IU/kg/week, and only 5 (20.8%) used > 500 IU/kg/week; most (87.5%, $n = 21$) received < daily ITI. In rescue ITI PwHA, 6 (35.3%) used < 300 IU/kg/week and 9 (52.9%) used > 500 IU/kg/week; most received daily ITI (64.7%, $n = 11$).

rFVIIIFc ITI was well tolerated, with no unexpected adverse events (AEs) or treatment discontinuation due to AEs.

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Discussion/Conclusion: This chart review study showed benefits of rFVIIIFc ITI, with a high ITI success rate in first-time ITI and several successful rescue ITI cases.

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PO104 | Insights from people with haemophilia in france: Patient perspectives on the concizumab pen-device

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Introduction: Concizumab is an anti-tissue factor pathway inhibitor (TFPI) monoclonal antibody in development as a once-daily subcutaneous prophylaxis administered via a pen-device for haemophilia A/B with and without inhibitors (HAwI/HBwI and HA/HB, respectively). Although emicizumab is approved as a subcutaneous prophylaxis for HAwI/HA in France, intravenous treatments are also commonly used to control bleeds, often negatively impacting quality of life. Presented here are patient perspectives on the concizumab pen-device from ethnographic interviews in France from patients with HAwI or HB.

Methods: Concizumab-naïve patients were screened to include diverse characteristics (age, gender, treatment types such as emicizumab for patients with HAwI/HA or various factor replacement therapies). Explorative qualitative research was conducted with semi-structured interviews at patients' homes from February to March 2023. As part of the interview, patients were presented with the concizumab pen-device, as well as information on the mode-of-action, efficacy and safety. With patient consent, all interviews were recorded and transcribed using Grain (Grain Intelligence Inc). Transcripts were coded (i.e., to label and organise data for identifying patterns of themes; a method commonly used for qualitative data analysis) using NVIVO 14 (QSR International) to identify core themes from the patient responses.

Results: A total of 13 patients were interviewed (HAwI: $n = 6$; HB: $n = 7$; male, $n = 12$; female, $n = 1$), of whom 11 were adults and two were children (8–10 years; interviewed with their mothers). Of six patients with HAwI, two were willing to try concizumab (33%), whereas four patients on emicizumab were hesitant or not willing to try (33% each). Of seven patients with HB, 5 (71%) were willing and 2 (29%) were hesitant to try concizumab. Patients highlighted that the mode of administration of concizumab can positively contribute to their autonomy due to the ease of storage of the transportable pen-device. Furthermore, the patients responded positively to the simplicity of administration of concizumab compared with intravenous treatments and commented that the pen-device is more socially accepted.

Discussion/Conclusion: The 13 patients in France who participated in the study perceived the concizumab pen-device positively, as it potentially allows social acceptance and seamless incorporation of the treatment routine in their daily life.

Disclosure of Interest: None declared.

PO105 | Surgeries in haemophilia patients: An experience of tertiary care hospital in northern india

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Introduction: Surgical procedures in people with haemophilia are challenging. Surgical success depends on factor replacement, pre- and postoperative interventions, laboratory monitoring, care and rehabilitation of patient. There is limited experience of surgery in PwH in Northern India.

Methods: A retrospective analysis was done in haemophilia patients registered under Adult Hematology Clinic (AHC), PGIMER from 2019 to 2023. Demographic data, diagnosis, replacement therapy and duration of hospital stay were recorded. Follow-up was done in routine AHC visits.

Results: Out of the $n = 72$ patients registered in AHC, 19 patients underwent 21 surgeries for both elective ($n = 5$) and emergency ($n = 16$) indications. Eighteen out of $n = 21$ procedures were major surgeries. Of $n = 21$ surgeries included in the study, the median age of patients is 24 years (5–66). Two out of 19 patients had haemophilia B while others ($n = 17$) were haemophilia A. Four patients had high

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titre of factor VIII inhibitors (>5 Bethesda Units) and one out of these four received both Factor Eight Bypassing Agent (FEIBA) and recombinant factor 7 while two were managed with FEIBA alone and one was managed with recombinant factor 7 alone. Five surgeries had a post operative complication of re-bleed at surgical site, three of which were done in patients with high titre inhibitors. Median stay in hospital was 21 days. Median duration of stay was 23 days in patients with inhibitors and was 12 days in patients without inhibitors. Mean units of packed red blood cells (PRBC) transfused perioperatively were 2.3. Mean units of PRBC transfused perioperatively in a patient with inhibitors were around 4.2 against 1.8 in patients without inhibitors. Sixteen out of $n = 21$ surgeries had optimal haemostatic control peri-operatively. Three out of four surgeries where bypassing agent was used experienced post-operative re-bleed.

Discussion/Conclusion: The results of our retrospective analysis, demonstrate that, in experienced comprehensive care various surgical procedures can successfully be performed in PwH. Bleeding complications are increased in patients with inhibitors. Patients with inhibitors required more amount of blood products perioperatively and had a longer stay in hospital.

Disclosure of Interest: None declared.

PO107 | Enhancing haemophilia assessment and monitoring with novel digital biomarkers

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Introduction: Assessing joint condition and musculoskeletal function in people with haemophilia is crucial but faces challenges in routine care. Daily monitoring of key parameters such as the elbow range of motion (RoM) is not feasible, hindering a comprehensive understanding of joint health. Tests for lower limb function like the Six-Minute Walk Test are restricted to medical settings limiting exhaustive monitoring. Advanced tools allowing real-time data collection in ecological conditions might accurately assess joint health and enable early, personalised interventions. In this setting, we have explored the feasibility of novel digital biomarkers (dBMKs).

Methods: Literature review and 22 interviews with experts were conducted to specify candidate dBMKs for objective tracking and monitoring of elbow and lower limb joints function. Healthy volunteers were recruited for a Proof-of-Concept study, assessing the feasibility and limits of a measurement process exclusively based on smartphone's sensors. Varying conditions of an automated keypoint detection model were tested for elbow RoM using a smartphone's camera ($n = 10$) and a gait characterisation model for step count and length via an inertial measurement unit using a digital walking test ($n = 1$). For each condition the mean absolute error (MAE) was computed.

Results: For the elbow RoM, participants were either photographed in full (FB) or half body (HB). True positive rates, that is, key points detected on a picture, were 0.92 for the FB and 0.70 for the HB. Among those pictures, key points' precision was evaluated using the Percentage of Correct Keypoints: PCK@arm0.2, at 0.97 (FB) and 0.90 (HB) and the MAE of the RoM was 4.45° and 5.45°, respectively. For the walking test, participant's smartphone was held in a front pocket (FP), hand (HD), a backpack (BP) or a crossbody bag (CB). Over 200 steps, CB showed the highest performance with an MAE of five steps (97.5% precision) while other MAE were $\geq$6 steps but $\leq$16. Similar results were found for the step length with CB condition showing highest precision (MAE = 2 cm), followed by BP (3 cm). FP resulted in poorer performance (8 cm).

Discussion/Conclusion: These first results suggest that dBMKs can accurately capture upper and lower limb function. Clinical validation is needed to confirm their potential in enhancing haemophilia assessment enabling detection and monitoring of disease progression in real-world conditions, for adapted care.

Disclosure of Interest: S. Lobet Consultant for: Dr. Lobet has received payments from Ad Scientiam as an Expert Consultant (Member of a Scientific Board of Haemophilia Experts), A. Lebreton Consultant for: Pr Lebreton has received payments from Ad Scientiam as an Expert Consultant (Member of a Scientific Board of Haemophilia Experts), A. Plaud Employee of: Dr. Plaud has received payments from Ad Scientiam as an employee, A. Feyt Employee of: Mr. Feyt has received payments from Ad Scientiam as an employee, C. Gorin Employee of: Dr. Gorin has received payments from Ad Scientiam as an employee, L. Carment Employee of: Dr. Carment has received payments from Ad Scientiam as an employee, E. Guilpain Employee of: Dr. Guilpain has received payments from Ad Scientiam has an employee, A. Petitmangin Employee of: Alexandre Petitmangin has received payments from Ad Scientiam as an employee, S. Zinaï Employee of: Dr. Zinaï has received payments from Ad Scientiam as an employee, L. Frenzel Consultant for: Dr. Frenzel has received payments from Ad Scientiam as an Expert Consultant (Member of a Scientific Board of Haemophilia Experts), C. Négrier Consultant for: Prof. Négrier has received payments from Ad Scientiam as an Expert Consultant (Member of a Scientific Board of Haemophilia Experts).

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PO108 | Activlim-hemo, a new valid, reliable, unidimensional and linear measure of activity limitations in haemophilia

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Introduction: With new therapies for people with haemophilia (PwH) the bleeding rate is no longer a sensitive assessment. Treatment efficacy now focusses on joint health and activity limitations. Modern psychometry offers functional assessments with linear measures and appropriate ordinal scores interpretation. This study aims validate ACTIVLIM-Hemo, an instrument developed with the Rasch probabilistic model, to measure activity limitations in PwH.

Methods: An experimental questionnaire including 92 activities of daily life, assessed as 'impossible', 'difficult' or 'easy', was submitted to 114 PwH; 63 PwH were reassessed after 12 days. The Rasch Rating Scale model was used to identify a final set of 22 activities and delineating a 0%–100% unidimensional scale unbiased by demographic and clinical status. An additional sample of 16 PwH (total $n = 130$ PwH) was assessed for joint health (HJHS 2.1), walking performance (TUG and 2MWT), pain (BPI), physical activity (IPAQ) and with the HAL, the most widely used activity limitations assessment in PwH. ACTIVLIM-Hemo and the HAL were compared for reliability and minimum detectable change (MDC95). Construct validity was assessed for both instruments by correlation and multiple linear regression including demographic and clinical indices.

Results: ACTIVLIM-Hemo showed a lower ceiling effect (1%) than the HAL (9%) and an excellent test–retest reproducibility (ICC = 0.978). A high reliability was observed for ACTIVLIM-Hemo (PSI = 0.92) and for the HAL ($a = 0.98$). The MDC95 for ACTIVLIM-Hemo was 11.6% and of 18/100 score points for the HAL. Joint health, pain severity and walking performance were identified as significant predictors of activity limitations, explaining 75% of the variance in ACTIVLIM-Hemo and 60% in HAL.

Discussion/Conclusion: ACTIVLIM-Hemo is an easy-to-administer, valid and reliable alternative to HAL in assessing activity limitations in PwH. Its invariant scale can be used across conditions and time to compare the functional status of PwH over a wide measurement range. The ACTIVILIM-Hemo and the HAL showed significant correlations with demographic and clinical indices, but ACTIVLIM-Hemo exhibited a more homogeneous construct. ACTIVLIM-Hemo makes a promising patient-centric tool for assessing responsiveness to treatment in individual follow-up. Its clinical application using an on-line calculation tool can be illustrated in a case report.

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PO109 | The VINCEREMO pilot study: Physical activity and prophylaxis in haemophilia: How, when and why. final results

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Introduction: In haemophilia there are concerns regarding safe management of physical activity, considering functional limits related to arthropathy, risk of injury and associated bleeding complications. We design a prospective pilot study (VincerEMO) to evaluate how an adequate and controlled training program can slow down the onset or evolution of arthropathy, improve musculoskeletal health and quality of life.

Methods: A prospective observational study was performed from April 2022 to April 2023 with the collaboration of the Sisport sport society. The study involved severe haemophilic A and B patients, age >18 years old, on regular prophylaxis with replacement products, with a joint function ≥50%. The participants, without changing the usual prophylaxis schedule, maintaining a trough level of at least 20% FVIII/FIX before training, were involved in controlled physical activity followed by trainers, specifically educated in haemophilia issues. They had been evaluated at baseline, 6 months and at the end of the study (12 months). Each evaluation included annual bleeding ratio (ABR), basal articular ultrasound according to the HEAD US score, Haemophilia Joint Health Status (HJHS), joint range, muscle strength, postural assessment and specific physical tests.

Results: Mean age of the nine patients included was 38 years old (range 22–52 years). Participants completed a year of controlled physical activity without an increase in ABR (no bleeding event experienced during study period was related to training sessions), maintaining baseline joint status (as assessable by HEAD US score, HJHS and NRS). A trend not statistically significant towards improvement in mean HEAD US score (15.55 vs. 13.11) and HJHS (14.4 vs. 11) from baseline to 12 months was observed. Some of the physical test performed showed a significant improvement at 6 months and 12 months from baseline (5 Rep Sit to Stand, Sit and Reach and 6 min Walking Test), meaning an improvement in legs strength, dorsal flexibility and aerobic resistance.

Discussion/Conclusion: This is the first pilot study evaluating the safety and impact of a controlled physical activity on joint health in people with severe haemophilia. Our results show how controlled physical activity performed with a trough level of 20% FVIII/FIX is safe, as no

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participant experienced bleedings or a worsening in joint status and it is effective in improve in articular functionality.

Disclosure of Interest: None declared.

PO110 | Frequency of ultrasound (US) for joint evaluation in haemophilia: The montreal study

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Introduction: For haemophilic patients, optimisation of joint outcomes is an unmet need.

Traditionally, most symptoms are ascribed to joint bleeding and addressed mainly by optimising prophylaxis. Recently, a new emphasis is on early detection, diagnosis and treatment of arthropathy beyond improving clotting factor replacement strategies. There is rising awareness that detection and management of asymptomatic findings are essential. For this purpose, the HEAD US (haemophilia early arthropathy detection) protocol was designed, in order to detect blood effusion and joint damage before clinical manifestations.

The aim of this study is to determine use of US in severe haemophilia A and B patients and to find any correlation between US score and haemophilia joint health score (HJHS), annualised bleeding rate (ABR) and numeric pain rating scale (NRS) evaluated at baseline, after 6 months (T1) and 12 months (T2) of regular prophylaxis.

Methods: Nineteen adult severe haemophilia A/B patients were included.

At each visit articular function was evaluated with HJHS and US. Joint pain (NRS), through level and prophylaxis efficacy with ABR was performed.

Results: Median age was 38 years old (IQR1 −3.33–50.5), five patients had haemophilia B and 14 had haemophilia A. Eight patients treated with extended half-life FVIII (median trough level 2%, IQR 1.7–4.1), five patients with standard life FVIII (median trough level 1.72%, IQR 1.5–29) and all haemophilia B patients with extended half-life FIX (median trough level 10%, IQR 7.5–12.5). Median target joints value was 2, without differences between haemophilia A and B.

Median HEAD US, NRS, HJHS and ABR at baseline and at T2 (12 months) are shown in table 1. As reported, no significant differences were found within the three timepoints.

A univariate correlation analysis was performed and no significant correlations within variables was found; although, a correlation coefficient >0.5 was observed between trough level and age (−0.572), trough level and ABR (−0.517), trough level and HEAD US (−0.515).

Discussion/Conclusion: US is an evolving technology increasingly used to assess joint health in haemophilia, but the exact frequency of performing is not defined yet. Despite reduced sample size, our analysis suggests that a 12 months evaluation after baseline may be too early to detect significant intraarticular changes. As a consequence, no correlation between HEAD US score and the others parameters evaluated in this work was found.

Disclosure of Interest: None declared.

PO111 | Achieving zero annual bleed rate with tailored prophylaxis in low and middle income countries: A retrospective observational study

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Introduction: Prophylaxis in haemophilia is a vital approach to improve the quality of life (QoL) in people with haemophilia, but access remains limited, in low-income countries like India. This study examines the effectiveness of personalised low-dose clotting factor concentrates (CFC) prophylaxis and emicizumab in children, aiming to achieve zero annual bleed rates (ABR), thereby enhancing QoL.

Methods: This retrospective observational study done at the Hemophilia Treatment Centre (HTC) Aluva, India, from May 2022, to June 2023. Study included 31 children under 18 with haemophilia A/B, who started prophylaxis with CFC since 2015 and completed one year. Data on ABR, Annual Joint Bleed Rate (AJBR), Haemophilia Joint Health Status (HJHS) score and Functional Independence Score Haemophilia (FISH) extracted from the HTC. Standard half-life CFCs used, with a starting frequency of twice a week for factor VIII and once a week for factor IX. Outcome is correlated with changes in ABR and AJBR during the last year of prophylaxis and in the 1 year prior to prophylaxis. Analysis was done using SPSS version24. Results were presented as mean for quantitative and as percentages for qualitative variables. Comparison achieved with standard paired *t*-test, and p value $< .05$ considered as significant.

Results: Among 31 children, 10 (32%) received emicizumab, 21 (68%) received CFC. Haemophilia A constituted 24(77%) of cases. The mean age and weight are 10.96 ± 5.3 and 35.81 ± 18.56, respectively. The CFC exhibited significant improvements, reducing the ABR from 14.90 to 2.90(p .000) and the AJBR from 4.95 to 1.43(p .004). The number of treated bleeds decreased from 14.90 to 2.95(p .000). Additionally, HJHS improved from 3.30 to 0.95, and FISH increased from 29.90 to 32.00(p .020). Children on emicizumab had exceptional results, all reporting zero ABR (p .027), and AJBR (p .131) even with lower doses (1.02 mg/kg/week), only four achieved zero ABR with CFC.

Discussion/Conclusion: This highlights the effectiveness of personalised low-dose CFC prophylaxis and emicizumab in reducing bleeding rates and emicizumab had remarkable outcomes, achieving zero bleeds even with lower doses. However, CFC struggled to achieve zero bleed rates. This underscores the need for alternative strategies and increased accessibility to emicizumab and newer drugs to achieve zero bleed rates in resource-limited settings.

Disclosure of Interest: None declared.

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PO112 | Clinical and economic impact of switching a standard to an extended factor VIII in a group of haemophila A patients—the experience of a portuguese centre

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Introduction: Extended-half-life (EHL) factor VIII (rFVIII) products changed the concept of prophylaxis in haemophilia A (HA), bringing a promise of better outcomes, with a reduced infusion burden and, potentially, economic benefits. In our centre, patients (pts) on prophylaxis with a standard half-life (SHL) recombinant FVIII (octocog alfa—Kovaltry®) were switched to the EHL FVIII (damactocog alfa pegol—Jivi®).

Our aim is to assess the impact of switching between these two products, considering both clinical and economic aspects.

Methods: We retrospectively evaluated dosage of FVIII, prophylaxis regimen, number of infusions (infs), though levels, total ABR and joint bleeding rate (jABR) and factor consumption (FC), in pts switched from SHL to EHL FVIII. Cost of treatment and its budget impact for our Centre was calculated considering prices in Portugal.

Results: Since February 2021, 13 severe and 1 moderate HA pts; all adults, median age 34.9 years (ages 14–68) started prophylaxis with EHL-rFVIII; personalised according to individual PK profile and clinical needs. In 9/14 (64%) of pts, interval between infs increased, and higher through levels were clearly achieved. Previously, 12/14 pts had through levels <3%, while with EHL 8/14 had FVIII levels 3%–5% and 3/14 >5%. Accordingly, a decrease of 25% in annual infs was observed (137 vs. 103 infs/pt/year), with a median of 1.98 infs/pt/week. ABR decreased from 1.29 to 0.5, and jABR from 1.07 to 0.29. There was also a decrease in spontaneous hemarthrosis (1.00 vs. 0.07) and just a patient reported a spontaneous hemarthrosis due to a missed dosage. On the contrary, the number of patients with zero bleedings increased (35.7% with SHL vs. 71.4 with EHL). Although none had target joints, six patients who had problem joints, reported less pain and improved mobility. There was no inhibitor development in the two pts with past inhibitors. Regarding FC, significant 26% decrease of UI FVIII/year and, by consequence, savings around 500,000 euros in annual treatment costs, were observed.

Discussion/Conclusion: In this group of patients, replacing SHL with EHL FVIII reduced the therapeutic burden and improved bleeding outcomes, in a group that was already very adherent and had a low bleeding rate. From an economic perspective, always important to healthcare authorities, this switching clearly allowed significant cost savings.

Disclosure of Interest: None declared.

PO113 | Efanesoctocog alfa prophylaxis outcomes in european patients from the XTEND-1 trial

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Introduction: Once-weekly, fixed-dose efanesoctocog alfa prophylaxis allowed patients in the XTEND-1 trial to achieve mean factor VIII (FVIII) activity levels in the non-haemophilic range (>40%) for most of the week as well as superior bleed protection when compared with their prestudy FVIII prophylaxis. We present here a subanalysis of prophylaxis outcomes for European patients from XTEND-1.

Methods: XTEND-1 (NCT04161495) was an open label, multinational, phase 3 trial evaluating the safety, efficacy and pharmacokinetics of efanesoctocog alfa (50 IU/kg) in previously treated patients ≥12 years of age with severe (<1%) haemophilia A. Data are presented on European patients enrolled in Arm A from Belgium, Bulgaria, France, Germany, Greece, Hungary, Italy, Netherlands, Spain and the UK. In Arm A, patients received prophylaxis with efanesoctocog alfa once weekly for 52 weeks. A subset of patients was included in an observational prestudy. The primary endpoint in Arm A was annualised bleed rate (ABR). Secondary endpoints included bleed treatment, quality of life (Haem-A-QoL physical health domain score, PROMIS Pain Intensity 3a T-score), joint health (Haemophilia Joint Health Score—Total score), consumption, safety and an intra-participant comparison of prestudy versus onstudy ABRs.

Results: In total, 67 European patients (mean age 34 years) received prophylaxis in Arm A. Model-based mean ABR (95% CI) was 0.56 (0.35; 0.89). Median ABR (IQR) was 0.0 (0.0; 1.0). Forty-seven patients (70%) had zero bleeds. Most bleeding episodes (32/34 [94%]) were resolved with one injection of efanesoctocog alfa. Improvements in physical health (mean change [SD]: −3.04 [14.94], $n = 51$), pain (−1.99 [8.14], $n = 60$) and joint health (−1.1 [5.8], $n = 53$) were observed between baseline and Week 52. For 42 patients with ≥6 months follow-up in both the prestudy and XTEND-1, the switch from prestudy FVIII prophylaxis to efanesoctocog alfa prophylaxis decreased the model-based mean ABR from 3.11 to 0.52 (rate ratio [95% CI]: 0.17 [0.10; 0.30], $p < .0001$). Mean (SD) weekly onstudy consumption was 50.7 (2.5) IU/kg ($n = 42$). Efanesoctocog alfa was well tolerated, and inhibitor development was not detected.

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Discussion/Conclusion: In European patients, efanesoctocog alfa improved bleed protection versus prestudy prophylaxis. Results were consistent with the XTEND-1 primary analysis. Funded by Sobi and Sanofi.

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PO114 | Monitoring of albutrepenonacog alpha during invasive procedures in patients with haemophilia B

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Introduction: Albutrepenonacog alpha (rFIX-FP) is a recombinant extended half-life factor IX fused to albumin, available since 2021 in France. We report herein our experience in monitoring plasma factor IX clotting activity (FIX:C) during invasive procedures in patients with haemophilia B (HB), using rFIX-FP.

Methods: Patients with HB followed at the Lyon Comprehensive Haemophilia Care Centre who underwent a surgery with rFIX-FP were included in this retrospective analysis. Considering the large variability of FIX:C according to the reagent use, FIX:C was evaluated with a standard calibration curve and with a specific calibration curve using SynthASil® reagent and HemosIL® FIX-deficient plasma (Werfen, Le Pré-Saint-Gervais, France). The results were compared using Mann Whitney U test and $p < .05$ was considered statistically significant.

Results: Eleven major (according to Solimeno) surgeries were performed in 10 patients (three severe, one moderate and six mild HB). The median and interquartile range (IQR) preoperative loading rFIX-FP dose infused was 89 (74.0–108.0) IU/kg. The median FIX:C measured 30 min after the rFIX-FP infusion was 122.5 (103.8–140.3) IU/dL with standard calibration curve and 171 (145.5–221) IU/dL with specific calibration curve ($p = .017$). Thus, there is a significantly difference in FIX recovery according to the calibration curve used for FIX:C measurement ($p = .0075$). The median FIX:C measured 2 h after the end of major surgeries reported herein was 107 (85.75–129.8) IU/dL and 167 (120.5–189.5) UI/dL, with standard and specific calibration curve respectively ($p = .044$). On the first post-operative day, FIX:C was 98 (72–116) IU/dL with standard calibration curve and 136 (107.5–187) IU/dL with specific calibration curve ($p = .0135$). The blood loss was considered similar to that observed in patient with no bleeding disorder. There is 21%–40% of differences between the two calibration curves for the measurement of FIX:C, which could be over the underestimation of 30% reported in the literature with SynthASil® reagent.

Discussion/Conclusion: Using a specific calibration curve to monitor rFIX-FP during surgeries in HB patients is effective, safe, well tolerated and associated with a reduction of rFIX-FP consumption and with cost saving.

Disclosure of Interest: None declared.

PO115 | Acquired haemophilia A and A difficult to treat inhibitor: Case report

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Introduction: Acquired haemophilia A (AHA) is a rare bleeding disorder mediated by an autoimmune mechanism in which autoantibodies against factor VIII (FVIII) lead to a potentially severe bleeding diathesis.

Methods: We report a case of a 67-year-old woman, who was referred to our institution for endovascular embolisation treatment of an acute left iliopsoas bleeding. The patient was previously admitted to another hospital, due to pain and oedema of the left lower limb, skin pallor and fatigue. On admission, multiple hematomas were noticed. Her medical history was significant for diabetes mellitus, hypothyroidism and mitral valvulopathy (submitted to valvuloplasty in 2022). Prior to admission, she was medicated with warfarin, metformin, dulaglutide, levothyroxine and bisoprolol. Laboratory evaluation showed microcytic anaemia with normal leucocytes and platelets count; prolonged activated partial thromboplastin time: 67.1″ (normal: 24.2–36.4″), normal prothrombin time and mixing tests did not correct with normal plasma. Based on the clinical picture, AHA was suspected. FVIII level

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was 0.05% and FVIII inhibitor was detected (5 Bethesda units) confirming the diagnosis. The patient started treatment with prednisolone (1 mg/kg/day) and activated prothrombin complex concentrate (FEIBA) with several suspensions and reintroductions all over 4 months, due to multiple spontaneous deep hematomas.

Results: After an extensive investigation for malignancy, infectious and immunological markers, no cause was found. Due to lack of response, and even increasing inhibitor's titres, the patient started cyclophosphamide (100 mg/day), which was suspended 18 days later due to hepatic toxicity, and switched to rituximab (375 mg/m^2/week). After discharge, she was maintained on rituximab until inhibitor's eradication, achieved 7 months after admission.

Discussion/Conclusion: Management and treatment of AHA requires a two-fold approach including haemostatic therapy and inhibitor eradication. Rapid diagnosis and initiation of treatment are crucial to prevent fatal outcomes. Most patients usually respond to immunosuppressive (IS) therapy with corticoids alone, although a combination with another therapy may be required. Management of AHA includes investigation and treatment of the underlying disease, although sometimes, underlying cause cannot be found. During discontinuation of IS, patient's vigilance is required to allow early identification of relapse or FVIII level rebound.

Disclosure of Interest: None declared.

PO116 | Health-related quality of life in adults with haemophilia B after gene therapy with fidanacogene elaparvovec in the BENEGENE-2 trial

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Introduction: The burden of the management and clinical sequelae of haemophilia B (HB) negatively impacts health-related quality of life (HRQoL), including physical and mental health and functional status. BENEGENE-2 (NCT03861273) is an ongoing phase 3 trial of fidanacogene elaparvovec, an adeno-associated virus gene therapy vector delivering a high-activity factor IX variant, FIX-R338L/FIX-Padua. Patient-reported outcome assessments (PROs) are presented for HRQoL, health status and functional status.

Methods: Adult males with HB (FIX:C ≤2 IU/dL) who completed ≥6 months of FIX prophylaxis received a single infusion of fidanacogene elaparvovec 5e11 vg/kg. Participants completed PROs pre- and post-infusion (Week 52), including the Haemophilia Quality of Life Questionnaire for Adults (Haem-A-QoL), Haemophilia Activities List (HAL), EQ-5D-5L, Patient Global Impression of Change–Haemophilia (PGIC-H) and Haemophilia Life Impacts Questionnaire (HLIQ).

Results: At baseline (pre-infusion), median age was 29 (range 18–62) years (N = 45). Data from pre-infusion to Week 52 were available for up to 42 participants, depending on the assessment/domain. The mean Haem-A-QoL total score decreased from pre-infusion by 11.2 (SD 9.1; $p < .001$), more than the clinically meaningful 7-point score reduction, suggesting an improvement in HRQoL. Scores for individual domains (including physical health, feeling, view of self, work/school, sport/leisure, treatment, future) also improved over time. For the HAL assessment, mean (SD) Complex Lower Extremity Activities and Basic Lower Extremity Activities component scores improved by 7.6 (19.6; $p = .024$) and 11.1 (18.2; $p < .001$), respectively, indicating improved functional status. Improvements in EQ-5D-5L index scores and EQ-VAS (treatment difference [95% CI]: 0.05 (0.02–0.08]; $p = .003$ and 5.8 (0.6–11.0]; $p = .030$, respectively) were observed from pre- to post-infusion, indicating improved health status. Most participants (78%) reported at least moderate improvements in their overall impression of life with haemophilia using the PGIC-H and improvements in most HLIQ domains related to life impacts associated with living with and treating haemophilia.

Discussion/Conclusion: Fidanacogene elaparvovec improved HRQoL, health and functional status in adults with HB, indicating a reduction in the burden associated with haemophilia.

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PO117 | Acquired haemophilia A: Searching for probable causes

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Introduction: Acquired haemophilia A (AHA) is a potentially life-threatening bleeding disorder caused by autoantibodies against coagulation factor VIII. Risk factors include older age, cancer, autoimmune disorders, medications and the postpartum

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state. Acquired clotting factor inhibitors are autoantibodies that either inhibit the activity or increase the clearance of a clotting factor.

Methods: We describe a clinical case of a 93-years-old woman presented to the emergencies on 14 October 2023 with bruises on upper limbs that appeared spontaneously 2 days before, with no trauma associated.

Results: The coagulation study performed was abnormal (aPTT 74.1″, PT 13.8″), and a prolonged aPTT study was carried out. The mixing study was suggestive of inhibitor presence and a deficiency of FVIII was detected (3%). We did the screen and titration of FVIII inhibitors: 12 Bethesda Units. The haemoglobin value was normal. She started immunosuppressive therapy with 1 mg/kg/day of prednisolone. Factor eight inhibitor bypassing activity (FEIBA) 3000 UI 12/12 h was started the following day because of a drop in haemoglobin value. Due to improvement in haemoglobin and absence of visible haemorrhage, FEIBA was suspended 4 days later. A body scan was performed which showed a right renal lesion highly suggestive of neoplasia. Due to the patient's age and comorbidities, it was decided against to perform any invasive maneuvers.

Discussion/Conclusion: This case demonstrates the importance of clinical suspicion and timely study of altered coagulation values. This patient was promptly diagnosed and started immunosuppression on time to decrease the inhibitor and reduce the risk of further bleeding. It also shows the relevance of studying underlined conditions; this patient has a lesion highly suggestive of neoplasia and it's probably the cause of AHA.

Disclosure of Interest: None declared.

PO118 | Reducing potential data gap after gene therapy using myGTR—a patient engagement tool from world federation of haemophilia gene therapy registry

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Introduction: The World Federation of Haemophilia (WFH) Gene Therapy Registry (GTR) is designed to collect long-term clinical data on people with haemophilia (PWH) who received Gene Therapy (GT). myGTR is a tool designed to collect patient-reported outcome (PRO) data and to complement clinical data from the WFH GTR. PRO data are critical, supporting the shared decision-making process and leading to more meaningful care and treatment. Efforts to keep both haemophilia treatment centre (HTC) and PWH engaged in the GTR are being implemented.

Methods: The GTR is developing a formal retention plan aimed at both HTCs and participating registries to ensure continued PWH recruitment and ongoing patient data collection. myGTR is the foundational element of the WFH GTR patient engagement plan. The GTR patient engagement plan includes different elements such as myGTR, access to dashboards for data visualisation of their data [benchmarked against other patients (future)], patient directed summaries of publicly available, high-level data and videos/podcasts with experts participating in the GTR. All elements will be available through a dedicated website which will include the latest registry and GT news.

Results: During the development of myGTR, focus groups indicated mobile app fatigue and a need for a simple tool. myGTR was developed as a web-based application. It is not available at any app store. Patients will receive alerts via their preferred contact method, either by email or text message to access myGTR and provide PRO data through an interactive digital assistant. The PRO data are bleeds, treatments and health related quality of life (HR-QOL) including the Patient Reported Outcomes Burdens and Experiences (PROBE), coreHEM Mental Health Outlook (coreHEM MHO) and EQ-5D-5L. At regular interval (four times during the first year, two times per year thereafter), the patients will be prompted to answer two simple questions about their health status since GT infusion. Then, they will be asked to complete two out of three HR-QOL questionnaires on a rotational basis.

Discussion/Conclusion: myGTR will enable PWH who receive GT to continue providing data on their health status and HR-QOL in a simple manner. This can improve patient retention, address potential data gap when patients reduce their visits to their HTC after GT, and continue to increase our understanding of benefits and risks of GT.

Disclosure of Interest: None declared.

PO119 | Case report: Treatment for wound complications of extremity compartment syndrome in an acquired haemophilia A patient

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Introduction: Acquired haemophilia A (AHA) is a rare haematology disease resulting from autoantibodies against endogenous factor VIII with a high risk for mortality. Due to its rarity and unknown, patients with AHA are usually hospitalised without a previous diagnosis. In patients with wound complications, AHA is an underlying factor impeding haemostatic treatment and possibly causing death if not detected. Currently, the literature on this disease diagnosis and treatment is limited.

Methods: To review a clinical case.

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Results: A 58-year-old man with a personal history of diabetes but no previous bleeding was hospitalised due to wound complications presented with sudden onset left forearm pain and swelling was found to have compartment syndrome requiring emergent fasciotomy and was complicated by persistent operative site bleeding. The initial blood investigations were as follows: haemoglobin (Hb) 5.3 g/dL, platelet (PLT) 272 x 109/L, white blood cell (WBC) 12.7 x 109/L, International normalised ratio (INR) 1.01, prothrombin time (PT) 10.2 s, activated partial thromboplastin time (aPTT) 68.6 s, fibrinogen 1.85 g/L. An aPTT mixing study was immediately performed, which showed isolated raised PTT was not corrected. The Rosner index was more than 15%, and factor VIII levels was 5.1%. Bethesda assay revealed factor VIII inhibitor of 79.69 Bethesda Unit (BU). Therefore, a diagnosis of acquired haemophilia A with high inhibitors was made. The patient was administered activated prothrombin complex concentrate (aPCC) at a dose of 50 units/kg every 12 h to brief cessation of bleeding, immunosuppressive therapy with methylprednisolone 60 mg and cyclophosphamide 100 mg daily. On day 17, the wound bled again. Factor VIII level was still low, and Bethesda assay with 148.55 BU. The patient was given vincristine 2 mg for 1 day and FEIBA infusion to cessation of bleeding. After 42 days of treatment, the bleeding signs were controlled, and the inhibitor was eradicated with a factor VIII concentration of 42%. The patient required surgery to debride and suture the wound.

Discussion/Conclusion: This case report describes the management of a life-threatening severe haemorrhage in a patient with AHA. Early recognition and treatment are critical to reduce morbidity and mortality in AHA. Through this case, we hope to contribute to clarifying the understanding of the management of AHA patients.

Disclosure of Interest: None declared.

PO120 | Impacts on functional outcomes following total knee arthroplasty in haemophilia patients: A comparative study of pain catastrophising and adaptation to artificial joints

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Introduction: Haemophilic arthropathy is a chronic joint disease that results from repeated bleeding episodes into the joints. Total knee arthroplasty in patients with haemophilic arthropathy is associated with unique challenges, including the risk of bleeding complications during the perioperative period, and comparative studies with matched osteoarthritis cohorts are limited. The aim of this study is to compare pain catastrophising, kinesiophobia, adaptation to artificial joint and functional outcomes following total knee arthroplasty in patients with haemophilic arthropathy and osteoarthritis.

Methods: The study included two male cohorts of haemophilic arthropathy and osteoarthritis patients treated with total knee arthroplasty. Twenty-five knees of 16 patients were in the haemophilia group, and 35 knees of 27 patients were in the osteoarthritis group. The primary outcome scores included preoperative and postoperative Pain Catastrophising Scale, Brief Fear of Movement Scale for Osteoarthritis, Forgotten Joint Score, Visual Analogue Scale (VAS), Hospital for Special Surgery Score (HSS) and Knee Society Score (KSS) questionnaires. Additionally, haemophilia patients with major postoperative bleeding were compared to those without.

Results: The osteoarthritis group had higher range-of-motion (95.5) and VAS (9.4) scores than the haemophilic arthropathy group, preoperatively ($p < .001$). Postoperative pain was also higher in the osteoarthritis group ($p < .001$). The haemophilic arthropathy group had higher preoperative fear of movement and higher pain catastrophising postoperatively ($p < .001$). Functional outcomes were similar between groups. Patients with major postoperative bleeding had more pain and pain catastrophising at the final follow-up ($p = .02$).

Discussion/Conclusion: Total knee arthroplasty provides similar functional outcomes between patients with haemophilic arthropathy and osteoarthritis. Haemophilia might lead to fear of movement and worse range of motion following total knee arthroplasty. Major postoperative bleeding can also impact functional outcomes, pain and pain catastrophising both before and after total knee arthroplasty in patients with haemophilic arthropathy.

Disclosure of Interest: None declared.

PO121 | Real-life single centre experience on the effectiveness of emicizumab prophylaxis in patients with haemophilia A with and without inhibitors associated with improvement of health-related quality of life

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Introduction: The use of emicizumab, a humanised bispecific recombinant monoclonal antibody designed to bridge activated factor IX and coagulation factor X, has played a central role in improving their quality of life of haemophilia A patients, not only through once monthly subcutaneous administration, first of its kind, but especially by significantly reducing bleeding episodes and prompt access to the Emergency Department (ED) in order to prevent further joint damage.

Methods: A real-life retrospective monocentric study on emicizumab treatment was conducted in patients with severe haemophilia A with and without inhibitor. A total of 14 patients with severe haemophilia A was treated with emicizumab, including eight patients with inhibitor and six patients without inhibitor. The mean age prior to emicizumab treatment was 16.8 years in seven patients with inhibitor and 32.8 years in three without, with a median treatment duration at last follow-up of 25 and 29 months respectively based on inhibitory status.

Results: The mean annual bleeding rate (ABR) in subjects with inhibitor before and following emicizumab were 2.17 versus 0.17, while in those

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without inhibitors the proportion was 2.33 versus 0.33. A total of ten patients had five or more target joints, including knees, elbows and ankles. The mean haemarthrosis in patients with inhibitor was 0.57 and 0.28 before and following emicizumab prophylaxis, while in patients without inhibitors was 0.66 and 0. There were no hospitalisations in course of emicizumab, nor adverse events in study group while with replacement therapy mean number hospital accesses was 0.67 for both patients. The quality of life (QoL) questionnaire (EQ-5D-5L) was given to patients before treatment switch and after a median follow-up of 12 months. The scores obtained in eight patients showed significant improvement of QoL from 11 to 6.4 in course of emicizumab. Moreover, the mean results were 2.86 and 1.43 respectively for pre- and post-emicizumab pain.

Discussion/Conclusion: Our real-life experience confirms the effectiveness of emicizumab in preventing both spontaneous and provoked bleedings along with preservation of the known target joints. Additionally, the health-related QoL was measured confirming improvement by patients themselves and reducing pain symptoms.

Disclosure of Interest: None declared.

PO122 | Emicizumab in people with moderate or mild haemophilia an aged ≥40 years, with and without comorbidities

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Introduction: Few data exist on older people with haemophilia A (PwHA), particularly those with comorbidities. We present a post hoc analysis of people with non-severe HA aged ≥40 years from the HAVEN 6 trial (NCT04158648).

Methods: HAVEN 6 is a Phase 3 trial in people with moderate/mild HA without FVIII inhibitors, warranting prophylaxis (investigator-assessed; Negrier, Lancet Haematol 2023). Emicizumab was given at one of the three approved doses. An age cutoff of ≥40 years was selected for this exploratory analysis to obtain an older population with comorbidities, including cardiovascular (CV) risk factors (history of CV disease, hypertension, hyperlipidaemia, diabetes, body mass index ≥30 kg/m^2), human immunodeficiency virus (HIV) and current or historical hepatitis C virus (HCV).

Results: At data cut-off (30 October 2021), 72 participants had been treated in HAVEN 6; 16 were aged ≥40 years and included in this analysis. Median (range) age was 50.5 (41–71) years, and all were male. Ten (62.5%) participants had moderate HA and 6 (37.5%) had mild HA. Nine (56.3%) participants had ≥1 CV risk factor, with 5 (31.3%) having ≥2. Three (18.8%) individuals had HCV only, 1 (6.3%) had HIV only, and 2 (12.5%) had HCV/HIV co-infection. Median (range) duration of emicizumab exposure was 1.1 (0.6–1.7) years. Fifteen (93.8%) participants had ≥1 adverse event (AE) and 3 (18.8%) had a serious AE, all unrelated to emicizumab. There were no fatal AEs, AEs leading to treatment withdrawal/modification/interruption, or thrombotic microangiopathies. One individual (with no CV risk factors or HIV/HCV infection) had a thromboembolic event (thrombosed haemorrhoid), unrelated to emicizumab. Three participants experienced a total of six treatment-related AEs: three injection-site reactions and one case each of fatigue, head discomfort and accidental overdose. The mean (95% confidence interval) ABR for treated bleeds for the 16 participants aged ≥40 years was 1.03 (0.03, 5.62), similar to that for the overall population of HAVEN 6 (0.94 [0.02, 5.48]). Eleven (68.8%) participants had zero bleeds, compared with 66.7% of the total population.

Discussion/Conclusion: The small population of people with moderate/mild HA aged ≥40 years precludes drawing firm conclusions from this analysis; however, the safety and efficacy of emicizumab did not differ notably from those observed overall in HAVEN 6.

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PO123 | Treatment preferences in previously treated patients with haemophilia A: Phase 3 XTEND-1 study of efanesoctocog alfa

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Introduction: Haemophilia A is a rare bleeding disorder that leads to recurrent joint bleeds causing debilitating pain. In the XTEND-1 trial of efanesoctocog alfa (ALTUVIIIO®; formerly BIVV001), a high-sustained factor VIII (FVIII) therapy, all 29 patients (Arm A $n = 17$; Arm B $n = 12$) who completed exit interviews reported preferring efanesoctocog alfa over pre-study treatment. This analysis aimed to understand treatment preferences of all patients in XTEND-1.

Methods: XTEND-1 (NCT04161495) was a Phase 3, open-label, multicentre study of the efficacy, safety and pharmacokinetics of efanesoctocog alfa in previously treated adults and adolescents aged ≥12 years with severe haemophilia A. Patients receiving prior standard-of-care FVIII prophylaxis received once-weekly (qw) prophylactic efanesoctocog alfa for 52 weeks (Arm A); patients on prior on-demand FVIII treatment received efanesoctocog alfa on-demand for 26 weeks, then prophylactic efanesoctocog alfa qw for 26 weeks (Arm B). A 2-item questionnaire was completed by patients at Week 52/end-of-study. Questions included treatment preference (prefer previous treatment, prefer current treatment, have no preference), and, if current treatment was preferred, the top three reasons as prespecified in the electronic case report form.

Results: A total of 130/133 patients in Arm A ($n = 67$ Europe, $n = 15$ US, $n = 48$ rest of world) and 25/26 patients in Arm B ($n = 14$ Europe, $n = 11$ rest of world) completed the survey at Week 52. Most patients (Arm A: 117 [90.0%]; Arm B: 25 [100.0%]) preferred their current treatment with efanesoctocog alfa to previous treatment. In Europe, 62 (92.5%) patients in Arm A and 14 (100%) in Arm B preferred efanesoctocog alfa, and in the US and rest of world, 55 (87.3%) in Arm A and 11 (100%) in Arm B preferred efanesoctocog alfa. Of 142 participants in pooled Arms A and B who preferred efanesoctocog alfa, the most common reasons were 'less frequent treatment' ($n = 115$, 81.0%), 'bleeds and bleed-related complications reduction' ($n = 98$, 69.0%) and 'feel better protected' ($n = 91$; 64.1%). Three participants (2.6%) in Arm A reported preferring previous treatment over efanesoctocog alfa, but reasons for this were not collected. The remaining ten participants (7.7%) had no preference.

Discussion/Conclusion: Nearly all patients in XTEND-1 preferred treatment with efanesoctocog alfa over their previous FVIII (prophylaxis or on-demand) treatment regimens.

Disclosure of Interest: E. Spasov: None declared, D. Quon Consultant for: Consulting/Advisory Boards: Bayer, Biomarin, CSL Behring, Genentech/Roche, Novo Nordisk, Pfizer, Sanofi, Takeda, Speaker Bureau of: Bayer, Biomarin, CSL Behring, Genentech/Roche, Novo Nordisk, Pfizer, Sanofi, Takeda, K. Fukutake Consultant for: has received consulting fees from Chugai Pharmaceutical Co., Ltd. and CellGenTech, Inc. and honoraria from Bayer Yakuhin, Ltd., Chugai Pharmaceutical Co., Ltd., CSL Behring K.K., Japan Blood Products Organization, KM Biologics, Novo Nordisk Pharma Ltd., Pfizer Japan Inc., Fujimoto Pharmaceutical Corporation and Takeda Pharmaceutical Company Limited, Sanofi K.K. and Sekisui Medical Co., Ltd., J. Msihid Shareholder of: May hold stock/stock options in Sanofi, Employee of: Sanofi, A. Willemze Shareholder of: May hold stock/stock options in Sanofi, Employee of: Sanofi, J. Dumont Shareholder of: May hold stock/stock options in Sanofi, Employee of: Sanofi, H. Palmborg Shareholder of: May hold stock/stock options in Sobi, Employee of: Sobi, N. Kragh Shareholder of: May hold stock/stock options in Sobi, Employee of: Sobi, A. Wilson Shareholder of: May hold stock/stock options in Sanofi, Employee of: Sanofi.

PO124 | Seven-year follow-up of valoctocogene roxaparvovec gene therapy for haemophilia A

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Introduction: Valoctocogene roxaparvovec is an adeno-associated virus vector serotype 5 (AAV5)-mediated gene therapy approved for severe haemophilia A (HA). We report outcomes 7 years after dosing.

Methods: In this open-label, phase 1/2 dose-escalation trial (NCT02576795), males ≥18 years with severe HA (factor VIII [FVIII] ≤1 IU/dL) who were previously receiving exogenous FVIII and had no history of FVIII inhibitors or anti-AAV5 antibodies received an infusion of 6×10^{13} ($n = 7$) or 4×10^{13} ($n = 6$) vg/kg valoctocogene roxaparvovec. Key exclusion criteria included significant liver

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dysfunction, fibrosis or liver cirrhosis. Efficacy was assessed by FVIII activity (chromogenic assay) and change from baseline (BL) in annualised rates of treated bleeds (ABRs) and exogenous FVIII infusions; safety was assessed with reported adverse events (AEs) or serious AEs (SAEs).

Results: All participants in the 6 x 10^{13} cohort and 5 in the 4 x 10^{13} cohort remain on study; a 4 x 10^{13} cohort participant was lost to follow-up after week 287. At years 7 and 6, median (interquartile range) FVIII activity was 10.3 (4.8–14.2) and 7.2 (4.5–8.9) IU/dL in the 6 x 10^{13} (n = 5) and 4 x 10^{13} (n = 4) cohorts, respectively. In the last year, estimated FVIII activity changed by −0.001 and −0.07 IU/dL/week for the 6 x 10^{13} and 4 x 10^{13} cohorts, respectively. During all follow-up, mean ABRs decreased from BL by 96% and 88% for the 6 x 10^{13} and 4 x 10^{13} cohorts at years 7 and 6, respectively. A 6 x 10^{13} cohort participant resumed prophylaxis after a non-treatment-related grade 4 SAE of spontaneous internal carotid artery bleeding in year 7. His FVIII activity was last assessed 26 weeks prior to the SAE at 5.1 IU/dL. Another 6 x 10^{13} cohort participant resumed prophylaxis in year 7 following ankle joint bleeds; 6 weeks prior to that, his FVIII activity was 1.9 IU/Dl. A 4 x 10^{13} cohort participant transiently returned to prophylaxis during year 5. Mean (median) annualised FVIII infusion rate for the 6 x 10^{13} and 4 x 10^{13} cohorts were 6.4 (1.6) and 9.3 (5.1) infusions/year over all follow-up, a decline of 95% and 93% from BL, respectively. In the last year, one participant in each cohort had a treatment-related AE: grade 1 hepatomegaly (6 x 10^{13}) and grade 1 splenomegaly (4 x 10^{13}); no treatment-related SAEs or alanine aminotransferase elevations occurred.

Discussion/Conclusion: While 2 participants resumed prophylaxis in year 7, the majority maintained haemostasis. Safety remains in line with previous reports.

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PO125 | French real-word data on rIX-Fp prophylaxis use in adolescent-adult patients with haemophilia B

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Introduction: The OrPHEe study is an observational study (NCT05086575) describing real-world efficacy and safety data on the use of rIX-FP for prophylaxis in patients with haemophilia B (HB) in France.

Methods: This interim analysis included data collected from October 2021 to August 2023. Dosing frequency, weekly consumption, and bleeds before and after switching to rIX-FP were recorded. Annualised (spontaneous) bleeding rates (A[s]BR) were calculated only in patients on prophylaxis with a follow-up period of ≥6 months. Results are presented as median (IQR). Wilcoxon matched-pairs signed rank tests were used to compare data pre- and post-switch to rIX-FP.

Results: Among 134 patients included, 97 were treated with rIX-FP prophylaxis. This analysis focused on 72 patients ≥12 years old, including 59 (82%) with severe HB. 52/72 (72%) were previously treated with prophylaxis (40 with rFIXFc, 12 with a standard half-life FIX).

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Nine patients had at least one target joint at inclusion, including eight previously with rFIXFc prophylaxis.

After switching to rIX-FP, the interval between infusions was 14 (7–14) days, with 21 days or more in four patients. Weekly consumption was 42 (35–53) IU/kg (n = 64, data missing [DM] for eight patients). ABR and AsBR were 0 (0–1.5) and 0 (0–0), respectively (n = 51 for both) after a follow-up period of 14 (10–18) months. 58/61 (95%) of investigators evaluated the efficacy of rIX-FP prophylaxis as 'Excellent' or 'Good', and 59/59 evaluated the safety as 'Good' (DM for 11 and 13 patients, respectively). Three adverse events were reported, including one related to rIX-FP (haemarthroses).

Patients previously treated with rFIXFc reduced their infusion frequency from every 7 (7–14) days with rFIXFc to 14 (7–14) days with rIX-FP (n = 38; DM for two patients; $p < .001$). Weekly consumption was also reduced with rIX-FP (from 61 [46–79] to 42 [35–51] IU/kg; $p < .0001$). Despite these reductions, patients treated with rIX-FP prophylaxis maintained good protection against bleeds (ABR: from 1 [0–2] to 1 [0–1]; AsBR: from 0 [0–1] to 0 [0–0]; n = 26 for both) during a follow-up period of 13 (8–18) months.

Discussion/Conclusion: To date, the OrPHEe study is the world's largest cohort of patients with HB treated with rIX-FP and demonstrates that patients ≥12 years old who switched to rIX-FP were able to reduce their injection frequency and FIX consumption whilst maintaining a good level of protection against bleeds.

Disclosure of Interest: None declared.

PO126 | Emicizumab prophylaxis in people with haemophilia A: Summary of 10 years of safety data on thromboembolic events and thrombotic microangiopathy

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Introduction: The HAVEN 1 Phase 3 trial outlined thromboembolic events (TEs) and thrombotic microangiopathies (TMAs) as risks in people with congenital haemophilia A (PwcHA) when taking emicizumab with activated prothrombin complex concentrate (aPCC) at >100 U/kg/24 h for ≥24 h. We report updated safety data on emicizumab prophylaxis in PwcHA, as >24,000 people have now received post-market emicizumab (as of 18 July 2023; Roche, data on file).

Methods: Emicizumab safety reports from clinical trials, registries, expanded access, compassionate use and spontaneous post-marketing reports were analysed for TEs/TMAs. TEs were identified using the Medical Dictionary for Regulatory Activities (MedDRA v26.0) search strategy: 'Embolic and Thrombotic Events' Standardised Medical Query (Broad). TMAs were defined as MedDRA preferred terms: haemolytic uremic syndrome, microangiopathic haemolytic anaemia, microangiopathy, TMA, thrombotic thrombocytopenic purpura and renal-limited TMA.

Results: As of 1 August 2023, 155 total events meeting TE/TMA criteria were found from 24 countries in the Roche Global Safety Database; 97 were in PwcHA, including 34 since the previous analysis (15 May 2022). Two TEs and the five TMAs were related to aPCC (>100 U/kg/24 h for ≥24 h); 90 TEs were not. The new TMA since last analysis was due to aPCC exceeding dose guidelines to treat diverticular haemorrhage in a patient with severe HA who then recovered. In 81 non-aPCC- and non-device-related TEs, median (range) age at event was 48 (0.8–84) years; 55 (67.9%) TEs were related to ≥1 cardiovascular/thrombosis-related risk factor and 26 (32.1%) reported insufficient information. Eleven (13.6%) of the 81 TEs and two (40%) of the five TMAs led to emicizumab discontinuation. Five (6.2%) TEs were fatal: two myocardial infarctions and one cerebrovascular event in three people with multiple risk factors, and two disseminated intravascular coagulation events related to pneumonia in two people >70 years old.

Discussion/Conclusion: No new safety concerns were observed since the last data cut-off and the benefit–risk profile remains positive. Health authorities no longer require special expedited safety reporting of TE/TMAs for emicizumab; however, monitoring and reporting of safety data are ongoing, with no new safety signals with increased patient emicizumab exposure found to date.

Disclosure of Interest: K. Sarouei Shareholder of: F. Hoffmann-La Roche Ltd, Employee of: Genentech, a member of the Roche Group, S. Barlera: None declared, L. Polito Shareholder of: F. Hoffmann-La Roche Ltd, Employee of: F. Hoffmann-La Roche Ltd, G. Tobaruela Shareholder of: F. Hoffmann-La Roche Ltd, Employee of: F. Hoffmann-La Roche Ltd, J. Biondo Employee of: Genentech, Inc.

PO127 | Real-world effectiveness and usage of recombinant factor IX Fc: Interim analysis in paediatric patients from the 24-month, prospective, non-interventional B-MORE study

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Introduction: B-MORE (NCT03901755) is an ongoing, 24-month prospective, non-interventional, international study evaluating the real-world effectiveness and usage of extended half-life recombinant factor IX Fc (rFIXFc; Alprolix®) in patients with haemophilia B (PwHB).

Methods: PwHB were prescribed rFIXFc on demand (OD) or prophylaxis (PPX) prior to/at B-MORE study entry. Interim data from the first 12 months of rFIXFc treatment (retrospective/prospective

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periods) were analysed for paediatric PwHB (age grouped by <12/12–<18 years) with ≥6 months on the same rFIXFc regimen.

Results: At data cut-off (6 October 2022), a total of 151 PwHB were enrolled in B-MORE; 69 paediatric PwHB were included in this analysis (62 of 69 initiated rFIXFc before enrolment) with a median (range) age of 8.3 (1–<18) years (no inhibitor history). Of these paediatric PwHB, 54 were <12 years (all males; 42 severe, 11 moderate, 1 mild disease; 10 were previously untreated) and 15 were 12–<18 years (1 female; 12 severe, 3 moderate disease). At enrolment, one patient (12–<18 years) had joint surgery history and no patients had target joints.

Overall, 67 PwHB received rFIXFc PPX (64 remained on PPX from rFIXFc initiation and 3 PwHB < 12 years switched from rFIXFc OD at initiation) and 2 PwHB ($n = 1$ < 12 years, mild disease; $n = 1$ 12–<18 years, severe) remained on rFIXFc OD from initiation. Median (range) duration on rFIXFc PPX was 33.5 (7—71) months for PwHB < 12 years ($n = 53$) and 30.2 (15—65) months for PwHB 12–<18 years ($n = 14$).

An intra-patient comparison of 31 PwHB (with ≥6 months prior FIX PPX and ≥9 months rFIXFc PPX) showed the mean (SD) total annualised bleeding rate reduced from 2.9 (4.8) pre-rFIXFc initiation to 1.0 (1.7) during the first 12 months in PwHB < 12 years ($n = 22$) and from 0.8 (1.0) to 0.4 (0.7) in PwHB 12–<18 years ($n = 9$). Mean (SD) weekly factor consumption and injection frequency were reduced by 26 (29) IU/kg and 0.7 (0.4) injections in PwHB < 12 years, and 25 (20) IU/kg and 1.2 (0.4) injections in PwHB 12–<18 years.

No inhibitor development or serious adverse events related to rFIXFc were reported at data cut-off.

Discussion/Conclusion: Interim real-world B-MORE data indicate rFIXFc is effective and well tolerated in paediatric PwHB, with improved bleed protection and reduced factor usage versus prior FIX PPX.

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PO128 | The efficacy, safety and pharmacokinetics of N8-GP in previously treated chinese patients with haemophilia A: Results from the phase 3b pathfinder10 study

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Introduction: N8-GP (turoctocog alfa pegol; Esperoct®) is a recombinant, glycoPEGylated extended half-life factor VIII (FVIII) replacement product approved for haemophilia A (HA) treatment. The pathfinder10 (NCT05082116) trial investigated N8-GP efficacy, safety and pharmacokinetics (PK) in previously treated Chinese patients with severe HA.

Methods: Patients (≥12 years) with severe HA, FVIII activity < 1%, ≥150 exposure days to FVIII products, no FVIII inhibitors (≥0.6 BU) or history were enrolled in this multi-centre, open-label, non-randomised, single-arm Phase 3b trial. Patients received 50 IU/kg N8-GP prophylaxis every 4 days for ≥28 weeks; twice-weekly dosing allowed at investigator's discretion. Bleeding episodes were treated with 20–75 IU/kg N8-GP. The primary endpoint was the number of bleeding episodes (spontaneous and traumatic) observed during the treatment period. Secondary endpoints included haemostatic effect, incidence rate of confirmed inhibitors, PK [FVIII activity trough level, incremental recovery (IR), area under the curve (AUC), half-life ($t_{½}$)].

Results: Thirty-six patients (13 adolescents aged 12–17, 23 adults aged 18–54) enrolled in and completed the trial. In the 12 months before trial entry, mean (SD) and median number of bleeding episodes for patients receiving prophylactic treatment were 11.0 (11.1) and 5.0. During prophylactic treatment, mean annualised bleeding rate (ABR) was 2.55 (95% CI: 1.24; 5.23), and median ABR 0.00. No bleeds were reported in 25/36 patients (69.4%) during the trial. The haemostatic success rate for treatment of bleeding episodes, assessed on a 4-point scale for haemostatic response, was 94.8% (95% CI: 73.2; 99.2). Most bleeds (49/52; 94.2%) were treated with ≤2 injections; 42/52 (80.8%) needed only one injection. Mean FVIII activity trough level was

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3.3 IU/dL (95% CI: 2.6; 4.3), mean post-dose recovery (peak level) was 126.1 IU/dL (95% CI: 116.9; 136.0). N8-GP terminal $t_{½}$ was 19.9 h (95% CI: 18.6, 21.2), ~1.6 times longer than non-modified recombinant FVIII products. IR at 30 min (single dose) was 2.3 (IU/dL)/(IU/kg) (95% CI: 2.1, 2.5). $AUC_{(0\text{-}96\,h)}$ at single dose was 31.8 h*(IU/mL) (95% CI: 28.9; 34.9). No patients developed inhibitors against FVIII during the trial; no safety concerns were identified.

Discussion/Conclusion: N8-GP appeared safe and efficacious in previously treated Chinese patients with severe HA.

Disclosure of Interest: J. Sun: None declared, Y. Chen: None declared, W. Li: None declared, R. Wu: None declared, Y. Feng'e: None declared, Z. Xiaojing: None declared, Z. Zeping: None declared, X. Bao Employee of: Novo Nordisk (China) Pharmaceuticals Co., Ltd, Beijing, China, L. Xiaoyan Employee of: Novo Nordisk (China) Pharmaceuticals Co., Ltd, Beijing, China, M. Zak Employee of: Novo Nordisk A/S, Y. Renchi Consultant for: Bayer, Novo Nordisk, Pfizer, F. Hoffmann-La Roche Ltd, Sanofi and Takeda.

PO129 | Comparing inhibitor development in (plasma derived vs. recombinant) FVIII/FIX concentrates in severe haemophilia: Reporting on 1392 PUPs from EUHASS and canadian registries

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Introduction: Severe haemophilia patients treated with concentrates are at risk of inhibitors development. Concentrate type may affect inhibitor risk. While the randomised SIPPET trial showed reduced inhibitor development with pdFVIII versus rFVIII, this has not been supported by a prospective study.

Methods: We assessed inhibitor development by type of concentrate during the first 50 EDs in PUPs with severe haemophilia A or B. For 11 and 8 years, respectively, the European Haemophilia Safety Surveillance (EUHASS) and Canadian Bleeding Disorders Registry (CBDR) registries have been monitoring adverse events using the same data capture system. Inhibitors are reported quarterly, and PUPs completing 50 EDs without inhibitor development annually. Cumulative inhibitor incidences and 95% confidence intervals (CIs) were compared without adjustment for other risk factors. A secondary analysis was performed comparing inhibitor development on pdFVIII and rFVIII after exclusion of data that were also reported to the international PedNet registry.

Results: Fifty-six European, and 23 Canadian centres reported inhibitor development in 312/1219 (26%; CI: 23–28) PUPs with severe haemophilia A and in 14/173 (8%; CI: 5–13) with severe haemophilia B. In PUPs with severe haemophilia A, inhibitor development was lower on pdFVIII (20%: CI: 14–26), than on standard half-life rFVIII (SHL-rFVIII, 27%: CI: 24–30; odds ratio 0.67 (CI 0.45–0.98); *p* .04). Extended half-life rFVIII (EHL-rFVIII, 22%; CI: 12–36) showed an intermediate inhibitor rate. The subgroup analysis showed that in the non-PedNet centres (767 PUPs), the protective effect of pdFVIII was more with an inhibitor development of 13.7% versus 26.1% on rFVIII (OR 0.45; CI 0.26–0.76) *p* .002). In contrast, in the PedNet centres (452 PUPs) inhibitor development was much higher on pdFVIII (33.3%) and similar to inhibitor development on rFVIII (27.6%; *p* value .369). These results suggest a centre effect. In PUPs with haemophilia B, Inhibitor development was similar for pdFIX (11%; CI: 3–25), SHL-rFIX (8%; CI: 3–15) and EHL-rFIXs (7%; CI: 1–22).

Discussion/Conclusion: While confirming expected rates of inhibitors in PUPs with haemophilia A and B, unadjusted inhibitor development rates were significantly lower with pdFVIII compared to SHL-rFVIII. This is the first prospective study to confirm the results from the SIPPET study.

Disclosure of Interest: None declared.

PO130 | Uptake of emicizumab in PUPs with severe haemophilia A and changes in inhibitor incidence

K. Fischer[1,*]; R. Lassila[2]; F. Peyvandi[3]; A. Gatt[4]; S. Gouw[5]; R. Hollingworth[6]; T. Lambert[7]; R. Kaczmarek[8]; M. Makris[9]

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Introduction: Since the first publication on emicizumab in 2016, the possibility of an effective prophylaxis without the burden of venous access is appealing for infants and toddlers with severe haemophilia A. Emicizumab is increasingly used for primary prophylaxis in previously untreated patients (PUPs) with severe haemophilia A (SHA) and consequently exposure to FVIII is reduced and/or postponed. We aimed to quantify the uptake of emicizumab and concomitant changes in the incidence of FVIII inhibitors.

Methods: The European Haemophilia Safety Surveillance System (EUHASS) has been monitoring adverse events according to concentrate in 83 European haemophilia treatment centres. Inhibitors were reported quarterly, and PUPs completing 50 exposure days without inhibitor development annually and per concentrate. Cumulative inhibitor incidences and 95% confidence intervals (CI) were compared without adjustment for other risk factors. For the present analysis, data on treatment and inhibitor development from 2016 until 2022 of PUPs with SHA were extracted and compared per treatment year.

Results: Since 2016, 831 PUPs were reported, of whom 131 (15.8%) developed an inhibitor against FVIII. Data per treatment year are shown in the table.

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Year	2016	2017	2018	2019	2020	2021	2022
Treated (N)	107	131	120	143	103	124	103
Receiving emicizumab	0.0%	1.5%	9.2%	9.0%	3.9%	25.0%	43.7%
FVIII inhibitor	21.5%	22.1%	22.5%	15.4%	11.7%	9.7%	5.8%

The use of emicizumab was first reported in 2017, but the proportions reaching 50 exposure days on emicizumab really started to increase in 2021, when already 25% of all PUPs were primarily treated with emicizumab. A trend was observed towards lower inhibitor incidences, from around 22% in 2016–2018 to around 6% in 2022. This is most likely related to the fact that treatment with FVIII occurs only very infrequently in patients on emicizumab, resulting in postponement of inhibitor development. No inhibitors against emicizumab or other/thrombotic side effects were reported in these PUPs.

Discussion/Conclusion: Primary prophylaxis with emicizumab is increasingly used in PUPs with SHA and the concomitant lower inhibitor incidence is expected to be temporary. These trends will make it more difficult to assess inhibitor incidence for newly introduced FVIII concentrates.

It is probable that the FVIII inhibitors will eventually develop when patients are treated with FVIII, up until 50 EDs, but this will have to be studied in registries.

Image: See above

Disclosure of Interest: None declared.

PO131 | Healthcare resource use and related costs of haemophilia B in French adult patients in 2021: A nationwide claims database analysis

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Introduction: There are few data on healthcare resource use and related costs of French haemophilia B (HB) patients. The aim of this study was to describe these features in HB adults according to severity in France in 2021.

Methods: This study used the French nationwide claims database (SNDS). HB patients alive on 1 January 2021, were identified by the ICD-10 code D67. A control group without HB matched on age, gender and region of residence was randomly selected in the database. Sub-group analyses were performed according to treatment pattern (as a proxy for severity). Direct costs were estimated in a collective perspective.

Results: A total of 991 adult patients with HB were identified. Mean age was 44 years and 81.6% were males.

Among the patient's population 776 (78.3%) and 209 (21.1%) patients without inhibitors were treated on demand and in prophylaxis respectively and less than 10 patients had inhibitors.

Compared to controls, patients with HB had significantly more frequent consultations with general practitioners (78.8% vs. 71.7%), hospital specialists (53.3% vs. 26.8%), nurses (68.8% vs. 50.5%), physiotherapists (20.7% vs. 14.6%) and to emergency room visits (17.7% vs. 12.1%). They were more frequently treated with analgesics (57.6% vs. 48.7%) but less frequently with non-steroid anti-inflammatory drugs (17.1% vs. 25.0%). The proportion of HB patients hospitalised all causes was higher than in controls, overall (25.5% vs. 15.0%) as well as for bleeding (2.0% vs. 0.1%) and orthopaedic surgery (6.8% vs. 3.5%).

The mean and median annual direct medical costs (drugs, consultations, hospitalisations, …) varied strongly according to treatment modalities:

€7400 and 1081€ for adults treated on demand without inhibitors;

—€178,512 and 156,188€ for adults treated in prophylaxis without inhibitors.

The costs related to antihaemophilic drugs accounted for 32% and 91% respectively in these two treatment groups.

Discussion/Conclusion: These results highlight the burden of HB in terms of healthcare resources utilisation and direct cost. The costs of HB patients varied greatly with disease severity and was mostly due to the use of antihaemophilic drugs.

Disclosure of Interest: None declared.

PO132 | Vector clearance following administration of fidanacogene elaparvovec gene therapy in adults with haemophilia B

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Introduction: Fidanacogene elaparvovec is a recombinant adeno-associated virus (AAV) gene therapy for haemophilia B that delivers a high-activity factor IX (FIX) variant (FIX-R338L; FIX Padua). An important safety endpoint in AAV gene therapy trials is the time required for viral vector DNA to clear from bodily fluids. We report vector clearance data from the phase 3 BENEGENE-2 trial (NCT03861273).

Methods: Male participants ≥18 years old with haemophilia B (FIX activity ≤2%) received a single infusion of fidanacogene elaparvovec [5e11 vector genomes (vg)/kg]. Vector DNA in plasma, peripheral blood mononuclear cells (PBMC), semen, saliva and urine was analysed with quantitative polymerase chain reaction. Measurements were made weekly until vector clearance, defined as three consecutive negative results (i.e., below limit of quantification).

Results: As of November 2022, 41 of 45 participants completed ≥15 months of follow-up. Vector clearance results were observed in a setting of no infusion-related serious adverse events, thrombotic events, FIX inhibitors or malignancies. Peak levels of vector DNA occurred within 2 weeks postinfusion. The highest vector DNA concentrations were found in plasma, the lowest in urine. In plasma, peak vector DNA concentration [mean (SD) and median (min, max)] was 2.008e9 (3.633e9) and 3.610e6 (1.880e3, 1.030e10) vg/mL, with a mean time to peak of 8.4 (SD 13.67) days. In urine, mean peak concentration was 4.360e4 (SD 8.539e4) and median 1.640e4 (min, max, 5.770e3, 3.230e5) vg/mL, with a mean time to peak of 1.8 (SD 0.60) days. After reaching peak, vector DNA concentration declined steadily. In general, PBMC were slowest to clear with mean (SD) and median (min, max) time to last undetectable vector of 163.3 (109.44) and 130.0 (39, 513) days. The mean (SD) and median (min, max) time to last undetectable vector in plasma were 98.6 (54.69) and 93.0 (30, 317) days; saliva, 42.4 (17.23) and 37.0 (29, 105) days; semen, 41.1 (20.09) and 35.0 (15, 104) days; and urine, 20.4 (13.26) and 21.0 (4, 87) days.

Discussion/Conclusion: Fidancogene elaparvovec was well tolerated and full clearance of vector DNA was observed in all participants. On average, clearance was achieved within 1—4 months, except in PBMC where clearance took ≤7 months. These results are consistent with those reported in an earlier phase 1/2a trial and other gene therapy studies.

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PO133 | Danish clinical experience of switching from standard half-life FVIII to damoctocog alfa pegol in patients with haemophilia A

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Introduction: Damoctocog alfa pegol (BAY 94-9027, Jivi®) is an extended half-life factor VIII (FVIII) treatment indicated for use in previously treated patients aged ≥12 years with haemophilia A. We report an intra-patient comparison when switching to damoctocog alfa pegol from previous standard-half-life (SHL) therapy, in a real-world setting.

Methods: This single-centre, retrospective cohort study was performed using a chart audit from the Haemophilia Centre, Aarhus University Hospital. Patients with severe or moderate haemophilia A aged ≥12 years who had received damoctocog alfa pegol for at least 6 months were included. Pre- and post-switch data on annualised bleeding rate (ABR), infusion frequency, utilisation and FVIII level were collected.

Results: Overall, 42 patients switched to damoctocog alfa pegol, 34 (81%) had severe disease and 8 (19%) had moderate disease. Median (Q1;Q3) age was 44.0 (29.0;56.0) years. Median (Q1;Q3) ABR pre- and post-switch was 2.00 (0.00;6.00) and 0.00 (0.00;1.00), respectively. Pre-switch, treatment with SHL therapy was most commonly received every other day (twice weekly [2 × *W*; *n* = 10], every 3 days [*n* = 1], three times weekly [*n* = 9], every other day [EOD; *n* = 14], four times weekly [*n* = 1], daily [*n* = 3] and on demand [*n* = 4]). Post-switch, treatment with damoctocog alfa pegol was most commonly received twice-weekly (weekly [*n* = 3], every 5 days [*n* = 7], 2 × *W* [*n* = 29], EOD [*n* = 1] and daily [*n* = 2]). For SHL FVIII versus damoctocog alfa pegol, mean (SD) annualised utilisation was 3514 (± 1225) IU/kg/year versus 3860 (± 789) IU/kg/year. Mean (SD) FVIII levels were 7.7 (6.4), 3.1 (2.6), 0.8 (1.1), 1.0 (1.2) and 1.0 (1.0) for Days 1–5 after last infusion for SHL FVIII versus 16.5 (9.2), 9.8 (3.9), 4.9 (5.9), 4.8 (3.3) and 2.0 (1.4) for damoctocog alfa pegol. Six patients had a history of inhibitors on their previous therapy. No patient developed an inhibitor at or following switch to damoctocog alfa pegol. No drug-related serious adverse events were recorded.

Discussion/Conclusion: This single-centre experience provides real-world evidence supporting the use of damoctocog alfa pegol as an effective alternative therapy for individuals currently receiving standard-half-life factor-replacement products.

Disclosure of Interest: L. Poulsen Grant/Research support from: Pfizer, Speaker Bureau of: Bayer, Novo Nordisk, Pfizer and Sobi., I. Adamsen Speaker Bureau of: Bayer, Novo Nordisk, Pfizer and Sobi.

PO134 | Quality of life in children with haemophilia A: Phase 3 XTEND-kids study of efanesoctocog alfa

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Introduction: Haemophilia A is a rare, genetic bleeding disorder characterised by recurrent joint bleeds, leading to reduced mobility and poor quality of life (QoL). This analysis aimed to evaluate QoL in children receiving efanesoctocog alfa (ALTUVIIIO®; formerly BIVV001), a high-sustained factor VIII (FVIII) therapy, in the XTEND-Kids study.

Methods: XTEND-Kids (NCT04759131), a Phase 3, open-label, multicentre study, assessed the safety, efficacy and pharmacokinetics of once-weekly efanesoctocog alfa prophylaxis in previously treated participants aged <12 years with severe haemophilia A. QoL was assessed using patient-reported outcome (PRO) measures completed at baseline, Week 26 and Week 52 (end-of-treatment) by patients or caregiver proxies. PROs included the haemophilia-specific Haemophilia Quality of Life Questionnaire for Children (Haemo-QoL; ≥4 years old, lower scores = better QoL), and the generic Patient-Reported Outcomes Measure Information System (PROMIS) Pain Intensity assessment [0 (no pain) to 10 (worse pain)] and EQ-5D-Y (scoring: no, some or a lot of problems; dimensions: mobility, looking after myself, usual activities, pain/discomfort, feeling worried/sad/unhappy).

Results: In total, 74 boys were enrolled; mean (SD) age 6.0 (2.9) years. Prior to enrolment, 73 (98.6%) were on FVIII prophylaxis, with one receiving an on-demand regimen. Mean (SD) Haemo-QoL Total scores trended towards improvement from baseline to Week 52 for the following age groups: children 8–<12 years (n = 10), −9.79 (12.18); caregiver proxy 8–<12 years (n = 9), −4.05 (10.77); children 4–7 years (n = 14), −2.46 (10.49); caregiver proxy 4–7 years (n = 23), −2.85 (11.82). Most improved Haemo-QoL domains at Week 52 reported by children aged 8–<12 years (n = 10) were 'Other People' (−17.50 [17.87]) and 'Sports and School' (−16.25 [20.67]). Mean (SD) baseline PROMIS Pain Intensity scores (5 to <12 years, assessed by proxy) were low (1.1 [1.95]; n = 29). Overall, children and caregivers reported no problems from baseline to Week 52 across all EQ-5D-Y dimensions.

Discussion/Conclusion: Improvements in QoL were observed in children using a haemophilia-specific PRO measure; however, impact of treatment could not be well captured using generic PRO tools. Baseline PRO scores for pain were low, likely due to lack of chronic joint damage and effects from haemophilia A, given patients' young age and prophylaxis use prior to study, hence improvements were difficult to observe.

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PO135 | The effectiveness and safety of every-7-days damoctocog alfa pegol prophylaxis in haemophilia A in phase 3, phase 4 and real-world studies

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Introduction: Damoctocog alfa pegol (BAY 94-9027, Jivi®) is an extended half-life factor VIII treatment approved for use in previously treated people with haemophilia A (PwHA) aged ≥12 years. Dosing regimens can be tailored to meet individual patient needs and may be extended to up to every 7 days (E7D).

Methods: This analysis reports efficacy and safety outcomes of the E7D regimen from the PROTECT VIII extension (NCT01580293), the phase 4 open-label post-marketing interventional (PMI; NCT04085458) and the HEM-POWR (NCT03932201) studies.

Results: Data from 55 participants (23 PROTECT VIII, 9 PMI study and 23 HEM-POWR) who received E7D damoctocog alfa pegol were included. All participants in the PROTECT VIII extension and the PMI study had severe haemophilia A. In HEM-POWR, 6/23 (26.1%) participants had mild/moderate disease and 17/23 (73.9%) had severe disease. At baseline, median age was 31, 36 and 38 years for the PROTECT VIII extension, PMI and HEM-POWR studies.

Median (quartile [Q]1; Q3) pre-study annualised bleeding rates (ABRs) were 3.0 (0.0; 12.0), 5.5 (0.0; 14.0) and 1.5 (0.0; 3.0) for the PROTECT VIII extension, PMI and HEM-POWR studies. Median (Q1; Q3) total, joint and spontaneous ABRs were 0.7 (0.0; 1.7), 0.4 (0.0; 1.0) and 0.3 (0.0; 0.8) in the PROTECT VIII extension; 0.6 (0.0; 1.1), 0.0 (0.0; 0.0) and 0.0 (0.0; 0.0) in the PMI study and 0.0 (0.0; 1.2), 0.0 (0.0; 0.9) and 0.0 (0.0; 1.1) in HEM-POWR. In total, 8/23 (34.8%), 7/9 (77.8%) and 13/23 (56.5%) PwHA receiving E7D prophylaxis experienced zero bleeds in the PROTECT VIII extension (during 1129 days), PMI (last 24 weeks of the study) and HEM-POWR (during 331 days) studies.

No study-drug-related treatment-emergent adverse events (TEAEs) were reported in PwHA receiving E7D prophylaxis in HEM-POWR. Study-drug-related TEAE data stratified by dosing regimen were unavailable for the other studies; however, rates of study-drug-related TEAEs were low (≤9.4%) across all studies.

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Discussion/Conclusion: This analysis confirms that the observed benefits of E7D damoctocog alfa pegol prophylaxis in people with haemophilia A from clinical trials extend to the real world. Damoctocog alfa pegol enables reduced-frequency prophylaxis with extended dosing intervals up to every 7 days, which is effective and well tolerated in previously treated people with haemophilia A across multiple settings.

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PO136 | Interim results from HA-SAFE: An observational study evaluating long-term safety of real-world treatment with damoctocog alfa pegol

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Introduction: Damoctocog alfa pegol is approved for prophylaxis and treatment of bleeds in previously treated patients with haemophilia A (PwHA) aged ≥12 years, with a two times per week, every 5 days or every 7 days dose that allows for the treatment regimen to be tailored to individual patient needs. The aim of HA-SAFE (NCT04461639) is to characterise in a real-world setting the long-term safety of damoctocog alfa pegol.

Methods: HA-SAFE is a multinational, open-label, prospective, non-interventional, multicentre, cohort study of PwHA receiving damoctocog alfa pegol as prophylaxis treatment. The study is being conducted in multiple countries in Europe with follow-up visits occurring during routine practice. Historical study-relevant data are collected from medical records and treatment-related data during visits. Patient diaries are provided and reviewed for adverse events (AEs) at each visit. The study aims to observe 50 patients for at least 4 years each. The primary objective of this study is the collection and analysis of AEs, AEs of special interest, serious adverse events and adverse reactions.

Results: A total of 62 patients have been enrolled. Overall, 56 patients were diagnosed with severe haemophilia A, and six with moderate disease. At the time of this protocol-specified interim analysis, the median number of days in the study for all patients (n = 62) was 68.5 days (range: 1–503). The median observation period for patients with at least one follow-up visit (n = 35) was 213 days (range: 23–503). Among the 62 patients, 22 patients (35%) experienced a total of 43 treatment-emergent adverse events (TEAEs). Eight patients (13%) experienced a treatment-emergent serious adverse event (TESAE). The majority of the reported TEAEs were of mild or moderate intensity and 38/43 were recovered/resolved or recovering/resolving. One of the reported events was a drug-related treatment-emergent adverse event of special interest, involving loss of drug effect and transient low-titre inhibitor development against factor VIII, and was classified as a TESAE. This event resolved without damoctocog alfa pegol discontinuation. There were no deaths.

Discussion/Conclusion: Based on these results obtained from the HA-SAFE study, it can be concluded that damoctocog alfa pegol treatment is well-tolerated, thus confirming a positive benefit-risk ratio.

Disclosure of Interest: J. Oldenburg Grant/Research support from: Bayer, Biotest, CSL Behring, Octapharma, Pfizer, Sobi and Takeda, Consultant for: Bayer, Biogen, Biomarin, Biotest, CSL Behring, Chugai, Freeline, Grifols, LFB, Novo Nordisk, Octapharma, Pfizer, Roche, Sobi, Sparks and Takeda, Speaker Bureau of: Bayer, Biogen, Biomarin, Biotest, CSL Behring, Chugai, Freeline, Grifols, LFB, Novo Nordisk, Octapharma, Pfizer, Roche, Sobi, Sparks and Takeda, M. T. Alvarez Román Grant/Research support from: Shire/Takeda, Speaker Bureau of: Amgen, Bayer, CSL Behring, Novartis, Novo Nordisk, Roche, Shire/Takeda and Sobi, H. Pergantou Consultant for: Takeda, Bayer, CSL Behring, Novo Nordisk, Pfizer, Roche and Sobi, S. Wenning Grant/Research support from: Bayer, Biomarin, Chugai, CSL Behring, Novo Nordisk, Octapharma, Pfizer, Roche, Swedish Orphan Biovitrum and Takeda, M. E. Mancuso Consultant for: Bayer, BioMarin, CSL Behring, Grifols, Kedrion, LFB, Novo Nordisk, Octapharma, Pfizer, Roche, Sanofi, Spark Therapeutics, Sobi, Takeda and UniQure.

PO138 | Safety profile of damoctocog alfa pegol: Fourth interim analysis of the real-world HEM-POWR study for previously treated patients with haemophilia A

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Introduction: Damoctocog alfa pegol (BAY 94-9027, Jivi®) is an extended half-life recombinant factor VIII (FVIII) product that was approved as treatment for previously treated patients (PTPs) aged ≥12 years with haemophilia A. Effectiveness and safety results from the real-world HEM-POWR study (NCT03932201) of damoctocog alfa pegol in PTPs have been previously reported. Here, we present safety results from the fourth interim analysis.

Methods: HEM-POWR is an open-label, prospective, phase 4 study in PTPs with mild, moderate or severe haemophilia A. The primary endpoint was annualised bleeding rate and secondary endpoints included safety. The safety analysis set (SAF) included PTPs who provided informed consent and had received ≥1 study dose in the observation period. Data were collected from patient diaries and physician records. Ethical approval was obtained for all sites.

Results: At data cut-off (1 August 2023), 339 PTPs were enrolled of which 332 (97.9%) were included in the SAF. The majority of patients (85.2%) were aged ≥18–<65 years; 13.6% (n = 45) had a history of FVIII inhibitors. At initial diagnosis, 81.6% (n = 271) had severe disease and 17.2% were mild/moderate (n = 57; data missing for 1.2% patients). A proportion of 43.4% of patients (n = 144) had ≥1 comorbidity, most commonly chronic pain (17.5%, n = 58) and hypertension (15.7%, n = 52). The mean [standard deviation (SD)] observation period was 582.8 (293.1) days. Overall, 30.1% (n = 100) patients reported any treatment-emergent adverse events (TEAE) and 9.3% (n = 31) serious TEAEs. The most common TEAEs were injury and procedural complications (10.2%, n = 34), and musculoskeletal and connective tissue disorders (9.0%, n = 30). Three patients (0.9%) had 1 adverse event of special interest, namely a low titre transient inhibitor, an epileptic absence and erythema. The inhibitor was a serious study drug-related TEAE but resolved within 5 months. One death (0.3%) was reported (acute spinal ischaemia leading to septic shock in aspiration pneumonia). Cause of death was considered unrelated to study drug administration.

Discussion/Conclusion: In line with previous analyses, damoctocog alfa pegol showed a favourable safety and tolerability profile in PTPs with mild/moderate and severe haemophilia A in a real-world setting.

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Disclosure of Interest: M. Reding Grant/Research support from: Receipt of institutional research support from Bayer and BioMarin, Speaker Bureau of: Member of advisory boards and/or speaker bureaus for Bayer, CSL Behring, Genentech, HEMA Biologics, Novo Nordisk, Sanofi and Takeda, M. Alvarez Román Speaker Bureau of: Speaker in advisory boards and sponsored symposia with Novo Nordisk, Bayer, Takeda, Roche, Pfizer, Octapharma, Amgen, Novartis, CSL Behring and Sobi, G. Castaman Consultant for: Participant of advisory boards for Alexion, Bayer, BioMarin, Takeda, CSL Behring, LFB, Novo Nordisk, Pfizer, Roche, Sanofi, Sobi and UniQure, consultant for Roche, Speaker Bureau of: Speaker at satellite symposia during scientific meetings for Bayer, Grifols, LFB, Roche, Sobi, Novo Nordisk, Werfen and Kedrion, member of steering committee of UniQure, M. Janbain Consultant for: Consultancy for Takeda, CSL Behring, Sanofi, BioMarin, Genentech and Octapharma, member of Bayer steering committee, Speaker Bureau of: Member of speaker bureau for Takeda, BioMarin, CSL Behring and Sanofi, T. Matsushita Grant/Research support from: Receipt of educational and investigational support from Chugai and Novo Nordisk, received honoraria from Takeda, Bayer, Sanofi, Chugai, CSL Behring, JB Pharma, KMB Pharma, Novo Nordisk, Octapharma and Sysmex, Consultant for: Member of advisory boards for Takeda, Bayer, Novo Nordisk, Chugai and Pfizer, K. Meijer Consultant for: Participation in trial steering committee for Bayer, receipt of consulting fees from UniQure, Speaker Bureau of: Receipt of speaker fees from Bayer and Alexion, K. Schmidt Employee of: Bayer, J. Oldenburg Grant/Research support from: Reimbursed for attending symposia/congresses and/or received honoraria and/or funds for research from Bayer, Biogen Idec, Biotest, Chugai, CSL Behring, Novo Nordisk, Octapharma, Pfizer, Roche, Swedish Orphan Biovitrum and Takeda.

PO139 | HEM-POWR study interim analysis four: Effectiveness of damoctocog alfa pegol treatment for previously treated patients with haemophilia A

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Introduction: Damoctocog alfa pegol (BAY 94-9027, Jivi®) is an approved extended half-life factor VIII treatment indicated for use in previously treated patients (PTPs) with haemophilia A aged ≥12 years. HEM-POWR (NCT03932201) is an ongoing, real-world study at multiple clinical sites; here we present effectiveness data from the fourth interim analysis of the HEM-POWR study.

Methods: HEM-POWR is a prospective, open-label, Phase 4 study, and includes PTPs with mild, moderate or severe haemophilia A receiving damoctocog alfa pegol prophylactically or on demand. The primary endpoint was annualised bleeding rate (ABR). The full analysis set (FAS) consisted of patients who met all inclusion criteria, with a first documented dose of damoctocog alfa pegol in the study and ≥1 documented infusion during the observation period. Data were collected in patient diaries and physician records, and statistics were descriptive. Ethical approval was obtained for all sites.

Results: At data cut-off (1 August 2023), the FAS included 227 patients. At initial diagnosis, 1.3% of patients had mild, 13.2% moderate and 83.7% had severe haemophilia A. The median (Q1, Q3) observation period was 728.0 (491.0, 876.0) days and 86.3% patients were aged ≥18–<65 years. Prior to initiation of damoctocog alfa pegol, the median (Q1, Q3) ABR was 1.0 (0.0, 3.0) and mean [standard deviation (SD)] was 2.9 (5.9). During observation period, the median (Q1, Q3) ABR was 0.5 (0.0, 1.6) and mean (SD) was 1.7 (3.9). Mean (SD) change in ABR from prior to damoctocog alfa pegol initiation for total

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bleeds was −1.3 (5.6), for spontaneous bleeds −1.0 (3.3), for joint bleeds −1.1 (4.9) and for spontaneous joint bleeds −0.9 (3.0). In patients with mild or moderate haemophilia at diagnosis (n = 33), the mean (SD) change from baseline in ABR was −1.0 (3.0) and for patients with severe haemophilia (n = 190) it was −1.4 (6.0). The proportion of patients with no affected joints was 38.5% (n = 87/226) prior to damoctocog alfa pegol initiation, 43.2% (n = 98/227) at initial visit and 69.2% (n = 83/120) at first follow-up.

Discussion/Conclusion: In this large real-world study, damoctocog alfa pegol continues to demonstrate long-term effectiveness in PTPs with mild, moderate and severe haemophilia A.

This study was funded by Bayer.

Disclosure of Interest: M. Reding Grant/Research support from: Receipt of institutional research support from Bayer and BioMarin, Speaker Bureau of: Member of advisory boards and/or speaker bureaus for Bayer, CSL Behring, Genentech, HEMA Biologics, Novo Nordisk, Sanofi and Takeda, M. Alvarez Román Speaker Bureau of: Speaker in advisory boards and sponsored symposia with Novo Nordisk, Bayer, Takeda, Roche, Pfizer, Octapharma, Amgen, Novartis, CSL Behring and Sobi, G. Castaman Consultant for: Participant of advisory boards for Alexion, Bayer, BioMarin, Takeda, CSL Behring, LFB, Novo Nordisk, Pfizer, Roche, Sanofi, Sobi and UniQure, consultant for Roche, Speaker Bureau of: Speaker at satellite symposia during scientific meetings for Bayer, Grifols, LFB, Roche, Sobi, Novo Nordisk, Werfen and Kedrion, member of steering committee of UniQure, M. Janbain Consultant for: Consultancy for Takeda, CSL Behring, Sanofi, BioMarin, Genentech and Octapharma, member of Bayer steering committee, Speaker Bureau of: Member of speaker bureau for Takeda, BioMarin, CSL Behring and Sanofi, T. Matsushita Grant/Research support from: Receipt of educational and investigational support from Chugai and Novo Nordisk, received honoraria from Takeda, Bayer, Sanofi, Chugai, CSL Behring, JB Pharma, KMB Pharma, Novo Nordisk, Octapharma and Sysmex, Consultant for: Member of advisory boards for Takeda, Bayer, Novo Nordisk, Chugai and Pfizer, K. Meijer Consultant for: Participation in trial steering committee for Bayer, receipt of consulting fees from UniQure, Speaker Bureau of: Receipt of speaker fees from Bayer and Alexion, K. Schmidt Employee of: Bayer, J. Oldenburg Grant/Research support from: Reimbursed for attending symposia/congresses and/or received honoraria and/or funds for research from Bayer, Biogen Idec, Biotest, Chugai, CSL Behring, Novo Nordisk, Octapharma, Pfizer, Roche, Swedish Orphan Biovitrum and Takeda.

PO140 | Predicting time-dependent changes in factor VIII clearance in haemophilia A patients undergoing surgery

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Introduction: Prior studies suggest that the pharmacokinetic (PK) profile of factor VIII (FVIII) in haemophilia A patients is altered in the perioperative period compared to the prophylactic setting. In this work we apply machine learning to model the evolution of perioperative FVIII clearance over time.

Methods: Data from 44 moderate and severe adult haemophilia A patients undergoing low or medium risk surgery (16/28) with a minimal follow-up of 36 h were used from the OPTI-CLOT trial. In this trial, patients first underwent a baseline PK profile, where FVIII samples were taken 4, 24 and 48 h after a test dose of a standard half-life FVIII concentrate. A population PK model was then developed based on these samples to represent PK of FVIII in the prophylactic setting. Next, individual estimates of the PK parameters were taken and the change in these parameters during the first 48 h after surgery was estimated. Gaussian Process (GP) models then were fit to learn how the individual estimates of FVIII clearance evolved during the complete follow-up time (mean: 175 h). Finally, the relationship between maximal change in clearance and pre-assessed surgical risk, blood group and von Willebrand factor antigen (VWF:Ag) levels were evaluated using t-tests.

Results: Before considering any time-dependent effects, FVIII clearance was on average 7% lower in the first 48 h post-surgery compared to the prophylactic setting. Based on the GPs, patients could be classified into one of three groups: those with no time-dependent changes in FVIII clearance (11/44), those with an increase in clearance (12/44), and those with a decrease in clearance (21/44). In the latter group, the mean additional decrease in FVIII clearance was 31% ± 14 SD. Perioperative changes in VWF: Ag were not correlated to changes in FVIII clearance. Larger changes in FVIII clearance were associated with blood group O and medium risk surgery, although not statistically significant. Patients seemed to recover to pre-surgical FVIII clearance at different rates, with 29 patients still having altered FVIII clearance at the end of follow-up.

Discussion/Conclusion: In our study population, most patients presented with time-dependent changes in FVIII clearance following surgery. By also considering time-dependent effects, individualised dosing of FVIII in haemophilia A patients undergoing surgery can potentially be improved.

Disclosure of Interest: None declared.

PO141 | Associations between depression, anxiety and stress with pain and joint status in patients with haemophilia

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Introduction: Patients with haemophilia (PwH) often suffer from psychological symptoms such as depression or anxiety. To date, uncertainty exists about the determinants predicting worse psychological outcomes. The purpose of this study was to investigate the extent of depressive, anxiety and stress-related symptoms in PwH compared to the healthy population and to determine the impact of pain and joint status in this regard.

Methods: Depression, anxiety and stress were queried in a total of 379 PwH and 271 healthy controls by handing out the well-established and validated Depression, Anxiety and Stress Scale 21 (DASS). Each psychological scale is comprised of seven questions, resulting in a total of 21 items. A higher score for each psychological parameter indicates a more negative emotional state. In addition, scores for the currently perceived pain intensity (NRS from 0 'no pain' to 10 'maximal pain'), pain persistence (from 0 = 'less than one month' to 6 = 'more than 5 years'), pain sensitivity (pressure pain thresholds of the subjectively most affected joint; PPT), and the orthopaedic joint status (Haemophilia Joint Health Score v2.1; HJHS) were assessed to analyse associations with psychological symptoms.

Results: For PwH, higher scores for depression, anxiety and stress were observed compared to the healthy cohort (all $p < .001$). Spearman's rank correlation revealed significant positive associations between each psychological outcome and pain intensity (depression: $\rho = 0.258$, anxiety: $\rho = 0.168$, stress: $\rho = 0.261$; all $p < .001$), pain persistence (depression: $\rho = 0.286$, anxiety: $\rho = 0.242$, stress: $\rho = 0.272$; all $p < .001$) and HJHS (depression: $\rho = 0.163$, $p = .002$; anxiety: $\rho = 0.111$; $p = .031$, stress: $\rho = 0.183$; $p < .001$). For PPT, significant inverse correlations were found with depression ($\rho = -0.208$, $p < .001$), anxiety ($\rho = -0.196$, $p = .002$) and stress ($\rho = -0.170$, $p = .008$).

Discussion/Conclusion: The results provide further evidence for a poorer psychological profile of PwH compared to the healthy population. Particularly pain-related outcomes, but also the HJHS seem to be related with more severe psychological consequences. However, although the correlation analyses yielded significant results, coefficient values are to be interpreted as weak, especially in terms of HJHS. Nonetheless, as arthropathy-related factors such as pain and joint degeneration appear to affect mental health, prevention of haemophilic arthropathy is of great importance.

Disclosure of Interest: None declared.

PO142 | Promising future for haemophilia a patients: Is B-domain-deleted factor VIII gene therapy safe and really holds the future?

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Introduction: Haemophilia is a congenital coagulopathy which is associated with a deficiency in coagulation factor VIII in haemophilia A. It is estimated to have an incidence of 1 in 10,000 live births and is considered a dangerous condition since it can lead to serious complications. However, reports have reported lack of adherence to prophylaxis and numerous adverse events in administering IV factors. Recent research suggests that gene therapy has the potential to be utilised for treating haemophilia in a safe and effective way. This is the first systematic review to examine the efficacy and safety of gene therapy for the treatment of haemophilia.

Methods: This systematic review was conducted in accordance with the PRISMA guidelines and employed a comprehensive approach to gather relevant literature in multiple databases. Inclusion criteria were defined to encompass randomised controlled trial (RCT) study designs involving patients with haemophilia underwent gene therapy. The primary outcomes of interest were bleeding rates and adverse events. Exclusion criteria were applied to studies with irretrievable full-text, incomplete outcome data, in vitro studies or those not published in English.

Results: In this investigation, a sample of 543 male participants were included. The analysis revealed that the cumulative median and mean values of acquired bleeding rate (ABR) across the compiled studies were consistently low with a mean range between 0.00 and 2.03. Furthermore, a discernible mean reduction in the consumption of factor VIII annually was found between −3561.5 and −4233. The discernible enhancements quality of life indicators suggest a positive impact attributable to the intervention. Notably, the safety profile of this treatment regimen displayed remarkable superiority, with a limited number of severe adverse events recorded, totalling 29 instances.

Discussion/Conclusion: We have derived compelling conclusions regarding the therapeutic potential of B-domain-deleted factor VIII gene therapy as a foremost prophylactic measure against bleed with favourable safety profile. In regard to these findings, we advise for the execution of additional clinical trials that include detailed documenting of ABR and factor VIII intake before and after treatment. Such trials will facilitate quantitative analysis, allowing for a thorough evaluation of the treatment's efficacy among haemophilia patients.

Disclosure of Interest: None declared.

PO143 | Integration of a clinical research unit and a paediatric haemophilia unit: Recruitment and follow-up of paediatric patients participating in a clinical trial

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Introduction: Haemophilia is a congenital disease linked to the X chromosome. Our hospital takes care of >100 children with congenital coagulopathies. Since a few years ago, treatment consisted of intravenous administration of substitute products several times per

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week. Our Clinical Trials Unit (CTU) coordinates >200 clinical trials with new therapies in paediatrics, including several substitutive and non-substitutive products for haemophilia and other coagulopathies.

Methods: Descriptive analysis of the operation and integration of the CTU and the Haemophilia Unit of a tertiary paediatric hospital.

Results: The paediatric HU working model is a patient/family centred that also integrates to the CTU. Appointments of both units are integrated in multidisciplinary team visits that include blood tests, physical and joint evaluation and/ or treatment administration to provide a regular follow-up. There are a total of 16 clinical trials open for haemophilia ($n = 36$).

After identifying a potential candidate for a clinical trial, the patient follows these steps:

General information and Informed Consent Form (ICF) signature after answering any question they can have.

Screening to confirm they meet all inclusion criteria. Necessary studies are coordinated and carried out by specialised clinical trial staff.

Treatment initiation and short and long-term follow up visits following the clinical trial schedule in the HU under the supervision of the multidisciplinary team. The CTU manages and organises all the trial visits that take place in the HU.

Patients that complete their participation in the trial continue their treatment within the regular care pathway. Professionals from the multidisciplinary team and the trial coordinator conduct together the final visit and the first standard of care. Thus, providing support and reinforcement to the patients.

Discussion/Conclusion: (1) A CTU with trained and specialised staff that coordinates with the HU provides a unique and individualised service capable of integrating trial visits with the regular follow-up of haemophilia patients.

(2) Patients could benefit from this integrated service. A future study could help us to draw any further conclusion.

Disclosure of Interest: None declared.

PO144 | Health-related quality of life and long-term joint damage in people with severe haemophilia A in Brazil

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Introduction: People with severe haemophilia A's (PwSHA) health-related quality of life (HRQoL) is impacted by many factors including bleeding, treatment burden and long-term joint damage. Currently there is lack of data on long-term joint damage and HRQoL for patients in Brazil. This analysis aims to describe the impact of joint damage on HRQoL in a sample of people with severe haemophilia A (PwSHA) in Brazil receiving prophylaxis without inhibitor diagnosis.

Methods: Brazilian clinical data were obtained via electronic case record forms (eCRF) collected during the CHESS LATAM burden-of-illness study, with cross sectional EQ5D-5L data from a corresponding patient survey (PPIE). EQ5D-5L data were also captured using a supplemental cross sectional patient survey (CHESS LATAM+) and pooled with the PPIE cohort. The Peruvian value set was used to estimate EQ5D-5L utility scores as no value set was available for Brazil. Of the available South American EQ5D-5L value sets, Peru was deemed to have the closest population characteristics to Brazil. Patients were stratified by the number of problem joints (PJ, defined as having chronic joint pain and/or limited range of movement due to compromised joint integrity) acquired, in categories of 0 PJ, 1 PJ, 2 PJ, 3 PJ and 4≥ PJ. Patients not receiving prophylaxis or with active inhibitor were excluded from the analysis.

Results: The majority of PwSHA in the Brazil eCRF cohort reported no active inhibitor and were receiving factor VIII prophylactically (124; 58%). Of these, 63 had 0 PJ, 37 had 1 PJ, 16 had 2 PJ, 4 had 3 PJ, and 5 had 4≥ PJ. Of those respondents with a completed EQ5D-5L, mean HRQoL scores from the pooled sample (66 patients) were 0.83 (0 PJ), 0.61 (1 PJ), 0.50 (2 PJ), 0.60 (3 PJ) and 0.31 (4≥ PJ).

Discussion/Conclusion: The analysis is the first to explore long-term joint damage using the problem joint metric in Brazil for PwSHA. The pooled EQ5D-5L results indicated substantial impact on HRQoL as long-term joint damage increased.

Disclosure of Interest: J. Evans Employee of: HCD Economics, T. Burke Employee of: HCD Economics.

PO145 | Real world evidence: Experience of using standard half-life factors with frequency less than twice a week in haemophilia A

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Introduction: Standard treatment for haemophilia A involves regular administration of recombinant factor VIII to replace the missing factor. However, the frequency of administration may vary depending on the severity of the disease and the individual needs of the patient. In this study, we explored the experience of using standard half-life factors at a frequency of less than twice a week in patients with haemophilia A. Our research focuses on understanding how this treatment frequency relates to factors such as age, severity and bleeding phenotype.

Methods: Our research methodology is based on a retrospective approach that uses the review of clinical records and administrative databases. We will make frequency tables to identify trend measures in the data and group the results. This will include the use of appropriate statistical tests to compare groups of patients and to evaluate the association between different variables. We hope that our findings will contribute to improved treatment management for these patients.

Results: In total, 54 patients with a diagnosis of haemophilia A in prophylaxis used standard half-life factors with two or fewer administrations per week. The analysis using frequency tables allowed us to establish that 31% of the patients used Hemofil M, 30% Advate and 22% BAY 81-8973. The average age of the population was 23 years,

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with an age range that varied from 1 to 74 years. It is important to note that 9% of the population registered moderate severity of the disease, while 91% presented severe severity. The annualised bleeding rate registered a value per patient of 1.2, which indicates effective control of bleeding episodes in this population.

Discussion/Conclusion: These findings suggest that the use of standard half-life factors less frequently than twice a week may be a viable option for some patients with haemophilia A. However, it is important to note that treatment effectiveness may vary depending on the patient's condition, medication used, the severity of the disease and the particular characteristics of each patient, which supports the importance of a personalised approach in the care process of patients with haemophilia. Furthermore, although our study population was relatively young on average, the results indicate that this treatment regimen may be suitable for a wide range of ages.

Disclosure of Interest: None declared.

PO146 | Real-world bleeding rates on emicizumab using digital treatment diary data, preliminary results

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Introduction: In The Netherlands, a digital treatment diary for people with a congenital bleeding disorder was introduced in 2018. In this mobile app, people log all bleeds and prophylactic and therapeutic infusions. Health care providers can access these data to evaluate treatment efficacy and change treatment plans. Since 2019 the majority of Dutch people with severe haemophilia A have switched to emicizumab for prophylaxis. However, the efficacy of emicizumab in preventing bleeds has not yet been evaluated in a real-world setting in The Netherlands using nationwide digital treatment diary data. We aim to assess the annual (joint) bleeding rate on emicizumab among people with severe haemophilia A. Our secondary aim is to assess the reliability of treatment diary data for secondary use in clinical research.

Methods: Dutch people with severe haemophilia A of all ages using emicizumab who have recently used the treatment diary were eligible. Treatment diary data were verified with electronic health record data. Annual bleeding rates (ABR), annual joint bleeding rates (AJBR) and proportions of people with zero treated bleeds were assessed. For this preliminary analysis, bleeding rates were calculated as the number of bleeds treated with at least one FVIII concentrate administration (documented in the treatment diary and/or electronic health records) divided by the follow-up duration. For final analyses a negative binomial regression model will be used.

Results: In total, 219 persons were eligible. Until now, data of 157 persons with severe haemophilia A on emicizumab have been collected, with a median age of 28 years [interquartile range (IQR) 16–51]. The median (IQR) duration of emicizumab use was 26 months (16–29). Median (IQR) real-world treated ABR and treated AJBR were 0.6 (0.0–1.5) and 0.0 (0.0–0.7), respectively. Of participants, 38% (59/157) had zero treated bleeds and 54% (84/157) had zero treated joint bleeds. Final data will be presented at the congress, as well as an evaluation of the reliability and completeness of bleeds in the treatment diary compared to electronic health records.

Discussion/Conclusion: Real-world bleeding rates in Dutch people with severe haemophilia A on emicizumab prophylaxis calculated using digital treatment diary and electronic health records data were comparable to other real-world studies. Here, we aim to showcase the value of the digital treatment diary to evaluate treatment efficacy.

Disclosure of Interest: None declared.

PO147 | Quality of life assessment and pharmacokinetic study in haemophilia A patients undergoing prophylactic treatment

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Introduction: The choice of personalised treatment plans significantly impacts haemophilia A patients' well-being. This study aims to investigate the pharmacokinetics of FVIII products and their association with quality of life in these patients.

Methods: Quality of life data were obtained via the distribution of Haem-A-Qol questionnaire to 29 Greek male patients with moderate or severe haemophilia A, receiving prophylactic treatment at the Hemophilia Center of Northern Greece. FVIII levels were measured from plasma samples(one-stage clotting assay, Pathromtin SL reagent) taken before and 2 h after administration of the factor concentrate, according to each patient's normal prophylaxis regimen. Pharmacokinetic models were generated using the McMaster PopPK clinical calculator.

Results: Findings revealed statistically significant variations in numerous quality-of-life dimensions in relation to the factor concentrate used for treatment. Variations included patients' life plans ($p = .007$),

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concerns about disease complications ($p = .001$), potential for deterioration ($p = .021$), pain ($p = .013$), anger ($p = .019$), discomfort during infusions ($p = .012$), disruptions in daily activities ($p = .001$) and social exclusion perception ($p = .04$).The feeling of social exclusion ($p = .047$) was notably elevated in severe haemophilia patients, along with infusion-related discomfort ($p = .014$). Moreover, total scores for physical health ($p = .015$), engagement in physical activities ($p = .04$) and treatment-related complications ($p = .04$) varied according to patients' age. Other aspects in accordance with baseline factors studied (severity of haemophilia, pharmacokinetics) showed no significant differences. For half-life, rurioctocog alfa pegol exhibited the longest duration (24.5 h), followed by damoctocog alfa pegol (20.5), octocog alfa (19.3), efmoroctocog alfa (18), moroctocog alfa (16.2) and INN-octocog alfa (12). Regarding average time required to reach 5% of FVIII levels, INN-octocog alfa had the shortest duration (38.2 h), with moroctocog alfa (71), octocog alfa (72.7), efmoroctocog alfa (79.3), damoctocog alfa pegol (92.2) and rurioctocog alfa pegol (110.9) following.

Discussion/Conclusion: Evaluation of pharmacokinetic parameters along with quality-of-life assessments could revolutionise the care of haemophilia patients. Choosing a personalised treatment regimen in correlation with the emotional and physical well-being of patients could lead to more effective clinical strategies.

Disclosure of Interest: None declared.

PO148 | Real world experience using emicizumab in paediatric patients: Clinical features and joint health evaluation

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Introduction: Background: Emicizumab is a humanised bispecific recombinant monoclonal antibody that binds to factor IX and factor X and mimics the function of factor VIII (FVIII). This drug solved some major challenges of haemophilia A (HA) treatment such as administration route (subcutaneous), frequency of administration (from weekly to monthly) and FVIII inhibitor.

Aim: To provide real world evidence from the use of emicizumab in a Paediatric Haemophilia Unit in Spain, from January 2017 to September 2023.

Methods: Retrospective study in a tertiary paediatric hospital in children 0–18 years-old diagnosed with severe haemophilia A under treatment with emicizumab. Apart from relevant clinical data, periodical joint evaluation was collected.

Results: Patients were divided in three groups. Group 1: untreated or minimally treated patients (PUPs; $n = 7$). Group 2: Inhibitor patients receiving concomitant immune tolerance treatment (ITI) ($n = 2$). Group 3: Patients with and without inhibitor receiving emicizumab as prophylaxis ($n = 9$). Median age was 1 (range 0–2), 1 (range 0–1) and 12 years (range 4–18), respectively. Median annual bleeding rate (ABR) in all groups was close to 0 (range 0–2). Only two bleeding events required replacement therapy or bypassing agents. Those two patients who received emicizumab during ITI eradicated inhibitor without major bleeding events. After ITI success, patients continued monotherapy with FVIII.

Periodical joint health evaluation using haemophilia joint health score (HJHS) and haemophilia early arthropathy detection with ultrasound (HEAD-US) was performed in 11 patients between 3 and 18 years-old. Ultrasound finding led us to intensify emicizumab treatment in four patients due to the presence of synovitis (from 15 to 7 days administration schedule). Two of these patients improved HJHS and HEAD-US score after these changes. Other two patients already had articular damage prior to emicizumab initiation. The drug allowed us to optimise the treatment with no major bleeding events unless the presence of arthropathy and also improving their quality of life.

Discussion/Conclusion: Emicizumab seems to be a safe and useful treatment in paediatric patients with HA, including those under ITI treatment. Periodic joint evaluation with ultrasound appears to be an interesting tool to monitorise treatment.

Disclosure of Interest: None declared.

PO150 | Acquired haemophilia—clinical manifestations and management; a single centre experience

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Introduction: Acquired haemophilia A (AHA), a rare bleeding disorder caused by neutralising autoantibodies against activity of coagulation VIII (FVIII:C) occurs in both men and women without a previous history of bleeding. Management of this disorder consists in rapid accurate diagnosis, control of bleeding and eradication of the inhibitor by immunosuppressive therapy (IST).

We report a retrospective cohort of 57 patients (pts) with AHA.

Methods: The diagnosis was based on a positive inhibitor measurement by the Bethesda method (NIJmegen modification, cut off <0.5 BU) in patients with bleeding tendency and aPTT prolongation.

Complete remission (CR) was defined as FVIII levels >50% with undetectable FVIII inhibitor.

Results: Between 2002 and 2023, 58 patients with a median age of 62 years (25–89), were diagnosed with AHA. In 27/58 patients (46.5%) the aetiology was idiopathic and in 31/58 (53.4%) was associated with autoimmune disease (24.1%), malignancy (12%), infection (3.4%), postpartum period (8.6%), drugs (3.4%) and vaccinations (1.7%). The most common symptoms in admission were muscle or soft tissue haematomas (85%).

Forty-one patients were high responders inhibitor titre >5 BU (7–742 BU) and 17 patients a low responders<5 BU (0.88–4 BU). Baseline

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FVIII:C was ≤1% in 12/58 pts, 1%–5% in 35/58 pts, and >5% in 11/58 pts. By passing agents for bleeding control were used in 43/58 pts (74.1%). All patients received IST: prednisolone 1 mg/kg/day per os for 4–6 weeks followed by tapered withdrawal (10 pts), prendisolone and cyclophosphamide 1.5–2.0 mg/kg/day for 6 weeks (47 pts) and cyclosporine 1 pt. Rituximab (375 mg/m^2 weekly for four cycles) was added to treat eight patients which did not respond to initial treatment. Median time to a negative inhibitor detection was 6 months (range 0.5–10). 43/58 (74.1%) had a CR. Thirteen pts (22.4%) relapsed 1–4 months after interruption of IST and associated with malignancy and uncontrolled underlying disease.

Mortality rate was 10.34% (6/58) due to malignancy 6.9% (4/58) and SARS-CoV2 infection 3.4% (2/58). None died due to bleeding or thrombotic complications.

Discussion/Conclusion: Prompt recognition and early initiation of IST together with control of severe bleeding using by passing agents are essential for the outcome of AHA. Inhibitor eradication strategy can be adapted to clinical severity and patient's comorbidities.

Disclosure of Interest: None declared.

PO152 | Clinical outcomes of prophylaxis with extended half-life coagulation factor concentrates or emicizumab in haemophilia

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Introduction: Nowadays, there are many people with haemophilia A or B (PwH A/B) switching from recombinant standard half-life (SHL) to extended half-life (EHL) factor VIII (FVIII) and factor IX (FIX) clotting factor concentrates (CFCs) respectively. Moreover, an increasing number of PwHA also switch from substitutive therapy with concentrates of FVIII to emicizumab. The aim of this study is to describe our experience in clinical practice of switching from SHL to an EHL FVIII/FIX CFC or emicizumab, and the result of the change on bleeding pattern, number of injections, FVIII/FIX administrated and economic outcomes after switching.

Methods: A retrospective study was conducted at a single comprehensive haemophilia centre including 25 PwHA with moderate/severe haemophilia A, who switched from a SHL either to an EHL FVIII CFC or emicizumab and four PwHB who switched from a SHL either to an EHL FIX CFC in the previous year.

Results: The study group comprised 23 PwHA (90%) and four PwHB (100%) with severe haemophilia.

Twenty-one PwH over 12 years of age (19 PwHA and two PwHB). Five PwHA with history of inhibitors against haemophilia A turn to emicizumab. In PwHA, the switch to rFVIII-EHL concentrate was associated with a 41.6% reduction in the number of weekly infusions from a median of 156 to 91 ($p < .015$). In PwHB, the switch to rFIX-EHL achieved a 60% of reduction in the number of weekly infusions from a median of 120 to 48 ($p < .05$). The most frequent reasons for switching to emicizumab were history of inhibitors, administration pathway and frecuency in administrations. PwHA that changed from SHL factor to emicizumab showed significant reduction in the frequency of administration. There was no significant change in annualised bleeding rates, median factor consumption or in economic burden of the prophylaxis.

Discussion/Conclusion: Changing from a prophylaxis with SHL factor concentrates to EHL products or emicizumab shows an improvement in the number of annual factor injections, maintaining excellent haemostatic coverage and without increasing the hospital economic burden. Prophylaxis with rFVIII-EHL, rFIX-EHL products and emicizumab have been shown to be safe in PwH, not developing inhibitors against FVIII, FIX or against emicizumab.

Disclosure of Interest: None declared.

PO153 | Positive clinical impact after switching to turoctocog alfa pegol: Iberian experience

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Introduction: Turoctocog alfa pegol (N8-GP) is a glycoPEGylated recombinant factor VIII (FVIII) with an extended half-life developed for treatment in patients with haemophilia A. It has proven to be safe and effective treatment. We present the largest cohort of PTPs switched to turoctocog alfa pegol. Our objective is to analyse the clinical impact in patients with haemophilia A after switching to turoctocog alfa pegol in patients from Iberian countries.

Methods: Observational, retrospective, multicentre study in centres in Spain and Portugal, which includes patients undergoing prophylaxis treatment with turoctocog alfa pegol. It includes as variables: age, frequency of administration and annualised bleeding rates. A comparison is made with the previous treatment of the same patients.

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Results: Since February 2020, 76 patients with haemophilia A started prophylaxis with turoctocog alfa pegol. The median follow-up was 27.6 months (range 2.3–44.97). The mean age was 34.8 years (range 15–56). 81.57% (62/76) were affected by severe haemophilia A. Fourteen patients had a diagnosis of moderate haemophilia A. 86.84% of patients came from a previous prophylaxis regimen (13.15% previously on demand).

Prophylaxis was initiated according to the personalised pharmacokinetic study with the support of WAPPS-hemo in 85.52% (65/76) and with the objective of reaching trough levels of >3–5 IU/dL.

The main reason for the change was to reduce the number of infusions in 42% of patients (32/76). Other reasons for the change were: to increase through level (12/76), to improve the adherence (9/76) and to improve clinical parameters (20/76).

All patients decreased or at least maintained the number of weekly infusions. The mean ABR decreased (1.72 [0–7] vs. 0.17 [0–2.31]).

No complications such as inhibitor development were observed after changing treatment. Treatment was discontinued in one patient due to entry into a clinical trial.

Discussion/Conclusion: In this study, turoctocog alfa pegol proved to be an effective therapeutic alternative as a prophylaxis regimen that has allowed us to reduce the treatment burden of patients, managing to reduce the number of infusions, reduce the ABR and/or increase the through levels.

Disclosure of Interest: None declared.

PO154 | Real world use of simoctocog alfa in persons with haemophilia A (PwHA) in spain

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Introduction: Simoctocog alfa (Nuwiq®) is a fourth generation recombinant factor VIII (FVIII) with proven efficacy for the prevention and treatment of bleeding episodes in patients with severe haemophilia A. The objective is to analyse the experience of long term prophylaxis with simoctocog alfa in PwHA in nine Spanish hospitals.

Methods: Observational, retrospective, multicentre study, which includes patients undergoing treatment in prophylaxis and immune tolerance induction with simoctocog alfa. Main analysed variables were age, frequency of administration and annualised bleeding rates.

Results: Since 2014 until Juny 2023, 35 PwHA started prophylaxis treatment and immune tolerance induction. with simoctocog alfa. Median age was 9 years (range 5 months–64 years)

77.14% PwHA (27/35) were severe haemophilia A. 34.28% (12/35) were previously untreated patients (PUPs). 2/12 (16.6%) PUPs developed inhibitor against FVIII. All of them had a successful immune tolerance induction with simoctocog alfa. One PUP with FVIII inhibitor started simoctocog alfa as a tolerance induction treatment.

The median ABR was 0 (range 0–4), the median AjBR was 0 (range 0–3).

Treatment was discontinued in six patients due to bleeding events despite prophylaxis (4/6 patients) and they switch to emicizumab. 2/6 patients discontinued simoctocog due to successful inmunotolerance.

Discussion/Conclusion: In our experience, simoctocog alfa is an effective treatment as immune tolerance induction in PwHA with inhibitor against FVIII and as a prophylaxis in PwHA without inhibitor.

Disclosure of Interest: None declared.

PO155 | Pharmacokinetic analysis in patients with haemophilia A in prophylaxis with turoctocog alfa pegol in one centre in spain

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Introduction: Prophylactic treatment with standard half-life (SHL) coagulation factors requires 3–4 weekly periodic infusions. Extended half-life (EHL) factor VIII (FVIII) provides improvements in half-life (t 1/2) and area under the curve (AUC) of 1.3 and 1.25 times compared to SHL products. Turoctocog alfa pegol is one of EHL products. The objective is to describe the pharmacokinetic profile of patients with haemophilia A on prophylaxis with turoctocog alfa pegol in a single centre in Spain.

Methods: Prospective, single centre study. Fourteen patients who started prophylaxis treatment with turoctocog alfa pegol were included. The pharmacokinetic study was using the population pharmacokinetic software WAPPS-hemo. FVIII levels were determined by one-stage assay and a minimal two to three simples are obtained.

Results: Since June 2020, 14 patients with severe haemophilia A started prophylaxis with turoctocog alfa pegol (median follow-up 25 months). The mean age was 29.81 years (15–50).

Prophylaxis was started according to the personalised pharmacokinetic study with the support of WAPPS-hemo and with the goal of reaching trough levels of 3–5 IU/dL. The average dose of 92.11 UI/kg/week.

The pharmacokinetic properties were: median half-life (T1/2; h) of 21.682 ± 6.969, median volume of distribution (Vss; L) of 58.625 ± 8.844 and median clearance (L/h) of 0.149 ± 0.047.

These parameters are better than those described in the Summary of product characteristics (SmPC): T1/2 (h): 19.9, Vss (L): 37.7 and Cl (L/h) of 0.14.

Discussion/Conclusion: In our experience, turoctocog alfa pegol shows an excellent pharmacokinetic profile, which allows us to reduce weekly infusions, ensuring haemostatic coverage and therefore the quality of life of these patients.

Disclosure of Interest: None declared.

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PO156 | Tele-psychological intervention for people diagnosed with haemophilia

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Introduction: Patients with chronic disorders like haemophilia, psychosocial variables have a substantial impact on quality of life. Interventions to support the psychosocial needs of patients and their families, such as providing information and assistance, answering questions and teaching coping mechanisms to lessen the impact of disabilities, may help to improve quality of life for patients' families and maximise patient outcomes.

Methods: The current study aimed to assess the psychiatric and psychosocial aspects of person diagnosed with haemophilia and provide online psychiatry and psychosocial intervention. A retrospective record-based study of participants who received treatment services from KHS Davangere from November 2022 to October 2023.

Results: Patients between age group from 15 to 46 received the services. Behavioural addiction, Attention Deficit Hyperactivity Disorder, Anxiety, Depression Tobacco dependence syndrome, adjustment disorder was commonly reported. The participants were provided with medical and psychological intervention including medication, psychoeducation, coping skill, attention enhancement skills, relaxation and mindfulness techniques, strategies to manage screen time on online basis. The assessment and intervention were carried out by Mental Health Professionals. The patients are in regular follow up with the treatment team and report improvements in psychological distress and functioning.

Discussion/Conclusion: Bleeding disorder has major impact on mental health of the individual and intern affects the QOL. The intervention by multi-disciplinary team including pathologist, psychiatrist, psychologist, psychosocial consultant benefits the client.

Disclosure of Interest: V. M. S.: None declared, S. Hanagavadi: None declared, P. Bhandary: None declared, M. E. R. Consultant for: No conflict of interest, N. Murthy Consultant for: No conflict of interest.

PO157 | The use of the haemophilia joint health score as a monitoring tool for children with severe haemophilia a on emicizumab prophylaxis

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Introduction: The Haemophilia Joint Health Score (HJHS) is an assessment tool designed for the use in patients with haemophilia for the early identification and monitoring of joint arthropathy. Within our centre, we currently have 65 children with a diagnosis of severe haemophilia A, who receive emicizumab as prophylaxis. Every child has an annual review, during which their HJHS is evaluated as part of their physiotherapy review. We sought to evaluate the changes in the HJHS in children with severe haemophilia A receiving prophylaxis with emicizumab.

Methods: We retrospectively collected and analysed the data of 65 children on emicizumab registered at our centre, over a period of 4 years. Patient characteristics collected included the duration of treatment with emicizumab, current inhibitor status and annual HJHS between 2019 and 2023.

Results: The ages of the patients range from 3 months to 16 years. Twenty-two patients were below the age of 6 so were excluded as they would be unable to comply with the functional components of the HJHS, and therefore would not achieve an accurate score. Of the remaining 43 patients, there was an average of three HJHS completed over the 4-year period. All patient's scores were between 0% and 3. 81% (35) of patients scored 0 on each of their annual HJHS, which remained consistent between 2019 and 2023. The remaining eight patients had one HJHS that scored between 1 and 3. On each of these occasions, patients were referred for a further ultrasound or MRI scan. The ultrasound scans showed no joint arthropathy, but all showed a degree of effusion which likely contributed to the change in their HJHS. The MRI scan showed no abnormalities. Four of these patients have since had additional HJHS the following year where their scores returned to 0.

Discussion/Conclusion: From our cohort we can conclude that 100% of patients with severe haemophilia A, on emicizumab for prophylaxis, maintain an HJHS of 3 or below. Of the patients who had a score between 1 and 3, further imaging showed no evidence of haemophilic arthropathy. 50% of these patients have since had a return to a HJHS of 0. Overall, 81% of patients have no changes in their HJHS of 0, indicating optimum joint health.

Disclosure of Interest: None declared.

PO158 | Experience of treatment in children with severe haemophilia B in A single centre

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Introduction: Haemophilia B is a hereditary X-linked recessive disorder that leads to a deficiency of factor IX (FIX). It is considered severe when FIX levels are <1% and can result in spontaneous musculoskeletal bleeding. The primary treatment approach is on-demand or prophylactic replacement therapy with FIX.

Our objective is to analyse the disease progression based on different treatment regimens used in patients under 18 years old with haemophilia B in our centre.

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Methods: For this purpose, we present a descriptive study of two patients under 18 years old diagnosed with haemophilia B and under our care, who have received treatment with various types of FIXs for prophylaxis.

Results: Firstly, we present a 4-year-old patient diagnosed with haemophilia B in 2019 with FXI levels <0.4%. Initially, on-demand treatment with short half-life FIX (SHL, Benefix) was initiated. After experiencing two hemarthrosis episodes in target joints (elbows), it was decided to start secondary prophylaxis with weekly Benefix at the age of 9 months. At 18 months, due to frequent injuries and difficulties with venous access, a switch was made to a long half-life (EHL) FIX, Alprolix, administered weekly. Since then, there have been no further hemarthrosis episodes, and the administration has been spaced to every 10–14 days.

Secondly, we have a 5-year-old child diagnosed with haemophilia B since birth, as he presented with a severe cephalohematoma following and instrumental delivery, requiring transfusions and daily SHL FIX (Benefix) for 14 days. Subsequently, on-demand treatment with Benefix was initiated, requiring factor for four instances due to traumas without hemarthrosis. Due to the increased frequency of infusions, primary prophylaxis with weekly Benefix was started at the age of 2, with a later switch to an EHL factor, Alprolix, which allowed for administration every 14 days. After this change, only one inconsequential hemarthrosis episode occurred, necessitating a dosage adjustment.

Discussion/Conclusion: In conclusion, in our experience the manifestation of haemophilia B varies and, early initiation of primary prophylaxis with factor IX is recommended to prevent joint damage. Specifically, using an EHL factor helps reduce the number of infusions.

Disclosure of Interest: None declared.

PO159 | Development of a core data set for individual treatment plans for patients with congenital bleeding disorders

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Introduction: Currently, in The Netherlands, there is no national consensus on the content of an individual treatment plan for people with a congenital bleeding disorder. A treatment plan contains all information needed by health care providers to prevent or treat bleeds. Each centre uses their own plan, with different data items and answering options, not fully adherent to (inter)national standards for reporting and exchanging health data. This lack of standardisation hampers data exchange between treatment centres and with the Dutch quality registry HemoNED. Moreover, the lack of data reusability increases administrative burden. Therefore, we set out to establish a standardised treatment plan for patients with a congenital bleeding disorder.

Methods: Initiated by the Dutch Association of Haemophilia Treaters, an interdisciplinary committee of haematologists, specialised nurses, data managers and HemoNED representatives drafted a core data set. FAIR data principles (findable, accessible, interoperable and reusable) were adopted. National treatment guidelines and Dutch Health and Care Information models were used as guidance to capture information. (Inter)national standards were applied, including: the Dutch G-Standard to register medication (based on ATC codes), LOINC to register test results and the Diagnosethesaurus (Dutch interface terminology based on SNOMED CT codes) to register diagnoses. Multiple feedback rounds were held, until consensus was reached among health care providers and patient representatives.

Results: Consensus was reached on the following data set: diagnosis; most recent length; weight and relevant laboratory parameters; factor VIII (FVIII) or factor IX (FIX) half-life (if applicable); history of gene therapy; inhibitor status and titre (for haemophilia); allergies or contraindications for relevant treatments; product, dose, and frequency of prophylactic therapy, home treatment and the presence of an extreme fear of injections. The treatment plan for bleeds included product choice and dose for three scenarios: mild, severe and life-threatening bleeds.

Discussion/Conclusion: National consensus has been achieved on a treatment plan for people with a congenital bleeding disorders. We are currently implementing this plan in the electronic health records of all Dutch haemophilia treatment centres to facilitate shared care, aid quality assessments, clinical research and ultimately, to improve the quality of care.

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PO161 | The MAPTO survey, mapping approaches to tolerance in PUP/MTP treatment around the world in the non-replacement era

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Introduction: Previously untreated patients (PUPs) and minimally treated patients [MTPs, i.e., <5 exposure days to factor VIII (FVIII)] with severe haemophilia are at risk for inhibitor development during the first 50 exposure days (EDs) to FVIII. Presently, many PUPs and MTPs receive prophylaxis with emicizumab instead of FVIII. Under emicizumab prophylaxis is FVIII exposure for breakthrough bleeds infrequent. Therefore, it may take years before PUPs or MTPs achieve a total of 50 EDs to FVIII. Yet, obtaining tolerance towards FVIII sooner may be preferred in order to avoid unexpected inhibitor development and treatment failure during breakthrough bleeds or emergency surgery. Tolerance may be achieved by regular low doses of FVIII alongside emicizumab. It is currently unknown whether regular low doses of FVIII have a tolerising effect and reduce inhibitor risk, or whether the effect is opposite and FVIII exposure triggers inhibitor development in PUPs/MTPs. Anecdotal information demonstrates that haemophilia treaters around the world have adopted different strategies. We lack more precise information on this heterogeneity in treatment paradigms. Aim: To describe current practices and perspectives of haemophilia health care providers worldwide on obtaining FVIII tolerance for PUPs/MTPs with severe haemophilia A who use emicizumab prophylaxis.

Methods: We are currently performing a global international survey among a total of >500 haemophilia treaters from all continents addressing real world approaches to obtain FVIII tolerance in PUPs/MTPs with severe haemophilia A on emicizumab prophylaxis and their experiences with the perspectives of parents on potential treatment approaches.

Results: Preliminary results will be presented during the EAHAD conference. We expect to reveal heterogeneous clinical practices, reflecting the uncertainty of clinicians on the best treatment for this vulnerable group of PUPs/MTPs with severe haemophilia A.

Discussion/Conclusion: We will not only learn about the perspectives of haemophilia health care providers, but also whether parents and children are willing to undergo intravenous injections for tolerisation purposes. This information will clarify a need for further research into FVIII tolerisation with additional FVIII exposure, alongside emicizumab prophylaxis.

Disclosure of Interest: None declared.

PO162 | Characteristics of girls with haemophilia A or B included in the pednet registry

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Introduction: Girls with haemophilia A (HA) and B (HB) are often underrecognised and only limited data is available. The aim of this study is to describe the characteristics of girls included in the PedNet registry. PedNet collects data on girls with factor VIII/IX (FVIII/FIX) levels up to 25%.

Methods: Girls* in the PedNet Registry (Clin.gov.trial NCT02979119) with baseline factor FVIII/FIX between <1% and 25% (<0.01–0.25 IU/mL) were included. Girls were followed from diagnosis to: 1 January 2023 or 18 years of age. Descriptive data are presented.

*Assigned at birth female. We use the word girl, but it does not mean it is not inclusive of other genders.

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Results: In total 23 girls were included, four severe (3 HA/1 HB), four moderate (2 HA/2 HB), 15 mild (10 HA/5 HB) with a total follow up duration of 177 years [median age last evaluation was 10.1 (IQR 7.0–14.6)]. Age at diagnosis was at a median of 0.4 years (IQR 0.1–1.2) for severe, 0.0 years (IQR 0.0–0.1) for moderate and 0.7 years (IQR 0.1–5.0) for mild haemophilia. Family history of haemophilia was the reason for diagnosis in 70%. Thirty percent were diagnosed due to bleeding, including one girl (severe HA) diagnosed after a traumatic intracranial haemorrhage and one girl was diagnosed due to excessive bleeding after heel prick test. Genotype was available for 86% and none of the girls developed an inhibitor.

Joint bleeding occurred in 75% of the severe girls, 50% of moderate and 13% of mild. Median age at first joint bleed was 1.3 years for severe, 5.4 years for moderate and 6.3 years for mild haemophilia.

All of the girls with severe and moderate haemophilia received factor concentrate at least once, in contrast to 5/15 with mild haemophilia. Prophylaxis was started in five girls (3/4 with severe, 2/4 with moderate and 0/15 with mild haemophilia). One girl with severe HA was lost to follow up before prophylaxis could be initiated. Age at start of prophylaxis was 1.0 years for severe and 8.6 years for moderate haemophilia. Five girls required surgery, most commonly dental surgery such as extractions and fillings.

Discussion/Conclusion: Data from this registry on girls with factor levels below 25% reveal a significant number of girls with joint bleeding and the need of regular prophylactic treatment. To ensure a timely diagnosis of girls with haemophilia, more awareness is needed and early screening of girls in families with haemophilia is recommended.

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PO163 | Gathering and disseminating standardised gene therapy data—the world federation of haemophilia gene therapy registry

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Introduction: The World Federation of Haemophilia (WFH) has launched the Gene Therapy Registry (GTR) aimed at gathering comprehensive data on all people with haemophilia (PWH) who receive gene therapy globally.

Methods: The GTR is a prospective, observational and longitudinal registry. It was designed to standardise and centralise global data collection by establishing a single, unified repository for the gathering and dissemination of gene therapy data, ensuring mutual benefit for all stakeholders. Data entry occurs once, either directly into the GTR platform or through data transfer from National Registries.

The GTR will disseminate specific de-identified data to various stakeholders. The GTR Scientific Advisory Board accesses global data for monitoring safety and efficacy. Haemophilia treatment centres (HTC) and National Registries will receive aggregated global safety data. Regulatory agencies and Health Technology Assessment organisations can request specific data to inform their decisions, while industry partners will receive product-specific data.

Results: The WFH is engaged with a broad network of HTCs and National Registries to establish mutually beneficial collaborations with the GTR. To foster dialogue and obtain feedback from our collaborators, the GTR National Registries & HTC Consortium has been established. This group includes representatives from Ireland, Sweden, Brazil and Saudi Arabia, and registries from Australia, Canada, France, Germany, Japan, The Netherlands, Spain, the United Kingdom and the United States.

Based on the GTR protocol, core data set and methodology, the European Medicines Agency (EMA) Committee for Medicinal Products for Human Use (CHMP) has shown strong support for the GTR. The CHMP endorses the GTR as the worldwide registry for consolidating all international data on PWH who receive gene therapy and encourages collaboration of all HTCs and National Registries, stating that the WFH GTR is of particular value for post approval safety and efficacy studies of gene therapies and recommending its use as a planned data source for mandated Phase IV studies.

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Discussion/Conclusion: The GTR simplifies the data entry process, facilitates efficient data sharing and provides valuable information to all stakeholders, advancing our understanding of gene therapy's safety, efficacy and long-term effects, ultimately contributing to improved patient care and treatment outcomes.

Disclosure of Interest: None declared.

PO164 | The world federation of haemophilia living guidelines model

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Introduction: Since the publication of the 3rd edition of the World Federation of Haemophilia's (WFH) Guidelines for the Management of Haemophilia in 2020, the WFH has been implementing a Living Guidelines Model (LGM) to ensure recommendations are kept current.

Methods: The LGM is being implemented by a multi-disciplinary Steering Committee (SC), a Guidelines Oversight Committee and topic-specific panels. All groups are composed of healthcare and allied healthcare professionals, people with haemophilia and caregivers, ensuring global representation. Individual recommendations will be updated on a prioritisation and rotational basis, established by the SC. Updates will be posted on the WFH website and in the *Haemophilia* Journal. The first topic selected centred on Adeno-Associated Virus (AAV) Gene Therapy for haemophilia A and B.

Results: The members of the Gene Therapy Panel include 35 healthcare professionals and allied healthcare professionals, people with haemophilia and/caregivers, with the latter two groups making up 25% of the total. The panellists received training in guideline methodology. Four research questions address safety, efficacy, quality of life and site preparedness. The literature search (PubMed, EMBASE and Cochrane Library) identified 44 eligible studies addressing one or more of the research questions. Data extraction is currently underway.

Discussion/Conclusion: Developing and updating WFH recommendations using the LGM allows for a systematic prioritisation of topics and evidence synthesis, with the unit of update as individual recommendations rather than chapters. The recommendations on AAV gene therapy for haemophilia will be published in mid-2024.

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PO165 | Body composition in patients with haemophilia and the impact of severity phenotype and age

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Introduction: Using bioimpedance analysis, literature described an increased body fat distribution and decreased lean mass in PwH compared to healthy controls. However, to provide more precise insights this investigation aims to determine body composition parameters in PwH compared to literature data on the non-haemophilic population by using dual x-ray absorptiometry (DXA), which is known to be the most accurate method. This study further evaluates the (potential) effect of the disease severity and the patients' age on body composition.

Methods: A total of 200 PwH underwent a 7-min whole body DXA screening, using Horizon™ (Hologic, USA; Apex Software; Auto Whole-Body V. 13.6.0.7). Body fat percentage, lean mass in relation to body height (lean/height^2) as well as appendicular fat and lean mass were examined and compared to male European reference data [1]. PwH were further discriminated by severity phenotypes [mild ($n = 44$), moderate ($n = 43$) and severe ($n = 115$)] as well as five age groups [18–29 ($n = 50$), 30–39 ($n = 47$), 40–49 ($n = 26$), 50–59 ($n = 43$) and 60–80 ($n = 38$)].

Results: PwH [aged median 40 (28–55; 1. IQ – 3. IQ) years] showed an overall mean body fat percentage of 29.3% ± 6.2 %. Similar values are seen in the European male population with a mean of 29.3 ± 7.3 %. Total lean/height^2 was 17.5 ± 4.9 kg and also similar compared to the non-haemophilic population (17.8 ± 1.8 kg). Moreover, fat mass did not differ between the severity phenotypes ($p = .470$), though lean mass was significantly lower in patients with severe haemophilia compared to patients with mild haemophilia ($p = .048$). Differentiating the PwH by age groups, the age group 18–29 shows significantly less fat in both total and appendicular compared to PwH of the three age groups older than 40 years (total: $p < .003$, appendicular: $p < .001$). Neither total lean mass (lean/height^2) nor appendicular lean mass differed across age groups ($p > .005$).

Discussion/Conclusion: This study for the first time provides valuable reference data for body composition parameters in PwH. Compared to the European male population, PwH showed similar results regarding total body fat and lean mass. However, patients with severe haemophilia show significantly less lean mass especially compared to patients with mild haemophilia. Body fat percentage and VAT did not differ between the severity phenotypes, but is increased with age.

Disclosure of Interest: None declared.

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PO166 | Psychometric evaluation of the haem-a-QoL in adults with haemophilia B

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Introduction: Haemophilia B can negatively impact health-related quality of life (HRQoL). Validated patient-reported outcomes (PROs) help us to understand treatment effects from the patient perspective in haemophilia B clinical trials. The Haemophilia Quality of Life Questionnaire for Adults (Haem-A-QoL) is a PRO that assesses 10 domains of HRQoL. Published evidence supports content validity and measurement properties of the Haem-A-QoL. Psychometric analyses were needed to generate supplemental evidence in haemophilia B patients and refine thresholds for clinically meaningful change.

Methods: A psychometric evaluation of the Haem-A-QoL was conducted using data from the phase 3, open-label, single arm BeneGene-2 trial of fidanacogene elaparvovec in 45 adult males with moderately severe to severe haemophilia B (NCT03861273). Data collected up to 12 months were used to analyse reliability, validity, responsiveness/ability to detect change, and meaningful within-patient change for the Haem-A-QoL total score and Physical Health domain (the latter was a BeneGene-2 secondary endpoint).

Results: Haem-A-QoL total score (Cronbach's alpha 0.91–0.96) and Physical Health (0.86–0.90) showed excellent internal consistency reliability, which was further supported by strong corrected item-total correlations. Test–retest reliability was moderate to good for Haem-A-QoL total score [intraclass correlation coefficient (ICC) 0.55–0.70] and Physical Health domain (0.56–0.86). Known-groups evidence was demonstrated by significant mean differences in Haem-A-QoL total and Physical Health domainusing the EQ-5D-5L and Haemophilia Life Impacts Questionnaire (HLIQ) items. Cross-sectional Spearman correlations ≥0.40 (absolute values) with EQ-5D-5L, Haemophilia Joint Health Score (HJHS) and HLIQ items supported convergent validity of the Haem-A-QoL total score and Physical Health domain. Using the same PROs, Spearman correlations ≥0.30 (absolute values) for score changes supported responsiveness of the Haem-A-QoL total score and Physical Health domain. Thresholds for meaningful within-patient improvement were estimated at 5–8 points for Haem-A-QoL total score and 6–12 points for Physical Health.

Discussion/Conclusion: Collectively, these psychometric analyses support existing literature on content validity and measurement properties of the Haem-A-QoL for use in clinical trials of haemophilia B, and corroborate published thresholds for clinically meaningful improvement.

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PO167 | The haemophilia activities list: Psychometric evaluation in adults with haemophilia B

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Introduction: Haemophilia B clinical trials may be enriched by including health-related quality of life (HRQoL) endpoints because patients with haemophilia B often experience impaired HRQoL. The Haemophilia Activities List (HAL) is a self-report measure assessing seven domains of physical functioning in adults with haemophilia. Further validation evidence was needed to support its fitness-for-purpose for use in clinical trials and to define thresholds for clinically meaningful change.

Methods: BeneGene-2 (NCT03861273) is a phase 3, open-label, single arm trial of fidanacogene elaparvovec. Data collected up to 12 months from 45 participants (adult males with moderately severe to severe haemophilia B) were used to evaluate psychometric properties of the HAL total score and Complex Lower Extremity Activity component score (the latter was a secondary endpoint in BeneGene-2). Reliability, validity and responsiveness (ability to detect change) were assessed, and thresholds for meaningful within-patient change were estimated.

Results: Strong evidence of internal consistency reliability was demonstrated for HAL total score (Cronbach's alpha 0.97–0.98 across assessments) and Complex Lower Extremity Activity (0.92–0.95). Corrected item-total correlations also supported internal consistency of Complex Lower Extremity Activity (0.33–0.89, $p < .05$). Test–retest reliability was moderate to good for HAL total score [intraclass correlation coefficient (ICC) 0.65–0.87] and Complex Lower Extremity Activity (0.67–0.89). Convergent evidence came from cross-sectional correlations ≥0.40 (absolute values) with EQ-5D-5L, Haemophilia Joint Health Score (HJHS) and Haemophilia Life Impacts Questionnaire (HLIQ) items. Known-groups evidence was demonstrated by significant mean differences in groups based on EQ-5D-5L and HLIQ item scores. Responsiveness was supported by significant mean differences in changes in HAL total score based on HLIQ item groups and changes in Complex Lower Extremity Activity based on PGIC-H. Thresholds for meaningful within-patient improvement were estimated at 3–6 points for HAL total score and 3–7 points for Complex Lower Extremity Activity.

Discussion/Conclusion: Collectively, these findings further validate the psychometric properties of the HAL for use in clinical trials for haemophilia B. The thresholds for clinically meaningful improvement

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derived in this study can aid in interpreting change in the context of a clinical trial.

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PO168 | Ultrasound in haemophilia and sports: Detection of bleedings and safe return to sport determination

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Introduction: Musculoeskeletal Ultrasound (MskUS) is the ideal method to detect and monitor intra-articular and intramuscular haemorrhages allowing haemophilic patients to return to their usual sport practice with the lowest risk of relapse as possible, or avoiding a new injury. It allows safely patient escort to careful re-incorporation to their sporting activity.

Methods: Our group of athletic patients (4–27 year old) is made up mostly of children and adolescents who play soccer recreationally, in a supervised way. One of them plays on a local competitive team and another plays semi-professional basketball. Basketball player suffers the most despite being in prophylaxis. A mild haemophilia A patient developed an acute compartmental syndrome after receiving an impact while playing soccer. Patients who perform swimming have not presented significant haemorrhages. Most severe muscular injuries occurred from direct impact while a minority caused by overload.

Results: MskUS is the ideal method for evaluating intra-articular bleeding as well as periarticular or muscular soft tissues haemorrhage. It is an economical, fast and radiation-free method that allows us to assess size of haematoma, its relationship with the bone plane to avoid the formation of myositis ossificans and monitoring of its size reduction until the injury is completely healed, allowing the safe return to usual sports activity. It can also detect uncommon bleeding manifestations as acute compartment syndrome when critical increase in pressure within a confined osseo-fascial compartment happens, declining perfusion pressure that can lead to irreversible tissue damage. It allows detection of small haematomas not available in physical examination as well as interstitial haemorrhage. Haemorrhagic involvement of the tendons and their sheaths are also valorated. Regarding the most limiting and disabling intra-articular haemorrhage due to its possible association with osteocartilaginous damage and synovial hypertrophy, it allows control of its resolution and even guides for evacuation of haemorrhage procedure.

Discussion/Conclusion: MskUS allows safe monitoring return times to sports activity. Working in an Interdisciplinary Team provides an efficient Diagnostic Method, a very useful tool for patient support, approaching current accompaniment requirements of our patients in their choices.

Disclosure of Interest: None declared.

PO169 | Risks of ignoring limits in non severe haemophilia: Advantages of the interdisciplinary team in emergency management

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Introduction: Bleedings in mild haemophilia can be underestimated and often minimised by the patient himself exceeding recommended limits to avoid injury and not recognising or missing alarm signals.

Teamworking has well known advantages and added values when members use their own specialised knowledge and that generated as result of each other's experience to work on common goals. It is specially useful in emergency situations, highlighting the importance of performance as an Interdisciplinary Team (IT).

Methods: A 17-year-old boy with mild haemophilia A presents with significant pain radiating to his knee after a soccer game. Ultrasound (US) is requested to assess possible joint bleeding. Pain increases with progressive functional impotence and difficulty walking. When performing US, minimal joint involvement was detected. Significant increase in the volume of the thigh caught radiologist attention valuing acute haemorrhage close to bone plane and interstitial haemorrhage on overlying muscular planes. Evaluation of the IT (haematologist, traumatologist and radiologist) was urgently activated suspecting acute compartment syndrome (ACS) based on clinical and US findings taking the required prophylactic measures.

Results: Compartment syndrome is an uncommon bleeding manifestation occurring when a critical increase in pressure within a confined osseo-fascial compartment happens. Subsequent decline in perfusion pressure can lead to irreversible tissue damage. When necessary treatment is prompt surgical fasciotomy.

Patients with mild haemophilia sometimes do not recognise themselves as haemophiliac, failing to get awared of the potential severity of their pathology, as the case of this patient who did not measure the risk of an impact while playing soccer, leading to an ACS. Beyond this, it is important to highlight the increase in suspicion that is generated with IT interaction, being useful to take into account this unusual entity that might otherwise have gone unnoticed.

Discussion/Conclusion: Regression of the process was long, not requiring invasive procedures for its resolution.

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Brainstorming functions better in interactive group sessions. Fluid and constant communication between the group reinforce the skills of each professional, which are enriched with the knowledge and experiences of the rest of the colleagues. The interaction of the team helps raise alarm signals, always in benefit for the patient.

Disclosure of Interest: None declared.

PO170 | Healthcare resource use and related costs of haemophilia A in french adult patients in 2021: A nationwide claims database analysis

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Introduction: There are few data on healthcare resource use and related costs of French haemophilia A (HA) patients. The aim of this study was to describe these features in HA adults according to severity in France in 2021.

Methods: This study used the French nationwide claims database (SNDS). HA patients were identified by the ICD-10 code D66. Adult patients alive on 1 January 2021 were selected. A control group without HA matched on age, gender and region of residence was randomly selected in the database. Sub-group analyses were performed according to the treatment pattern (as a proxy for severity). Direct costs were estimated in a collective perspective.

Results: A total of 4149 adult patients with HA were identified. Mean age was 44 years and 96.8% were males.

Among the patient's population, 3237 (78.0%) and 790 (19.0%) patients without inhibitors were treated on demand and in prophylaxis, respectively, and 28 (0.7%) and 94 (2.3%) patients with inhibitors were treated on demand and in prophylaxis, respectively.

Compared to controls, patients with HA had significantly more frequent consultations with general practitioners (76.9% vs. 68.4%) and hospital specialists (54.5% vs. 25.6%), nurses (68.5% vs. 49.8%), physiotherapists (19.7% vs. 13.4%) and visits to emergency room visits (15.1% vs. 12.1%). They were more frequently treated with analgesics (53.8% vs. 45.9%) and corticosteroids (16.2% vs. 12.5%) but less frequently with non-steroid anti-inflammatory drugs (16.7% vs. 22.7%). The proportion of HA patients hospitalised was higher than controls, overall (22.5% vs. 14.2%) and for bleeding (2.0% vs. 0.2%) and orthopedic surgery (6.4% vs. 3.6%).

The mean and median annual direct medical costs varied strongly according to treatment modalities and presence of inhibitors:

—€12,817 and €1220 for adults treated on demand without inhibitors;

—€90,368 and €36,141 for adults treated on demand with inhibitors;

—€297,643 and €261,302 for adults treated in prophylaxis without inhibitors;

—€445,132 and €437,865 for adults treated in prophylaxis with inhibitors.

Most of the costs was related to antihaemophilic drugs: 65%, 61%, 94% and 93% respectively in the four treatment groups.

Discussion/Conclusion: These results highlight the burden of HA in terms of healthcare resources utilisation and cost. The cost of haemophilia A varied greatly with disease severity and was mostly due to the use of antihaemophilic drugs.

Disclosure of Interest: None declared.

PO171 | The evaluation of joint health and health-related quality of life in children with haemophilia: A cross-sectional single-centre study

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Introduction: Although prophylactic therapy is the gold standard of care in the management of children with haemophilia, it does not completely eliminate the risk of developing symptomatic haemophilic arthropathy and/or subclinical joint bleeding. Therefore, early evaluation and the diagnosis of arthropathy should be the mainstay of the follow-up. There are some recommended outcome assessment measures of body structure and function to investigate the impact of bleeding on the joints. Our aims in our study were to investigate the joint health and overall health with physical examination, and radiological imaging to determine early subclinical haemophilic arthropathy, and to assess health-related quality of life of the patients.

Methods: Thirty-nine children with haemophilia (35 with haemophilia A, four with HB) who were older than 4 years and followed up regularly in our centre were evaluated. Concurrent joint health assessments with HJHS 2.1 and HEAD-US, and simultaneous health-related quality of life scales (EQ-5D-3L, EQ-VAS, Haemo-QoL/ Haem-A-QoL) were done.

Results: Twenty-four had severe haemophilia, eight with moderate and seven with mild haemophilia. The median age of the patients was 13 years (4.4–24.15). All severe patients and two patients with moderate haemophilia were on prophylactic therapy. None of the patients had positive inhibitor. The lifetime bleeding and annual joint bleeding rates were correlated with the HEAD-US, but not with annual bleeding rate. HJHS and HEAD-US scores were not correlated at the patient level whereas negligible positive correlation was found at the joint level. HEAD-US scores varied with the severity of haemophilia. Health-related quality of life scales did not change with the severity of haemophilia, nor was it correlated with HEAD-US and HJHS.

Discussion/Conclusion: In conclusion; it is important to evaluate the HEAD-US and HJHS scores together, since the correlation is weak. In terms of the development of haemophilic arthropathy in childhood, the group that needs to be the most focused is children with severe haemophilia. Even subclinical arthropathy was not detected in patients

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with mild haemophilia, no difference was found between mild, moderate or severe haemophilia in terms of health-related quality of life scales. Therefore, although the severity of haemophilia and the joint scores of patients may vary, mild and moderate haemophilia should not be ignored when the health is evaluated as a whole.

Disclosure of Interest: None declared.

PO172 | Inhibitor development in mild haemophilia A: Four patients

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Introduction: Mild haemophilia A is an X-linked bleeding disorder defined by factor VIII (FVIII) levels between 5 and 40 U/dL. Diagnosis occurs later in life compared to severe or moderate disease. Although bleeding episodes are particularly common after trauma, their unexpected occurrence can be potentially life-threatening if diagnosis is missed or delayed. The inhibitor risk is reported to be 20%–30% in severe haemophilia A and 3%–13% in mild haemophilia A. However, unlike severe or moderate haemophilia A, mild haemophilia A has a lifelong risk of inhibitor formation. Because inhibitors often cross-react with the patient's endogenous FVIII, reducing endogenous FVIII plasma levels to less than 1 U/dL, inhibitors can dramatically alter the clinical phenotype. Some specific F8 missense mutations predispose to inhibitor development.

Methods: In this study, the demographic information and genetic mutations of four patients diagnosed with mild haemophilia A who developed inhibitors and from three different families treated in our clinic were evaluated.

Results: In this study, inhibitor development was observed in four of six mild haemophilia A patients carrying two different mutations shown in three different families. These mutations were not reported as mutations with high inhibitory risk in previous studies.

Discussion/Conclusion: Knowing the mutations that have a high inhibitory risk in mild haemophilia A patients is important to closely follow the patients in this regard. The fact that these patients with mild bleeding clinics lead very active lives compared to patients with severe haemophilia, and when inhibitors develop, they turn into heavy bleeding clinics like patients with severe haemophilia, makes the management of these patients difficult. While the development of inhibitors at an early age in patients with severe haemophilia makes it easier for the family and the patient to accept this situation, the development of inhibitors in mild haemophilia patients at later ages makes the acceptance process difficult. If a patient diagnosed with mild haemophilia says that their family member has a severe haemophilia individual, this should raise the possibility that this individual may have developed an inhibitor. It is also difficult for patients with mild haemophilia A to use bypass medications because they do not receive prophylaxis and do not know how to self-administer intravenous medication at home due to rare factor infusions.

Disclosure of Interest: None declared.

PO173 | Real-world experience of emicizumab prophylaxis in children with severe haemophilia A: I year follow-up study in egypt

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Introduction: Emicizumab is a novel prophylactic medication used to treat patients with haemophilia A. It is indicated to minimise the frequency of bleeding episodes and the severity of serious bleeding in patients with haemophilia A with and without inhibitors. Real-world data and study data regarding prophylactic therapy with emicizumab in paediatric cohorts with haemophilia A is limited in Egypt.

This study aimed to investigate the real-world experience of Egyptian haemophilia A children with and without inhibitor on emicizumab.

Methods: This prospective study was conducted at Pediatric Hematology Clinic, Zagazig University in collaboration with Pediatric Department, Kafrelsheikh University Hospital, and Pediatric Department, Mansoura University Hospital, Egypt from April 2021 to August 2023. Fifty-nine children with severe haemophilia A received emicizumab prophylaxis. The mean age of patients included in the study was 6.67 ± 4.5 years. Out of them, 30 children were with factor VIII (FVIII) inhibitors (50.9%), and 29 children were negative for inhibitors (49.1%). Full medical history and meticulous clinical examination was done. In addition, annual bleeding rates (ABR), Haemophilia Joint Health Score (HJHS) and Functional Independence Score in Haemophilia (FISH) were assessed before receiving emicizumab prophylaxis and after 12 months of regular emicizumab prophylaxis.

Results: A significant reduction was observed in median ABR, from 48 (Interquartile range 36–48) to 0 (IQR 0.0–1), and HJHS, from median 15 (IQR 6.5–21.5) to 9 (IQR 2.5–14).

Moreover, there is statistically significant improvement in FISH score after one year of prophylactic therapy with emicizumab in haemophilic children (p-value $< .001$).

Discussion/Conclusion: Emicizumab prophylaxis markedly decreases bleeding episodes, improves functional ability and joint status in children with severe haemophilia A.

Disclosure of Interest: None declared.

PO174 | Successful management of haematuria with bypassing agents for paediatric congenital haemophilia a with inhibitor: A case report and literature review

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Introduction: The appearance of an inhibitory antibody to factor VIII (FVIII) is a rare but serious complication of haemophilia treatment of patients with haemophilia A. Haemophilia patients with inhibitors receive bypassing agents for treatment or prevention of bleeds.

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Haematuria is a frequent occurrence in persons with haemophilia resulting in a worsening of quality of life.

Methods: Herein, we report a paediatric congenital severe haemophilia A with inhibitor who presented with macroscopic haematuria was treated with bypassing agents.

Results: Case: A 14-year-old male with severe haemophilia A with inhibitor was admitted to paediatric haematology unit with asymptomatic macroscopic haematuria. Vital signs were stable. Radiologic imaging studies of the abdomen and pelvic ultrasonography were performed to determine a microthrombus in his urinary bladder. The patient was diagnosed with severe haemophilia A (FVIII level: 1%) when he was 8 months old. However, he was on episodic therapy due to the non-compliant family, and he had a high FVIII inhibitor titre (9.4 BU). The patient was started on vigorous hydration and placed on complete bed rest. The patient had been administered two doses of aPCC. Two days later, after receiving four doses of aPCC, the haematuria persisted. aPCC was discontinued and rFVIIa was started at 90 μg/kg per dose. There doses is total. Then treatment with rFVIIa at 90 μg/kg per dose every 6 h was continued in the hospital 4 days. Four days later, after receiving 19 doses of rFVIIa, the haematuria resolved. An ultrasound of his urinary bladder showed normal results. The rFVIIa were discontinued, as was hyperhydration. The patient was discharged with aPCC 3 days a week as a secondary prophylaxis. He is on follow-up in outpatient clinic with no bleeding and normal kidney functions.

Discussion/Conclusion: In congenital haemophilia A, the development of inhibitors against FVIII continues to be the most serious complication of haemophilia A management. Even though haematuria in haemophilia is usually considered a benign condition, data in the literature are different. Macroscopic haematuria is a significant problem in haemophilic subjects. For the right management of haematuria with possible renal dysfunction, more studies are necessary.

Disclosure of Interest: None declared.

PO175 | Long-term analysis of real clinical practice of emicizumab treatment in patients with severe haemophilia A with and without FVIII inhibitors

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Introduction: Patients with severe haemophilia A (PwHA) have benefits from prophylaxis. Emicizumab demonstrated valid evidence of effectiveness and safety from clinical trials but a long-term real-world data of emicizumab treatment is high interesting. The goal is to evaluate the effectiveness and safety of emicizumab in real clinical practice.

Methods: The retrospective analysis of data from 33 adult PwHA on emicizumab was made. Eight PwHA with inhibitors, and 25 PwHA without inhibitors. At the time of data collection, all PwHA had been receiving emicizumab therapy for at least 6 months. Effectiveness indicators were the number of all bleeding episodes, joint bleedings, treated bleedings and spontaneous bleedings. An analysis of adverse events related to emicizumab was made.

Results: Mean follow-up of emicizumab treatment was 19.4 months for the group of PwHA with inhibitors and 27.8 months for the group of PwHA without inhibitors. Ten patients received emicizumab for more than 24 months, and 10 for more than 36 months. Thus, the majority of the observed cohort received emicizumab therapy more than 2 years. Six out of eight PwHA with inhibitors experienced life-threatening bleedings before starting emicizumab treatment, while among PwHA without inhibitors this frequency was lower – 16% of PwHA. The use of emicizumab resulted in a statistically significant reduction in the frequency of all types of bleedings, regardless of the presence of inhibitors. The median changes were: for all bleedings −14.8 for PwHA with inhibitors (p-value .01368) and −4.5 for PwHA without inhibitors (p-value < .001), for spontaneous bleedings – 14.6 for PwHA with inhibitors (p-value < .001) and −4.0 for PwHA without inhibitors (p-value < .001), for treated bleedings – 13.7 for PwHA with inhibitors(p-value .1403) and – 4.0 for PwHA without inhibitors (p-value < .001), for hemarthrosis – 16.87 for PwHA with inhibitors (p-value .1415) and – 3.0 for PwHA without inhibitors (p-value < .001). An adverse event related to emicizumab was registered for only one patient: a local hematoma was developed after the emicizumab injection.

Discussion/Conclusion: The long-term use of emicizumab in real clinical practice led to a significant reduction in the frequency of all types of bleedings, regardless of the presence of inhibitors. Emicizumab demonstrated good safety in the cohort.

Disclosure of Interest: None declared.

PO176 | Hacettepe experience including circumsission with extended half-life factor VIII fusion protein (rFVIIIFc) that has recently become available in turkiye

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Introduction: The extended half-life (EHL) factor VIII (FVIII) concentrate rFVIIIFc was the first approved Fc-fusion protein for the treatment of patients with haemophilia A in all age groups in Europe in 2015. It was available since March 2023 in Turkiye, but a compassionate use program was first initiated in 2020 in a small number of patients. From the day of the availability 20 severe haemophilia A patients were received rFVIIIFc in our department. Here, we would like to show our encouraging 6-month single-centre experience with rFVIIIFc, a promising therapeutic agent even in low- and middle-income countries.

Methods: The joint bleeding frequency of 20 severe haemophilia A patients treated with rFVIIIFc in the last 6 months, the surgeries in which they experienced and other bleeding events, treatment doses

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they received were retrospectively reviewed. One patient was on compassionate use program since 2020. Median age is 13 years (range 3–28 years) and all were previously treated patients without inhibitor.

Results: Circumcision operation was done in a 7 years old boy who was on rFVIIFc treatment with a dose of 60 U/kg, 4 days interval. Treatment of 1 x 1250 Unit rFVIIIFc was given as the day before circumcision is a prophylaxis day and 1 x 1250 U just before circumcision surgery and no bleeding during and after the operation was reported. Prophylaxis was continued from the 5th day after the last dose. Another 13-year-old boy had a traumatic cut on his hand, so he needed stitches. Before this event, he did not need additional factor replacement because he received a dose of 50 U/kg rFVIIIFc as prophylaxy on that day. In the other three patients, changes were made in dosage and frequency of administration due to existing joint problems.

Discussion/Conclusion: Joint bleeding was not observed in any of the patients who received treatment at the appropriate dose and interval with EHL, which has been available for a short time in our country, and the bleeding caused by circumcision and traumatic incision could be effectively controlled without the need for additional doses. It was thought that it would be appropriate to re-evaluate the results in a longer follow-up period by increasing the number of patients.

Disclosure of Interest: None declared.

PO177 | Carriers—the great psychological darkness beyond bleeding events

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Introduction: Genetic counselling, testing, and prenatal diagnosis are vital for comprehensive haemophilia care. Haemophilia carriers often experience reduced QoL, particularly in mental health. However, the broader evaluation of QoL, considering physiological, psychological and social factors, remains limited in the literature and clinical practice.

Methods: A novel single-centre approach enrolled 20 confirmed haemophilic carriers in a coaching program. Comprehensive physician examinations were conducted, documenting patient characteristics and medical history. The coaching program assessed physiological and psychological burdens. Qualitative data on QoL were collected across all life stages, following WHO guidelines. Patients' qualitative statements about their QoL were clustered based on frequency.

Results: Participants (average age 28.7) were mostly mothers with an average of 2.2 children per participant, including one pregnant participant. Twelve had haemophilia A, and eight had haemophilia B, with no discernible differences in QoL between the groups. Participants' concerns fell into nine thematic clusters, with heavy menstrual bleeding and concerns about their children's well-being being top priorities.

Discussion/Conclusion: Being a haemophilia carrier significantly impacts women's QoL, necessitating innovative management strategies. Currently, minimal support and resources are available for these individuals. Recommendations include improving support, allocating more resources and conducting further research to better understand the challenges faced by haemophilia carriers.

Disclosure of Interest: None declared.

PO178 | Optimising joint health in haemophilia patients: Insights from a retrospective cohort study

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Introduction: Effective management of joint damage in haemophilic patients is crucial.[1,2]

This retrospective cohort study aimed to compare outcomes between proactive and reactive approaches guided by joint ultrasound in treating severe haemophilia patients at the Haemophilia Comprehensive Care Centre (HCCC) in Duisburg, Germany

Methods: Historically, the centre followed reactive guidelines, conducting joint ultrasounds upon patient discomfort or bleeding reports. Treatment, including radiosynoviorthesis (RSO), was adjusted as needed. In 2020, a proactive strategy was adopted, with annual ultrasounds on all ankle and knee joints. Quarterly ultrasounds were conducted if 'silent symptoms' or joint degradation occurred.

Results: Between 2020 and 2022, 1193 joints in 688 patients were examined, with 103 having severe haemophilia A or B. A total of 656 joint ultrasounds were performed, resulting in therapy adjustments. Prior to 2020, seven RSOs of ankle joints and three RSOs of knees were performed, compared to only two RSOs of ankle joints after 2020.

Discussion/Conclusion: These findings demonstrate that proactive ultrasound monitoring of ankle and knee joints, coupled with appropriate prophylactic factor therapy adjustments, reduced joint degradation in terms of severity and frequency. This approach provides valuable insights for enhancing joint health in haemophilia patients.

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Disclosure of Interest: None declared.

PO179 | Use of low-dose eloctaae~ three times a week in prophylaxis in a volleyball player patient with severe haemophilia A

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Introduction: For efmoroctococcus alfa (Elocta), although the recommended dose is 50 IU/kg every 3–5 days in long-term prophylaxis, dose adjustment may be made in the range of 25–65 IU/kg depending on the patient's response, and in some cases, especially in younger patients, shorter dose administration intervals or higher doses may be required. Here, we present a volleyball player patient who was given 1500 (21 μ/kg) standard half-life (SHL) recombinant factor VIII (FVIII) three times a week and was switched to Elocta prophylaxis at the same dose and observed an increase in quality of life.

Methods: The patient was diagnosed in 2008 at the age of 5.5 months and was started on FVIII prophylaxis at the age of 2 years. There was no major bleeding during the follow-up. In 2020, she started training with the school volleyball team under FVIII prophylaxis. However, since he gained weight during this period, it was observed that he complained of pain in the arm and leg joints, which reduced the quality of life, especially on the days when he did not take prophylaxis. In March 2023, Elocta prophylaxis (1500 IU, three times a week) was introduced.

Results: It was observed that our patient, who continued volleyball training regularly with this prophylaxis, did not have joint pain and bleeding for seven months.

Discussion/Conclusion: While classical (SHL) FVIII drugs are halved in the blood after 8–12 h, this period can increase up to 14–18 h in extended half-life factors. In other words, it increases the current half-life by about 1.5 times. As in our patient, when a patient who does active sports and uses 3 x 1500 IU FVIII/week switches to extended half-life factor at the same dose, it has been observed that the factor activity continues longer and he maintains a more active and painless sports life.

Disclosure of Interest: None declared.

PO181 | The histopathological landscape of synovitis in haemophilic arthropathy

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Introduction: Despite the dramatic improvement in the management of patients with haemophilia, some patients still experience synovitis as a consequence of subclinical or clinically overt recurrent joint bleeding. A deeper knowledge of haemophilic synovitis may help personalise treatment to prevent or delay the development of haemophilic arthropathy. We studied the histopathological aspects of the synovial membrane of patients with haemophilia undergoing orthopaedic surgery.

Methods: Synovial membrane samples were collected during surgery, following good clinical practice. haematoxylin–eosin colouration and immunohistochemical analysis were performed. Two synovitis scores currently used for rheumatoid arthritis were applied, namely the Krenn and the Humby scores. We evaluated synovial collagen fibrosis by means of Masson trichromic staining and iron deposits with Perls histochemical stain.

Results: Nine patients (six severe haemophilia A, one moderate haemophilia A and two severe haemophilia B), mean age of 41 ± 14 years, were included during orthopaedic surgery (four total knee replacement, one arthroscopic knee synovectomy, two total ankle replacement and two arthroscopic ankle debridement).

All samples were characterised by synovial hyperplasia and haemosiderin deposits. In seven out of nine samples a pauci-immune infiltrate was observed, whereas in two samples a lymphoid-myeloid infiltrate with lymphoid aggregates was present. All cases showed ≥1 grade fibrosis, with eight out of nine cases showing moderate to severe subintimal fibrosis and only one case with lympho-myeloid infiltrate exhibiting mild fibrosis. Cases showed mild (33%), moderate (33%) or severe (33%) iron deposition with equal distribution.

Discussion/Conclusion: In haemophilic arthropathy, we found typical characteristics of the blood-induced synovial hyperplasia in the majority of the studied synovial membranes, with a pauci-immune infiltrate as in osteoarthritis. By contrast, lymphoid aggregates as observed in inflammatory arthritis were less frequent. Fibrosis and iron deposition were more frequent than in osteoarthritis. It should be noted that all the samples were collected from patients undergoing orthopaedic surgery due to long-lasting synovitis. A larger study may help clarify if a different histopathological landscape exists at different stages of arthropathy and if the presence of specific features may predict the response to different therapeutic approaches.

Disclosure of Interest: None declared.

PO182 | Simulation of extended half-life replacement fix therapy dosing to achieve comparable fix activity to that of fidanacogene elaparvovec gene therapy in haemophilia B patients

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Introduction: Standard-of-care for severe haemophilia B is prophylactic coagulation factor IX (FIX) replacement therapy [such as eftrenonacog alfa (Alprolix) 50 IU/kg once weekly or 100 IU/kg every 10 days]. Fidanacogene elaparvovec gene therapy (referred as GTx) is a recombinant adeno-associated virus vector carrying the gene that encodes for a high activity variant of human FIX. The objectives were to determine the dose and frequency of FIX prophylaxis (using Alprolix as the example) required to maintain trough FIX activity at levels predicted for GTx up to 25 years.

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Methods: A previously developed longitudinal pharmacometrics model of FIX activity (Actin FSL one-stage assay) following GTx administration was used as a reference response for 25 years. FIX activity following Alprolix dosing was simulated for 500 virtual individuals using a published population pharmacokinetic model.[1] At each year for 25 years, the dose (fixed once weekly) and frequency (fixed 50 IU/kg) required to achieve trough FIX activity comparable to the time-matched mean GTx response was determined for each individual.

Results: The mean GTx response at Years 1, 5, 10 and 25 were 15.3, 11.2, 8.12 and 4.40 IU/dL, respectively. The median [90% prediction interval (PI)] Alprolix dose required to maintain trough FIX activity at the reference during Years 1, 5, 10 and 25 were 251 (145, 493), 174 (101, 342), 117 (67.8, 230) and 47.8 (27.7, 94.0) IU/kg, respectively. The median (90% PI) cumulative dose required in the first 1, 5, 10 and 25 years was 13,047 (7546, 25,653), 54,494 (31,516, 107,147), 90,088 (52,104, 177,134) and 146,630 (84,804, 288,302) IU/kg, respectively. The median (90% PI) frequency required during Years 1, 5, 10 and 25 were every 2.72 (2.06, 3.56), 3.42 (2.54, 4.51), 4.35 (3.23, 5.84) and 7.18 (5.24, 9.72) days, respectively.

Discussion/Conclusion: The simulated Alprolix doses and frequencies required to maintain reference FIX activity levels comparable to GTx exceeded 100 IU/kg once weekly and 50 IU/kg once weekly in the first 10 years. These are conservative estimates as additional doses might be needed for on-demand treatment of bleeds. This reinforces that GTx results in FIX activity not achievable within the labelled posology for Alprolix.

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Disclosure of Interest: J. Wojciechowski Employee of: Pfizer, Inc, P. Gaitonde Employee of: Pfizer, Inc, L. Wilcox Employee of: Pfizer, Inc.

PO183 | Women living with bleeding disorders: Insights from a nordic survey study

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Introduction: Women with bleeding disorders, including carriers, face multiple, additional challenges compared to men with bleeding disorders, including heavy menstrual bleeding and increased risk of bleeding complications during pregnancy and childbirth. These women may also face obstacles with regular follow-up, social perception and reduced quality of life. This survey aims at gaining insights in the women's current perspective and need for improved information and support in four Nordic countries.

Methods: Web-based surveys sent via local patient organisations to their members were carried out by women diagnosed with or being carriers of a bleeding disorder in Denmark (D), Finland (F), Norway (N) and Sweden (S). The surveys consisted of 31 (F,N) and 46 (D,S) questions about medical history associated with bleeding phenotype, family planning and childbirth, healthcare, support and information, and social perception. The survey designs used skip logic and respondents could also choose to skip questions.

Results: In total, 303 women across the four Nordic countries responded (D, $n = 64$, F, $n = 46$, N, $n = 69$, S, $n = 124$), and 66% ($n = 199$) were older than 40 years. Fifty four percent ($n = 163$) reported having a diagnosis of a bleeding disorder and 42% ($n = 126$) reported being carriers. As many as 77% ($n = 231$) experienced problems related to bleeding, 56% ($n = 128$) stated having frequent bleeding problems (several times per week to monthly), 87% ($n = 201$) experienced heavy menstrual bleeding. Despite having experienced frequent bleeding problems, only 45% ($n = 109$) were under regular follow-up. This proportion varied across the individual countries and the gap between women who experienced frequent bleeding problems and those reporting to be under regular follow-up was 22%–27% (F,N) and 3%–5% (D,S). Interestingly, about half of the respondents (48%, $n = 108$) did not know about their carrier or diagnostic status before their first pregnancy and a total of 41% ($n = 166$) experienced bleeding complications during pregnancy and/or childbirth (any parity). In S and D, 47% ($n = 57$) of the women required medication supporting coagulation immediately after childbirth, and across the four Nordic countries, 24% ($n = 52$) reported the need of factor concentrate immediately after childbirth.

Discussion/Conclusion: The survey results from the lived experience of women with bleeding disorders in four Nordic countries revealed unmet needs about management of bleeding, support and follow-up.

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PO184 | Systematic literature review to evaluate haemophilia A therapies in paediatric patients without inhibitors

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Introduction: Haemophilia A (HA) is a rare bleeding disorder caused by a deficiency of factor VIII (FVIII), characterised by recurrent joint bleeds. Management includes standard of care prophylaxis with FVIII replacement therapy or non-factor therapy such as emicizumab, or on-demand treatment. This study aimed to evaluate the effect of HA therapies on bleeding and safety in paediatric patients without inhibitors by conducting a systematic literature review (SLR) of recent publications.

Methods: The SLR identified Phase 3/4 randomised controlled trials (RCTs) and non-RCTs in patients with HA without inhibitors published in English, reporting the prophylactic use of factor or non-factor therapies. Searches were run from January 2012 to November 2022 (conference abstracts included 2020 onwards) in Ovid MEDLINE, Embase and Cochrane databases; clinical trial registries were searched to identify completed/ongoing trials. Outcomes included: annualised bleeding rates [ABRs, including spontaneous ABR (AsBR)], proportion of patients without bleeds, adverse events (AEs) and inhibitor development. This analysis focused on results in paediatric patients (untreated and treated, <12 years).

Results: Of 33 studies (52 articles) identified, 16 (21 articles; 2012–2022) reported outcomes in children receiving FVIII prophylaxis (n = 11 single-arm, n = 5 multi-arm). The only reported comparator was on-demand treatment (n = 6 studies). At the time of the SLR, no published articles reported on efficacy of non-factor therapies in children with HA without inhibitors. The most frequently reported age at inclusion was <12 years (n = 10) or <6 years (n = 3) (n = 1 < 1 years; n = 2 not specified) and length of follow-up was 6–60 months (n = 13, n = 3 not specified). The most frequently reported outcome was development of inhibitors (n = 15 studies; 0%–7.6% of previously treated patients, 24.0%–43.1% of previously untreated patients). Other reported outcomes included: overall ABR (n = 14; median 1.5–4.8), total AEs (n = 12; 50.8% at 4.5 months to 83.6% at 9 months in previously treated patients), AsBR (n = 11; median 0), and percentage of patients without bleeds (n = 9; 22.6%–46.4% after ≥6 months prophylaxis).

Discussion/Conclusion: This SLR demonstrated that FVIII prophylaxis results in a low number of bleeding events in children with HA. As of November 2022, no published data from large RCT or non-RCT studies of non-factor therapies were available in children without inhibitors.

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PO185 | HIV comorbid infection and etranacogene dezaparvovec therapy: Efficacy and safety results from phase 2b and pivotal phase 3 HOPE-B trials 3 years after administration

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Introduction: Potential hepatotoxicity of liver-directed adeno-associated viral (AAV) vectors in patients (pts) receiving HIV medications have excluded those with HIV from participating in gene therapy haemophilia trials. Pts with controlled HIV comorbid infection were enrolled in phase 2b (NCT03489291) and phase 3 HOPE-B (NCT03569891) trials of etranacogene dezaparvovec (formerly AMT-061); here, we evaluate the individual efficacy and safety outcomes in the subset of pts with comorbid HIV infection.

Methods: A single injection of etranacogene dezaparvovec [2×10^{13} gc/kg, an AAV5 vector containing factor IX (FIX) Padua R338L transgene under the control of the liver-specific promoter LP-1] was administered to adult pts with severe or moderately severe haemophilia B. Pts with uncontrolled HIV (CD4+ counts ≤200/μL) were excluded.

Results: Of 57 pts in phase 2b and phase 3 HOPE-B trials, five had comorbid HIV infection [median (range) age 49 years (38–54)], four of whom had a history of hepatitis C virus with a negative viral load. Three of five pts with comorbid HIV infection had preexisting AAV5 neutralising antibodies with median (range) titre of 20 (0–99). Annualised bleeding rate (ABR) decreased compared to previous extended half-life FIX prophylaxis; median (range) ABR during FIX prophylaxis was 5 (1–10.4). One pt recorded no bleeds in the 36 months after receiving etranacogene dezaparvovec; the overall median (range) ABR was 0.64 (0–5.7). Median (range) uncontaminated endogenous FIX at 36 months post treatment was 32.3% (31.5%–58%). Three pts received no FIX infusions through 36 months.

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Seven treatment-related adverse events (AEs) were reported in three pts, and no treatment-related serious AEs were reported. Treatment-related alanine aminotransferase (ALT) elevation of moderate severity occurred in one pt (20%, similar to pts without comorbid HIV) 35 days posttreatment and resolved within 15 days with use of corticosteroids. His FIX levels later declined to 2%–5%, and he resumed prophylaxis per protocol at Month 30 posttreatment.

Discussion/Conclusion: Etranacogene dezaparvovec was found safe and effective in a subset of pts with controlled comorbid HIV infection. Owing to the small number of pts with HIV enrolled in trials, long-term collection of data and special attention in the real-world setting is recommended.

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PO186 | Immunogenicity and safety of marstacimab, an anti-tissue factor pathway inhibitor, in participants with haemophilia A or B and without inhibitors

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Introduction: Marstacimab (PF-06741086) targets tissue factor pathway inhibitor. BASIS is an open-label phase 3 study of marstacimab in people with haemophilia A (HA) or haemophilia B (HB). This analysis examined marstacimab immunogenicity and safety.

Methods: Data were from male participants (pts) aged 12 to <75 years with severe HA (<1% factor VIII) or moderately severe to severe HB (≤2% factor IX) without inhibitors in the 1 year BASIS study (NCT03938792) and its long-term extension (LTE; NCT05145127). Pts received a subcutaneous 300-mg dose of marstacimab followed by weekly 150-mg doses. Non-neutralising antidrug antibodies (ADAs), neutralising antibodies (NAbs), adverse events (AEs), treatment-emergent AEs (TEAEs), serious AEs (SAEs) and AEs of special interest (AESIs), including anaphylactic reactions and injection site reactions (ISRs), were recorded.

Results: Of 116 pts who received marstacimab in BASIS, 87 continued in the LTE [median treatment, 193 (range 34–483) days] and 44 had data at day 180. Baseline ADA titres were positive in 2/116 (1.7%) with no titre increase during treatment. Of 116 pts across BASIS and its LTE, ADAs were seen in 23 (19.8%) and NAbs in 6 (5.2%). ADA titres were low and resolved in 22/23 (95.7%) by BASIS end. ADA response was transient in the majority (61%) of ADA-positive pts. In the LTE, 1/44 (2.3%) was ADA-positive. All NAb titres were low and transient (maximum duration, 2 months). No pts were NAb-positive at BASIS end or during the LTE. ADA positivity had no noticeable effect on marstacimab pharmacokinetics or the incidence or severity of TEAEs, SAEs and AESIs. Among the 23 ADA-positive pts, six were NAb-positive and safety findings were consistent with ADA-negative pts. During BASIS and the LTE, TEAEs occurred in 13/23 (56.5%) ADA-positive and 67/93 (72.0%) ADA-negative pts; SAEs in 1/23 (4.3%) who were ADA-positive and 8/93 (8.6%) ADA-negative. AESI incidence was similar between ADA-positive [12/23 (52.2%)] and ADA-negative [52/93 (55.9%)]. No ADA-positive pts reported AESIs of anaphylaxis or angioedema; 2/23 (8.7%) reported ISRs.

Discussion/Conclusion: Most ADA titres were low and transient and all NAbs were transient, with no clinically meaningful differences by ADA status in marstacimab exposure, TEAEs, SAEs, AESIs, or discontinuations due to AEs.

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PO187 | Genetic diagnosis of von willebrand disease: Preliminary results

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Introduction: Genetic variations affect the plasma level and function of the von Willebrand factor (vWF), resulting in impaired haemostasis. There are difficulties in diagnosing and determining the type of disease. The objective of the present study is to evaluate the genetic variations who are diagnosed with von Willebrand disease (vWD) Type2 or who have differences in typing in the same patients due to laboratory differences, and the impact of these variations on the clinical phenotypes.

Methods: Eighteen patients were enrolled. Demographic and clinical data for all patients, Bleeding Assessment Tool (BAT) scores and blood

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samples for genetic analysis were collected. DNA samples extracted from the patient's blood samples were sequenced using the Twist HC Exome Panel.

Results: The median age of the patients was 21.5 years (range: 5–54), with 13 females. The median BAT score was 9 (range: 7–21). All patients except one had a family history. Following WES analysis, data for 551,654 variants in 21,560 genes were obtained: 39.07% of the variants/mutations obtained are synonymous, 37.44% are missense, 8% are intronic, 4.39% are intergenic, 0.86% are splice donor/acceptor, 0.78% are frameshift, 0.33% consist of nonsense mutations and others. According to the initial pathogenicity prediction classification, %0.008 is classified as group A (pathogenic), %1.79 is classified as group B (likely pathogenic), %14.5 is classified as group C (uncertain significance) and %83.7 is classified as group D (likely benign, benign or no clinical significance) variants. Among the analysed results, when examined in terms of genes directly related to bleeding, three patients (from the same family) were found to carry one pathogenic mutation in the F8 gene, six patients (from five different families) had five different mutations in the VWF gene and one patient was found to carry one pathogenic mutation in F9 gene. Three patients with F8 mutations and two patients with VWF mutations belonged to the same family.

Discussion/Conclusion: The diagnosis of VWD still presents challenges. Our findings suggest that genetic testing holds promise for cases initially suspected to be VWD. In this investigation, the identified F8, F9 and VWF mutations elucidated the aetiology of bleeding symptoms in the 10 patients participating in the study. This study remains ongoing, we anticipate further updates and new data will continue to be obtained.

Disclosure of Interest: None declared.

PO188 | Evaluation of thrombin generation assay profiles in patients with von willebrand disease

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Introduction: Thrombin generation assay (TGA) is a global coagulation assay used for monitoring of thrombin formation, reflecting the effect of both procoagulant and anticoagulant factors on the blood coagulation process. The aim of the present study was to evaluate TGA profiles in patients with von Willebrand disease (VWD) and assess the differences in TGA parameters between VWD types.

Methods: Thrombin generation was assessed using the fluorimetric TGA RB assay composed of tissue factor and negatively charged phospholipids that was applied on the automated Ceveron s100 analyser (Technoclone, Wien, Austria). Citrate plasma samples from 50 patients (11 males and 39 females) with phenotypically and genetically confirmed diagnosis of VWD (21 with type 1, 23 with type 2 and 6 with type 3 VWD) were analysed. TGA parameters were derived from the respective curve and comprised peak height (Peak), lag phase (tLag), time to peak (tPeak), area under the curve (AUC) and velocity index (VI). Comparison of TGA parameters between groups of patients with different VWD types was assessed using the Kruskal–Wallis test and Conover's post-hoc pairwise multiple comparisons, $p < .05$ was considered statistically significant.

Results: In type three patients tLag was significantly prolonged (median 12.1 min, IQR: 9.2–12.8) compared to type 1 (median 8.5 min, IQR: 7.3–9.7) and type 2 (median 7.9, IQR: 7.0–9.5), with $p = .020$. Equally, statistically significant difference was obtained for tPeak between type 3 VWD patients (median 22.0 min, IQR: 20.4–24.4) compared to type 1 (median 15.6 min, IQR: 13.0–17.5) and type 2 (median 14.8 min, IQR: 13.4–18.1), yielding a $p = .005$. VI was significantly lower in patients with type 3 (median 16.2 nM/min, IQR: 15.0–27.5), in contrast to type 1 (median 32.9 nM/min, IQR: 23.1–43.8) and type 2 VWD (median 35.1 nM/min, IQR: 23.0–48.9), $p = .032$. Peak and AUC did not yield statistically significant differences between the compared groups of patients, with $p = .265$ and $p = .413$, respectively.

Discussion/Conclusion: TGA profiles in patients with type 3 VWD revealed that thrombin generation is postponed and is characterised by a markedly slower kinetic pattern compared to patients with type 1 and type 2 VWD. This can be explained by severe deficiency of von Willebrand factor in patients with type 3 VWD which results in hypocoagulability.

Disclosure of Interest: None declared.

PO189 | Frequency of type 2N vWD among patients with mild or moderate factor VIII deficiency in iran

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Introduction: Type 2N von Willebrand disease (vWD) is a rare autosomal recessive disease that compromises the binding capacity of von Willebrand factor (vWF) to factor VIII (FVIII) leading to the accelerated clearance rate of FVIII in the patient's plasma. Thus, affected individuals will have clinical manifestations and primary laboratory findings similar to patients with mild or moderate haemophilia A. Due to differences in genetic counselling and treatment, it is crucial to differentiate these conditions from each other. This study aims to identify type 2N vWD patients among mild or moderate FVIII deficient individuals using genetic analysis as diagnostic method.

Methods: Based on FVIII:C levels between 50% and 1% and FVIII:C/vWF:Ag ratios below 1, 15 participants from referred patients to Iranian Blood Transfusion Organisation in a 6-month period were selected for further evaluations. For molecular investigations, the genomic content of each sample was extracted by silica-based method and amplified using a thermal cycler. Subsequently, PCR products were

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sequenced by Sanger's sequencing method on exons 18 through 20 of *the VWF* gene. Afterward, all gathered sequence data were analysed using NCBI's BLAST database and Chromas Pro.

Results: Results of the current study revealed that out of 15 selected participants with mild or moderate factor VIII deficiency, three patients had known type 2N vWD mutations. Detected mutations were p.Arg16Gln ($n = 2$) and p.Thr789Pro ($n = 1$). These cases were males with mean BAT score of 8.6 ± 2.6. In addition, laboratory findings for these patients showed factor VIII level as 13.3% ± 6.1%, vWF:Ag value as 50.3 ± 6.5 IU/day, and the FVIII:C/vWF:Ag ratio as 0.27 ± 0.12. In addition, the clinical history of these affected patients showed that two of them were misdiagnosed as haemophilia A at a young age; while the other one was not diagnosed until he was 33 years old.

Discussion/Conclusion: Compared to a few conducted studies with the same approach as this study, which estimated that only 10% of patients with decreased FVIII:C levels and FVIII:C/vWF:Ag ratios below 1 might be type 2N vWD cases; the current study revealed that 20% of the participants were patients with known type 2N vWD mutations, which is predictable due to the higher rate of consanguineous marriages in Iran. It seems that due to limited access to accurate diagnostic assays for type 2N vWD in our country, there is a high possibility of misdiagnosing or underdiagnosing patients with this disease.

Disclosure of Interest: None declared.

PO190 | Clinical pharmacokinetic analysis of vwf parameters following FVIII/VWF concentrates in patients with immune-mediated aVWS: A case series

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Introduction: Immune-mediated acquired von Willebrand syndrome (aVWS) is a heterogeneous and potentially life-threatening acquired bleeding disorder with laboratory and clinical features similar to congenital Von Willebrand disease. aVWS usually occurs at advanced age with different underlying disorders (e.g., lymphoproliferative) contributing to aVWS pathophysiology. aVWS patients are at risk for severe bleeding, necessitating urgent diagnostic workup and therapy. Despite the development of various diagnostic algorithms, early diagnosis of aVWS remains challenging due to the insensitivity of current assays. We report on the role of pharmacokinetics of von Willebrand factor (VWF) parameters following factor VIII (FVIII)/VWF administration (Haemate P®) in diagnosing aVWS.

Methods: Four patients were diagnosed with aVWS in the Antwerp University Hospital (Belgium), 2012–2023. Underlying IgG monoclonal gammopathy of clinical significance (MGCS; 2/4), monoclonal B-cell lymphocytosis (MBL; 1/4) and Waldenström macroglobulinemia (WM; 1/4) were identified. Von Willebrand factor antigen (VWF:Ag) and VWF dependent platelet binding activity (VWF:GPIbM) were measured using automated immunoturbidimetric assay, VWF collagen binding (VWF:CB) with ELISA and FVIII coagulant activity (FVIII:C) using one-stage FVIII:C assay.

Results: All four patients showed marked discrepancy between VWF:GPIbM, VWF:CB and FVIII:C compared to VWF:Ag, indicating functional defects. This improved only briefly after Haemate P® administration with a preserved VWF:Ag half-life contrasting with an early loss of VWF activity in 3/4 patients, suggesting an inhibitor to VWF primarily targeting functional domains (A1, A2, A3) rather than accelerating elimination of VWF protein (1/4). The VWF:Ag half-life in the patient with MBL was 7 h, and in the patients with MGCS 2 and 2.5 h, respectively. Three patients were treated with high-dose intravenous immunoglobulin (IVIG), correcting FVIII and VWF activities in only one patient, while limited impact was observed in the other two patients. Treatment of WM resulted in complete remission of aVWS in the fourth patient.

Discussion/Conclusion: Pharmacokinetic analysis of VWF parameters following FVIII/VWF concentrates is valuable in aVWS diagnosis, indicating inhibitor characteristics. Where possible, treatment should target the underlying disease; alternatively, regular infusions IVIG may sustain adequate VWF parameter levels.

Disclosure of Interest: None declared.

PO191 | The relation between heavy menstrual bleeding, menstrual phases and plasma clotting factor concentration: A systematic review and meta-analysis

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Introduction: Cyclic variation in sex-hormones have been reported to cause fluctuation in clotting factor levels. In normal cycles, most clotting factors levels appear lowest in the follicular phase. This phenomenon has not been investigated in women with HMB, but may impact the timing to diagnose an underlying bleeding disorder.

Aim: To compare clotting factor fluctuation in the follicular versus the luteal phase, between patients with and without HMB.

Methods: A Pubmed/MEDLINE systematic literature review using keywords on HMB, clotting factors and Von Willebrand factor (VWF). Inclusion criteria were measurement of levels of factor (F) II, FV, FVII, FVIII, FIX, FX, FXI, FXIII, fibrinogen, or VWF activity or antigen in normal or HMB cycles. We used measurements of HMB cycles from subjects identified as having HMB in the selected articles. The Newcastle Ottawa scale was used for quality assessment. If the moment of blood sampling was known, it was coded as the follicular (week 1—2) or the luteal phase (week 3—4). We conducted a meta-analysis to determine the effect of HMB or the follicular phase on clotting factor levels using R Studio 2023.06.0.

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Results: The search yielded 2158 articles of which 21 met the inclusion criteria. Overall, the articles were of moderate to good quality. Insufficient data was available for FXIII. In normal cycles, all other clotting factor levels were similar between the follicular phase and the luteal phase. Since all HMB measurements were done during the follicular phase or unknown phase, it was not possible to determine the difference in clotting factor levels between the follicular and luteal phase. When pooling the follicular, luteal and unknown phase measurements, HMB cycles had slightly higher FVIII (pooled difference 21.8 IU/dL, 95% CI 4.5–39.1, $p = .01$) and FV levels (pooled difference 15.8 IU/dL, 95% CI 6.0–25.5, $p = .002$) as compared to normal cycles. We found no significant differences for other clotting factors.

Discussion/Conclusion: Our study provides evidence that HMB cycles have higher FVIII and FV levels as compared to normal cycles. The menstrual cycle phase does not seem to influence clotting factor levels. However, data was scarce, especially for HMB cycles. Whether clotting factor levels influence HMB and if this depends on the menstrual phases needs further study.

Disclosure of Interest: None declared.

PO192 | The use of protein a-conjugated magnetic nanoparticles in the von Willebrand factor purification technology

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Introduction: Magnetic nanoparticles (MNPs), due to their excellent chemical and physical properties, have been widely employed for different biomedical applications. Methods of purification and production of a high-quality product in biotechnology are important. The purification step is particularly critical. Proteins are the most important type of biological macromolecules, and play an important role in all living organisms.

Von Willebrand factor (VWF) is a haemostatic, multimeric glycoprotein, one of the key components of the haemostasis system. Von Willebrand disease (VWD) is the most common autosomal inherited disorder of the haemostasis system and the cause is a genetic deficiency of quantitative and/or qualitative abnormal multimeric structure of the VWF molecule. The basic principle of VWD treatment is based on the normalisation of VWF and/or factor VIII (FVIII) levels.

Aim: To investigate the possibility of using MNPs in the technology of isolation and purification of VWF.

Methods: By the co-precipitation method were synthesised MNPs with different core sizes (from 80 to 250 nm) and protein A as functional group. Measurement of the VWF activity was determined using VWF:RCo assay. For fractionation of MNPs a tripod with a constant field neodymium magnet (0.24 T; Sphere Sim, Lviv) was used.

Results: The VWF concentrate was obtained by the method of affinity chromatography on the silica sorbents. The initial activity of VWF was 0.63 IU/mL. The activity of VWF was determined: (1) upon addition of MNPs (up to a final concentration of MNPs 50 μg/mL); (2) after 60 min of incubation and (3) after separation of MNPs on a permanent neodymium magnet (24 h).

The following results were obtained: MNP(1)-protein A-80 nm: after 60 min—0.11 IU/mL, after magnetic separation—0.13 IU/mL; MNP(2)-protein A-80 nm: after 60 min—0.25 IU/mL, after magnetic separation—0.16 IU/mL; MNP-protein A-100 nm: after 60 min—0.41 IU/mL, after magnetic separation—0.14 IU/mL; MNP-protein A-130 nm: after 60 min—0.13 IU/mL, after magnetic separation—0.11 IU/mL; MNP-protein A-250 nm: after 60 min—0.37 IU/mL, after magnetic separation—0.12 IU/mL.

Discussion/Conclusion: Experimental studies have confirmed that synthesised MNPs may be effective use in technological schemes for the purification of VWF from blood plasma by the method magneto-affinity chromatography (bioseparation).

Disclosure of Interest: None declared.

PO193 | Females with von Willebrand disease: The silent majority in Brazil

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Introduction: Von Willebrand disease (VWd) is one of the most common hereditary bleeding disorders in Brazil. As women experience the haemostatic bleeding challenges of menstruation and childbirth, they are disproportionately affected by VWd. Healthcare planning in developing countries is hampered due to a lack of clear collated summaries of its basic epidemiological data.

Methods: Estimates of the size and characteristics of VWd populations are necessary for healthcare planning and resource needs assessment. Therefore, we carried out a retrospective, transversal, epidemiological investigation of the period from 2017 to 2021 in Brazil, with surveillance data from the Brazilian Ministry of Health/Secretariat of Specialised Health Care, and from the General Coordination of Blood and Blood Products.

Results: In 2017, Brazil registered 8531 cases of VWd, 33.34% ($N = 2844$) were males (M), and 66.66% ($N = 5.687$) were females (F). In 2018, 33.19% ($N = 2.973$) M, and ($N = 5984$) 66.81% F of 8957 VWd. In 2019, among 9.462 diagnoses, 33.09% ($N = 3131$) were M and 66.91% ($N = 6331$) F. There were a total of 9.768 VWF cases in n 2020, 32.95% ($N = 3219$) M and 67.05% ($N = 6.549$) F. In 2021, 32.71% ($N = 3347$) were men and 67.29% ($N = 6884$) were women.

Discussion/Conclusion: VWd disproportionately affects females in Brazil, and its diagnosis is often delayed in Latin countries. Women are more symptomatic than men from the additional haemostatic challenges of menstruation and childbirth. In addition, they were likelier to have anaemia, thrombocytopenia, hypertension, and cardiomyopathy. There is limited data available on specific aspects of women with VWd, such as the incidence of bleeding events and other

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complications during pregnancy and childbirth. Our results call for further research at the public health level for women. The burden of obstetric and gynaecological symptoms among women may lead to increased diagnostic testing, however, a lack of congenital bleeding disorder awareness among health professionals are significant barrier to patient care.

This study advances the public discussion on the prevalence of VWd in women in Latin America. It is incumbent on our community to guarantee guidelines and training for multidisciplinary care for women with VWd. Developing a specific care approach would reduce unnecessary surgical interventions and improve their quality of life.

Disclosure of Interest: None declared.

PO194 | Managing von Willebrand disease with inhibitors during prophylaxis with a plasma derived von Willebrand factor/factor VIII concentrate—the WIL-31 study

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Introduction: Long-term prophylaxis with von Willebrand factor (VWF) concentrates is used for people with von Willebrand disease (VWD) with frequent and severe bleeds. The WIL-31 study demonstrated the efficacy of prophylaxis with a plasma-derived VWF/factor VIII (pdVWF/FVIII) concentrate containing VWF and FVIII in a 1:1 activity ratio (Wilate®) in adults and children with VWD of all types. Although VWF inhibitors are rare, they can severely impact clinical management. Here, management of two patients with VWD and inhibitors during prophylaxis is described.

Methods: WIL-31 (NCT04052698) was a prospective, non-controlled, international, multicentre phase 3 trial that enrolled male/female patients aged ≥6 years with VWD type 1 (VWF:RCo < 30 IU/dL), type 2 (except 2N) or type 3. Prior to WIL-31, patients received VWF concentrates on-demand during a 6-month, prospective, observational, run-in study (WIL-29); patients with at least six bleeding episodes, of which ≥2 were treated with a VWF concentrate, could enter WIL-31. During WIL-31, patients received pdVWF/FVIII prophylaxis 2−3× per week at 20–40 IU/kg for 12 months. FVIII and VWF activity were assessed throughout the study. Retention samples were collected at screening and baseline visits.

Results: Inhibitor testing was performed in 2/33 patients due to activity levels (2nd study visit) indicating VWF inhibitors, though neither patient had clinical signs. VWF inhibitors were detected in both brothers and were present prior to WIL-31 as samples taken at screening were positive. During and before WIL-29, both boys had been treated on-demand with another pdVWF/FVIII. They were diagnosed shortly after birth with VWD (suspected type 2A from family history). Both parents had VWD with no family history of VWF inhibitors. After WIL-31, the boys were reclassified to type 3 following next-generation sequencing. Baseline VWF activity indicated low VWF:RCo levels (0.092 and 0.65 IU/mL). Mean total annualised bleeding rates decreased by 85% and 91% during WIL-31 versus WIL-29, in each patient, respectively. All bleeding events during WIL-31 were spontaneous nose bleeds. Both used the same dosing regimen throughout WIL-31. In one patient, the inhibitors resolved by the end of the study.

Discussion/Conclusion: Despite VWF inhibitors in two patients, prophylaxis with a pdVWF/FVIII concentrate was effective compared to on-demand treatment.

Disclosure of Interest: C. Khayat Speaker Bureau of: Octapharma, CSL Behring, R. Sidonio Grant/Research support from: Genentech, Octapharma, Takeda, Speaker Bureau of: Genentech, Takeda, Octapharma, Guardian Therapeutics, Bayer, Novo Nordisk, UniQure, Biomarin, Spark, Pfizer, A. Pavlova Grant/Research support from: Octapharma, Bayer, Novo Nordisk.

PO195 | Hypersensitivity to von Willebrand factor and von Willebrand disease: A case-report

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Introduction: von Willebrand disease (VWD) is a common, inherited bleeding disorder. The current classification includes types 1 and 3, which are characterised by quantitative deficiencies of von Willebrand factor (VWF), as well as types 2A, 2B, 2 M and 2N, which are qualitative variants. For type 1 VWD patients with baseline VWF level <0.30 IU/mL, desmopressin is a valid treatment option and it is recommended to perform a prior trial of desmopressin and treating based on the results. A contraindication to the use of desmopressin is uncontrolled arterial hypertension.

Methods: We describe a clinical case of a 56-year-old woman, diagnosed with type 1 VWD 10 years earlier and confirmed desmopressin responsiveness. The patient developed arterial hypertension of difficult control.

At 51 year-old, she had a hysterectomy, under treatment with VWF. During the 4th FVW administration, the patient presented with a generalised rash, dyspnoea and low back pain lasting 15 min. She was treated with hydrocortisone 200 mg, ev and O2 mask support. The patient subsequently improved without further care. Since the patient needed to have dental implants surgery, there was a need to find a therapeutic alternative to prevent bleeding.

Results: In order to allow surgery carried out, patient had an immunoallergology consultation and FVW hypersensitivity was confirmed. The possibility of rapid drug desensitisation was raised but alternative therapeutic options were considered. In collaboration with internal medicine, antihypertensive therapy was optimised and patient's

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arterial hypertension controlled. Surgery was performed under desmopressin in combination with tranexamic acid and was uneventful.

Discussion/Conclusion: von Willebrand's patient management may not be straightforward when there are comorbidities that contraindicate certain therapies and, in rare cases, FVW hypersensitivity. Cooperation between different medical specialties is key for the development of therapeutic strategies.

Disclosure of Interest: None declared.

PO196 | Von Willebrand disease in children and adolescents: A single centre experience

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Introduction: Von Willebrand disease (vWD) is mainly characterised by mucosal bleeding—often occurring during invasive procedures. vWD is categorised in three major types; however, diagnostic assessment is complicated and bleeding phenotype may vary. Aim of the present study was to report on the experience of a single referral paediatric centre regarding diagnosis, follow-up and management of patients with vWD.

Methods: Medical records of paediatric patients with vWD were retrospectively reviewed. Demographics, disease type, reason for testing, bleeding episodes and disease management were reported.

Results: In total, 48 patients were evaluated. Mean age at diagnosis was 6.7 years and median time on follow up 3 years. vWD type I was diagnosed in 17(35.4%), type II in 25(52.1%) and type III in 0(0%) patients. Based on Lavin and O'Donnel, 6(12.5%) patients presented with slightly reduced von Willebrand factor levels, were characterised as low vWD.

In 27(56.3%) patients diagnostic work up was done in the presence of family history, while in 12(25%) following repeated mucosal bleeding. Perioperative bleeding was the cause of investigation in 5(10.4%) patients and abnormal values found in routine laboratory work up in 4(8.3%).

Bleeding episodes were reported in 35(72.9%) patients, with median bleeding score 1(0–12). In specific, 16(45.7%) patients presented with bleeds originating in more than one organ, while 19 patients constantly presented with the same haemorrhagic source: in 12(34.3%) isolated epistaxis was reported, in 3(8.6%) menorrhagia, in 3(8.6%) subcutaneous hematomas and in 1(2.9%) gum bleeding. Bleeding score was correlated to disease type ($p = .026$) and was higher in patients with vWD type II.

In 21(43.7%) patients reported episodes were treated with tranexamic acid, while in nine cases missing factor was required. During follow-up, 13(27.1%) patients underwent invasive procedures—minor surgeries in 76.9% of the cases. Postoperative bleeds were reported in 2(4.1%) cases and involved prolonged bleeding after tooth extraction.

Discussion/Conclusion: Bleeding episodes in this paediatric cohort were limited and easy to manage, most probably, due to the absence of the severest form of vWD in the Greek population. In that context, a severe bleeding phenotype is not to always be expected when investigating a congenital bleeding disorder and that high suspicion remains the key to early diagnosis—enabling appropriate management when needed.

Disclosure of Interest: None declared.

PO197 | Cost model of long-term prophylaxis with von Willebrand factor concentrate

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Introduction: Prophylaxis with plasma-derived von Willebrand factor (VWF)/factor VIII (FVIII) concentrates is an alternative for persons with severe von Willebrand disease (VWD) when treatment with desmopressin failed. Clinical efficacy of VWF/FVIII concentrates is stablished in the literature, but nowadays there is a lack of evidence in term of costs and quality of life (QoL).

To describe a cost model based on VWF dosage of commercialised VWF products in Spain (HamateP®, Wilate® and Fandhi®) for long-term prophylaxis.

Methods: Cost analyse was based on the range of dosage of VWF:RCo ristocetin cofactor per kg of body weight for each plasma-derived VWF concentrate according to previous reports from Miesbach et al. 2021 and Jimenez-Yuste et al. 2022. The range of dosage was stablished following the recommendation of Summary Product Characteristics (SmPC). The unitary cost of each treatment was obtained from acquisition cost from Spanish National Health System (NHS). We analysed three scenarios of patients based on doses of VWF/kg of weight, twice a week. The range of doses tested was Haemate-P® 10–70 IU/kg (Real World Evidence), Fanhdi® 10–70 IU/kg (Real World Evidence) and Wilate® 20–40 IU/kg (SmPC).

Results: Between 69 and 75 kg: at low doses, Wilate represents an increase up to €40,872 per year and Fanhdi €21,216 per year versus Haemate; at high doses, Wilate represents an increase up to €21,840 per year and Fanhdi €85,488 per year versus Haemate. Between 25 and 34 kg: at low doses, Wilate represents an increase up to €20,592 per year and Fanhdi €624 per year versus Haemate. At high doses, Wilate represents an increase up to €20,904 per year and Fanhdi €42,432 per year versus Haemate. In all cases Haemate-P® prophylasis was the most economic choice versus Fanhdi® and Wilate® according to cost from SNS. In all patients, both, total vWF IU consumption per year and vial use per year were higher with Fanhdi® and Wilate® versus Haemate-P®.

Discussion/Conclusion: In our model, long-term prophylaxis with Haemate-P® was more efficient than Fanhdi® and Wilate® for persons with severe VWD, in terms of pharmacological cost acquisition. More pharmacoeconomic analysis will be necessary to assess

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cost-effectiveness from society perspective in long-term prophylasis in persons with VWD.

Disclosure of Interest: None declared.

PO198 | Von Willebrand Disease diagnostic situations in paediatric patients, a study from the FranceCoag Registry

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Introduction: Diagnosis of von Willebrand disease (VWD) can be difficult especially in children with fewer haemostatic challenges. Patients are usually diagnosed through three different features: bleeding symptoms, family history or fortuitous discovery. Published data about diagnosing symptoms of VWD in children are scarce. We took advantage of FranceCoag, the French cohort of inherited bleeding disorders, to describe diagnosing features and first specific treatment during childhood.

Methods: We included patients registered in the multicentre cohort FranceCoag, including about 14,000 patients diagnosed with an inherited bleeding disorder. Included patients were diagnosed for a VWD (FW:Ag < 30% or Type 2) between 2003 and 2022, while younger than 18 years. Diagnosing features, severe bleedings and treatment requirement were analysed until patients were 18 years old.

Results: A total of 1054 patients out of 3578 VWD patients from the FranceCoag cohort were included. 8% ($n = 73$) presented with a very severe VWD (VWF:Act < 5% or FVIII:C < 5%), 39% ($n = 374$) with severe VWD (VWF:Act 5%–15% and FVIII:C > 5%) and 54% ($n = 518$) with moderate VWD (VWF:Act 16%–40% and FVIII:C > 5%). 49% were male. Median age at diagnosis was 3.7 years (Q1: 1.3–Q2: 8.2). Median follow-up was 6.5 years for very severe VWD, 3.9 for severe and 2.8 for moderate VWD. 60% of the patients were diagnosed in the context of family history, 22% due to bleeding features and 17% fortuitously. Overall, 68% did not necessitate treatment during follow-up. Median age at first treatment was 4,7 years (Q1: 2–Q3 :10). First treatment was non-substitutive in 17% of the patients ($n = 57$) while substitutive VWF was used in 40% of the patients ($n = 135$). Prophylaxis was required in only 24 patients (2.3%). Only 20 severe bleedings were reported: nine intracranial haemorrhages, nine gastro-intestinal bleedings and two uterine bleedings. Median age at time of severe bleeding was 6 years (Q1: 3.8–Q2: 10.4).

Discussion/Conclusion: Our results underline the importance of familial screening in children with fortuitous discovery remaining rare. In our cohort, the need for specific treatment was marginal in line with the paucity of severe bleedings reported.

Disclosure of Interest: None declared.

PO199 | Acquired von Willebrand syndrome and molecular targeted anticancer therapy: About a case

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Introduction: Acquired von Willebrand syndrome (aVWS) is a clinical and biological entity similar to congenital von Willebrand disease (VWD). Its incidence, which is most likely underestimated, remains low with fewer than 800 cases described in the literature. The pathologies associated with aVWS are numerous and varied: from lymphoproliferative syndromes to autoimmune diseases. The therapeutic strategy consists in identifying the underlying pathology in order to treat the underlying condition. Management focuses on correction of the underlying cause if possible.

Methods: The case concerns a 79-year-old male patient with hypertension who presented with VWD diagnosed 10 years ago, with lower gastrointestinal (GI) bleeding. The phenotype was suggestive of type 2 VWD with factor VIII (FVIII) activity, von Willebrand factor antigen (VWF:Ag) and activity (VWF:Ac) levels respectively at 40, 20 and <10 IU/dL, associated with a loss of high molecular weight multimers (HMWM).

Results: An acquired aetiology was evoked as there was no personal or family history of bleeding. The ratio between von Willebrand factor propeptide (VWF:pp) and VWF:Ag was found to be 3.95 (<2.4), thus further supporting this hypothesis. A complete clinical and biological assessment led to the diagnosis of a monoclonal gammapathy of undetermined significance (MGUS) with IgM kappa, GI angiodysplasia and calcified aortic stenosis. The peak monoclonal immunoglobulin level has remained stably low. The clinical course was marked by the discovery of a non-small-cell bronchial carcinoma treated by sotorasib, a molecular therapy which selectively and irreversibly targets $KRAS^{G12C}$.

After initiation of this treatment, a reduction of haemorrhagic symptoms was observed, suggesting a regression of his aVWS. Haemostasis was normalised on several occasions, 1 year after the start of this therapy. The biological assessment confirmed this hypothesis with an FVIII, VWF:Ag and VWF:Ac respectively at 189, 151 and 124 IU/dL (ratio VWF:Ac/VWF:Ag: 0.82), and a normalisation of VWF:pp/VWF:Ag ratio at 0.99. The analysis of multimers repartition showed an HMWM restoration, while protein electrophoresis no longer showed gammopathy. Unfortunately, the patient died of carcinological pleurisy.

Discussion/Conclusion: To the best of our knowledge, this is the only case described in which MGUS complicated by an aVWS was cured by sotorasib.

Disclosure of Interest: None declared.

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PO200 | Treatment issues in bleeding and acute thrombotic event scenario in elderly patients with inherited bleeding disorders: A case report

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Introduction: Bleeding events are one of the main challenges in inherited bleeding disorders (IBDs), including von Willebrand disease (vWD). As patients get older, they can develop comorbidities with increased thrombotic risk, such as atrial fibrillation (AF).

Methods: We reviewed clinical records of an 86-year-old male diagnosed with vWD type 2A, who had angiectasia-induced gastrointestinal bleeding (GIB) and pulmonary thromboembolism with deep vein thrombosis (DVT), following treatment with plasma-derived vWF/factor VIII concentrate (pdvWF/FVIII), needing anticoagulation.

Results: A vWD type 2A patient (vWFAg: 46.7%, vWFRco: 17.3%, FVIIIC: 0.59 UI/mL) with past hepatitis C infection, AF (CHA2DS2–VASc score 5, HAS-BLED score 4), chronic kidney disease, arterial hypertension, dilated cardiomyopathy, pulmonary hypertension and DVT. He had recurrent epistaxis and angiectasia-induced GIB, treated on-demand with pdvWF/FVIII. He started oral anticoagulation with dabigatran 8 years ago.

In June 2023, he was admitted to local hospital and then referred to our hospital due to upper GIB. He was treated with adrenalin, argon plasma, packed red blood cells (PRBCs) transfusions and pdvWF/FVIII. Dabigatran was suspended. He was discharged on D17.

One month later, he was readmitted with GIB and treated with pdvWF/FVIII and PRBC, discharged on D16.

After 10 days, despite pdvWF/FVIII 2x/week, he was readmitted with haemorrhagic shock, due to melena and severe anaemia. He was transfused with PRBC and pdvWF/FVIII. At D1 pdvWF/FVIII was reduced and started tranexamic acid 1 g bid. At D2 he developed intermediate-high risk pulmonary embolism, started unfractionated heparin (UFH) and entered a level 2 unit. At D14 he developed septic shock due to multidrug resistant *Staphylococcus haemolyticus*. A multidisciplinary team decided in favour of palliative care due to poor prognosis (uncontrolled infection, new DVT under UFH and worsening condition) and recent multiple bleeding complications. He was discharged at D19 to community palliative care.

Discussion/Conclusion: In elderly patients with IBD, thrombotic risk/events have difficult management treatment issues, despite newer specific orientation guidelines. Approach is made case-to-case in multidisciplinary teams, balancing the haemorrhagic risk versus the thrombotic factors.

Disclosure of Interest: None declared.

PO201 | Von Willebrand Disease in association with neurodevelopmental disorder—a rare case report

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Introduction: The von Willebrand factor (vWF) protein plays an essential role in blood clotting and it is encoded by the vWF gene. The prevalence rate of vWF disease is found to be about 125 in every million of the population.

Methods: An 8 year old child was presented to us with the symptoms and rare bleeding events and under management with cryoprecipitate and factor VIII (FVIII). In addition to the bleeding events, the child also expressed the features of neurodevelopmental with delayed development and speech. The family pedigree of the child was normal and the parents were non-consanguineously married. The parent of the child was on their second pregnancy and was concerned about the manifestation of bleeding events as observed in the previous child. The whole exome sequencing was performed on the whole blood DNA isolated from the index child.

Results: The vWF disease was identified by the mutation in vWF gene with c.2443-1G > C variant at IVS 18 which is a substitution of C instead of G. This mutation is estimated to effect the consensus splice site which is causative of the pathogenic condition. However, there were no significant mutations identified for the neurodevelopmental problem exhibited by the index.

Discussion/Conclusion: The von Willebrand disease (vWD) was identified with an intronic variant c.2443-1G > C and this has been observed in the homozygous and heterozygous states in patients affected with vWD. The variant has also been identified in one allele among the general population.

Disclosure of Interest: None declared.

PO202 | A case report of type-2B Von Willebrand Disease and gastrointestinal bleeding

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Introduction: Gastrointestinal bleeding (GIB) associated with angiodysplasia is a severe symptom that presents in some patients with Von Willebrand disease (VWD). It is difficult to diagnose and manage and is associated mainly with type 2A/3 cases, although there could be more cases of congenital/acquired, non-diagnosed angiodysplasias. Despite the importance of vascular malformations, their natural history and the techniques used for diagnosis are not

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clearly defined, and there are no recommendations nor data on the impact on efficacy of prophylaxis.

Methods: We report the case of a 50-year-old woman with type-2B VWD, with a Von Willebrand factor (VWF) mutation in exon 28, c.3922C > T, p.Arg1308Cys, who was hospitalised for melena in December 2022.

Results: She initially received (Haemate® P) VWF:Rco 35 IU/kg every 12 h for 2 days, then every 24 h, plus (Amchafibrin®) 500 mg/3 tablets/8 h. No findings on endoscopy nor on colonoscopy were determined. A month later, (Haemate-P®) administration was further spaced to every 48 h, and by the end of January 2023 the patient was prescribed with a Tuesday/Thursday/Saturday (Haemate-P®) regimen, plus (Amchafibrin®) 500 mg/3 tablets/12 h on the days without factor. Two days later the patient presented in the hospital's emergency room with new episodes of melena that required admission, after which (Haemate-P®) daily plus (Amchafibrin®) 500 mg/intravenously/8 h were administered. One day later, the patient underwent a video capsule endoscopy (VCE) revealing which two segments of proximal jejunum with active bleeding and recent clots. No clear angioectasias nor hematic debris were identified on two-way push enteroscopy, suggesting that bleeding was the result of punctiform angioectasias. A high probability of repeat bleeding was determined, so compassionate use of 90 mg/month (Somatuline autogel®) was authorised, although only two doses were administered due to allergic symptoms, while a 2-days/week (Haemate-P®) prophylaxis regimen was prescribed. The patient remained free of bleeding after 10 months.

Discussion/Conclusion: The choice of rescue treatments and the time at which they have to be discontinued in VWD patients with GIB are still based on data from case reports/series, and research is needed to optimise treatments when an acute haemorrhage occurs, at prophylaxis, and when considering adjuvant therapies. VCE explorations will undoubtedly be useful for identifying the source of GIB, facilitating therapeutic decision-taking.

Disclosure of Interest: None declared.

PO203 | Challenges in managing severe von Willebrand disease: Insights from algiers centre

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Introduction: Dealing with bleeding episodes in patients with Von Willebrand disease (VWD) particularly in severe cases such as type 3 poses significant challenges and adversely impacts their short-term and long-term quality of life. Efforts to prevent bleeding are crucial in enhancing the overall well-being of these patients.

Objective: The objective of this study is to evaluate the efficacy and safety of prophylactic treatment using VWF concentrate in a cohort of VWD patients with recurrent bleeding at our centre.

Methods: Algiers centre currently provides monitoring and treatment to a total of 200 VWD patients out of which 82 (41%) are diagnosed with type 3. This study focusses on a cohort of 36 patients, aged between 3 and 50 years old. Various variables were recorded including the standard dosage (IU VWF:RCo per kg) per infusion during prophylaxis as well as the frequency of infusions per week or per menstrual cycle. The rates were calculated for the periods before and during prophylaxis. The primary reasons for initiating prophylaxis in patients with severe VWD.

Results: A total of 36 patients received short- or long-term prophylactic treatment, with a classic dosage range of 30–50 IU/kg administered two to three times per week (Wilfactin or Immunate). Prophylaxis was initiated for various indications such as epistaxis 5 patients (P) gingivorrhagia, 3 P menorrhagia, 6 P postpartum, 7 P intracranial haemorrhage, 1 P hemarthrosis, 8 P angiodysplasia, 5 P and Psoas1 P prophylaxis effectively managed bleeding in most of the cases and significantly reduced the need for hospitalisation. Notably, no thromboembolic events were reported, indicating the safety of this regimen.

Discussion/Conclusion: Short-term or long-term prophylaxis with VWF concentrate demonstrates its efficacy in managing severe forms of VWD significantly improving patients' quality of life. These findings underscore the necessity of a national consensus and the formulation of recommendations in this regard.

Disclosure of Interest: None declared.

PO204 | Prevalence of Von Willebrand Disease among women with Heavy Menstrual Bleeding

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Introduction: Von Willebrand disease (vWD) is the most common inherited bleeding disorder in the world with 1% prevalence among the general population and in 5%–20% of women with heavy menstrual bleeding (HMB). Diagnosis remains a challenge in Low Middle Income Countries (LMIC). We screened consecutive females in the reproductive age group presenting with Heavy Menstrual Bleeding in Punjab.

Methods: This is a prospective multicentric study from six centres in Punjab between June 2021 and May 2023, to estimate the prevalence of vWD in women suffering from HMB in the absence of uterine aetiology. The Condensed Molecular and Clinical Markers for the Diagnosis and Management of Type 1 von Willebrand Disease (MCMDM-1) bleeding questionnaire tool was used to assess the bleeding phenotype in patients.

Results: An Interim analysis of 23 women with HMB, with median age of 27 years (14–40) were screened and 4 (17%) women were confirmed to have vWD. Twenty one (95%) patients were from Punjab representing nine different districts. Only one of the four vWD patients had a positive family history. The MCMDM score ranges were 1–3 (65%), 4–6 (22%) and 7–10 (13%). Three (75%) of the patients with vWD had a score more than 4 and one patient had a score of 3. All of them had Type I vWD. The average RiCof and vWAg levels in the diagnosed patient was 36.4% (14.1%–50.9%) and 27.6 IU/dL (12.8–48.9 IU/dL).

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Discussion/Conclusion: vWD should always be considered as one of the possible bleeding disorders in women with HMB without a gynaecologic pathology. The application of the MCMDM-1 bleeding questionnaire demonstrated its tendency towards effectiveness in the initial screening process.

Disclosure of Interest: None declared.

PO205 | Lenalidomide has its place in the treatment of acquired von Willebrand disease

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Introduction: Acquired Von Willebrand syndrome (AVWS) is a rare, underdiagnosed and often delayed-diagnosed bleeding disorder. AVWS is associated with lymphoproliferative disorders, including monoclonal gammopathy of undetermined significance (MGUS) and multiple myeloma. Its haemorrhagic symptoms and adequate treatment are complicated.

Methods: Our patient is a 65-year-old woman who, in the pre-anaesthesia study prior to cholecystectomy, was diagnosed with AVWS.

Results: She presented values of VWF antigen [VWF:Ag] level of 15 IU/mL; VWF ristocetin cofactor [VWF:RCo] level of 8 IU/mL, VIIIF 17 IU/mL, which was associated with an underlying MGUS and a small IgG paraprotein (0.8 g/L).

The patient did not respond to desmopressin, VWF/VIIIF (Wilate®) was associated with rapid clearance ($t1/2 < 1$ h), and again had limited efficacy in managing his bleeding. A response was achieved with intravenous immunoglobulins (1 g/kg,), although with loss of response in approximately 20–30 days, which allowed surgical intervention.

New readmission due to a large abdominal hematoma after a respiratory infection that required a new admission and treatment with immunoglobulins associated with prednisone. The treatment needs to be continued for months until the abdominal hematoma improves. Treatment with rituximab was performed without achieving a response. Given a new gluteal hematoma after a fall, it was decided to start treatment with lenalidomide at 25 mg/day. After 8 months of sustained response with lenalidomide at 25 mg/day, we began to reduce the dose to 10 mg/day. She received a total of six cycles, maintaining a response. She subsequently received two cycles of 5 mg and recently suspended it without observing haemorrhagic symptoms or changes in VWF, not even in monoclonal peak.

Discussion/Conclusion: Lenalidomide is an oral treatment resulted in significant clinical improvement, and marked increases in plasma VWF antigen (VWF:Ag) and VWF ristocetin cofactor levels. Lenalidomide treatment was associated with a significant increase in plasma VWF levels, despite no major change in paraprotein level. This case adds to the few cases already reported of good results of lenalidomide in AVWS associated with MGUS.

Disclosure of Interest: None declared.

PO206 | Recombinant von Willebrand factor treatment outcomes in uk adults with von Willebrand disease: A retrospective chart review study

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Introduction: Recombinant von Willebrand factor (rVWF) is indicated in the UK in adult patients (pts) with von Willebrand disease (VWD), when desmopressin treatment is ineffective/not indicated, for the treatment of haemorrhage and the treatment/prevention of surgical bleeds. Consequently, data on rVWF treatment outcomes in pts with VWD in real-world settings are needed. This UK retrospective chart review evaluated real-world experience with rVWF in on-demand (OD) and surgical settings.

Methods: Adult pts with congenital VWD receiving rVWF for OD treatment of spontaneous/traumatic bleeds or prophylaxis/treatment of surgical bleeds at seven UK sites were included. Assessments included bleed control, bleed resolution, treatment satisfaction (investigator-reported 4-point rating scale), dosing and safety. Data were summarised descriptively.

Results: $N = 32$ pts [mean (SD) age, 48.3(19.5) years; 68.8% female] were included. $n = 12$ pts received OD treatment for one spontaneous/traumatic bleed each (most frequently pregnancy and muscle haematoma); 8/12 bleeds were mild. The mean (SD) number of infusions, dose/infusion (IU/kg) and total rVWF consumption (IU) were 2.3(2.6), 30.7(13.6) IU/kg and 4870.8(4443.9) IU, respectively. All pts who received OD treatment achieved bleed control and bleed resolution. $n = 20$ pts were treated in surgery: ($n = 12$: major; $n = 8$: minor). Pts who had surgery may have received intermittent prophylaxis pre-, during and post-surgery. $n = 10$ pts were treated with rVWF as a pre- and/or post-surgical prophylaxis with a mean (SD) number of infusions of 1.1(0.3) and 6.3(5.6), mean (SD) dose/infusion (IU/kg) of 44.4(17.8) and 23.0(10.2) IU/kg, and the mean (SD) total consumption was 3510.0(2171.0) IU and 8130.0(3770.8) IU, respectively. During surgery, pts treated with rVWF received a mean (SD) of 2.1(1.4) infusions, and total consumption of 31.6(9.5) IU/kg and 5627.3(3160.9) IU. Of the 11 pts who received rVWF during surgery, eight achieved bleed resolution [not applicable: three pts; treated pre-surgery (not prophylaxis)]. All pts treated with rVWF rated treatment satisfaction as excellent or good.

Discussion/Conclusion: The outcomes of this real-world chart review reflect results in-line with clinical trials with rVWF. However, on average rVWF dose/infusion values for bleeding episodes were lower than licensed recommendations, suggesting a difference in real-world utilisation versus clinical trials.

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PO207 | Successful control of bleeding in a patient with acquired von Willebrand syndrome using high-purity human von Willebrand factor

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Introduction: Acquired von Willebrand syndrome (AvWS) is a rare bleeding disorder that typically affects older patients with an underlying disorder for example cardiovascular disease or malignancy. The pathophysiology of the disorder is complex, involving a variety of mechanisms leading to increased degradation and clearance of von Willebrand factor (vWF).

Methods: The case of a 77 year-old man who developed AvWS following treatment for prostate cancer is described.

Results: AvWS was diagnosed in 2015 following bleeding due to radiation proctitis. The patient reported excessive bruising and bleeding following minor cuts during the preceding 18–24 months. An acquired bleeding disorder was suspected; diagnosis was confirmed after extensive investigations including several endoscopies. The laboratory phenotype was consistent with Type 2 von Willebrand disease: vWF activity 8 IU/dL and vWF antigen 20 IU/dL. He was anaemic with haemoglobin (Hb) 62 g/L.

Following 8 months of hyperbaric oxygen therapy, which did control bleeding but was unsustainable, he underwent an unsuccessful trial of 1 g/kg IVIg. Thereafter long-term prophylaxis (LTP) with factor VIII (FVIII)/vWF concentrate (*Wilate*) 3000 IU every 12 h, then every 8 h was commenced. There was minimal control of bleeding, so after 2 weeks therapy was switched to a formulation with a lower FVIII:vWF ratio (*Voncento*) initially at 4800 IU every 12 h, settling to 2400 IU x3/week. Although successful in controlling bleeding, FVIII accumulation was a concern. Additionally, regular blood transfusions and iron infusions were required to treat recurrent anaemia.

In December 2020, the patient was switched to high purity human vWF concentrate (*Willfact*) which has very low FVIII content. The patient started 3000 IU x3/week and maintains this dose to date. Bleeding remains well-controlled, and although Hb occasionally falls below the threshold of 90 g/L, he responds to iron infusion alone; blood transfusion has not been required since October 2020.

Discussion/Conclusion: Treatment with high purity human vWF provides good control of bleeding in patients with AvWS and avoids potential FVIII accumulation. Given the success of LTP with vWF concentrate in controlling bleeding, commencing *Willfact* earlier may have avoided the need for hyperbaric oxygen and blood transfusions.

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PO208 | Management of women with inherid bleeding disorders during pregnancy; a single centre experience

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Introduction: Women with inherited bleeding disorders have an increased risk of bleeding during pregnancy and delivery. Carriers of haemophilia A and B may have reduced factor levels. Von Willebrand disease (VWD) is a more heterogeneous bleeding disorder with various types and subtypes and with different bleeding risks and also different management strategies.

The aim of our study is to evaluate the treatment and complications during pregnancy, delivery and postpartum period. We report a retrospective cohort of 49 women with congenital bleeding disorders.

Methods: Haemophilia carriers received counselling about genetic transmission and prenatal diagnosis while planning for management of pregnancy and delivery were discussed for all women.

The levels of coagulation factors were measured during 3rd trimester of pregnancy, peripartum period and the complications were recorded.

Results: Between 2015 and 2023, 49 women with a congenital bleeding disorder, median age of 31 years (21–42 years) were included in the study. Thirty-five women had VWD (type 3 three pts, type 2A six pts, type 1 severe two pts, type1 moderate five pts and type 1 mild 19 pts), three with FVII deficiency, nine haemophilia carriers and two had storage pool disease. Miscarriage or termination of pregnancy due to abnormal foetal development occurred in 4/49 (8%). Haemostatic treatment was given to prevent bleeding during peripartum period if activity of FVIII/FIX/VWAg was <40%–50%. The 59% of our patients underwent caesarean delivery with general anaesthesia. Vaginal delivery with epidural anaesthesia underwent in 3/49 (6%).

Twenty-three pts (46.9%) received before and after delivery VWF/FVIII concentrate. Desmopressin was administered postpartum in 11/49 with a previously demonstrated good response while rFVIIa was given in 2 women with FVII deficiency. In all cases antifibrinolytic treatment was used. Complications include gestational diabetes 2/49 (4%), preeclampsia 2/49 (4%), premature delivery 3/49 (6%) and placental abruption 4/49 (8%).

Postpartum haemorrhage (PPH) was not reported.

Antithrombotic therapy during pregnancy/postpartum period was given in 3/49 (6%) with thrombotic condition.

Discussion/Conclusion: Pregnancy in women with hereditary bleeding disorders is a period of high risk and a treatment plan for delivery

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should be made. This requires a multidisciplinary team that includes haemophilia treat, an obstetrician, a clinical anaesthesiologist with expertise in bleeding disorders.

Disclosure of Interest: None declared.

PO209 | A series of unfortunate events—case study of challenging vaginal bleed management associated with type 2 von Willebrand Disease (vWD)

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Introduction: A case study highlighting the management of heavy menstrual bleeding (HMB) in a 45-year-old woman with Type 2 vWD. Previously a mild phenotype, suddenly increased to 10 months of acute vaginal bleeding requiring combined management from inherited bleeding disorder (IBD) and gynaecological teams to manage bleeding and enable a return to previous quality of life.

Methods: A&E presentation with HMB. Transvaginal ultrasound scan (T/V US) results showed two significant fibroids (one subserosal and one intramural). Requiring Norethisterone, IV iron infusion and plasma derived von Willebrand factor concentrate (pdvWF). This cycle was repeated on multiple occasions with additional outpatient appointments, further scans and hysteroscopies, significant pdvWF doses, blood transfusions and ultimately a hysterectomy.

Results: In total across 10 months, this patient was seen eight times through A&E attendances with three hospital admissions; two haematology day unit attendances; 45 haemophilia day unit attendances and four haemophilia/gynaecology outpatient attendances. She received four blood transfusions, five iron infusions; 201,000 IU pdvWF alongside three T/V US; one hysteroscopy (with an additional two failed appointments) and finally a hysterectomy.

Discussion/Conclusion: Conservative management of this patient's HMB proved unsuccessful. Bleeding was only successfully controlled, and quality of life resumed following a hysterectomy. Although a significant surgical intervention, in particular when completed in a patient with a significant IBD, this was the patient's choice. This was not initially felt appropriate as a result of increased bleeding and cardiovascular risks when completed in women under 50 years. Further questions were posed as a result of this case including: the need for more regular, available gynaecology appointments to openly discuss known associated risks for treatment options; management of patient/clinician expectations; increased opportunities needed to openly discuss between patient and specialists involved, to plan treatment whilst addressing the balance of risk in unmanaged bleeding with planned surgical bleeding risks.

Disclosure of Interest: None declared.

PO210 | Efficacy and safety of plasma-derived VWF concentrates in a cohort of 93 patients with type 3 von Willebrand disease enrolled in 3WINTERS-IPS: results of the 2-year prospective clinical observation

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Introduction: von Willebrand disease type 3 (VWD3) is a very rare and severe inherited bleeding disorders characterised by unmeasurable levels of von Willebrand factor (VWF). Plasma-derived VWF concentrates (pd-VWFC) are the mainstay of treatment of VWD3.

Aims: One of the aims of 3Winters-Ips was to collect prospective data on efficacy/safety of pd-VWFC in a well characterised cohort of VWD3 enrolled in European (EU) and Iranian (IR) centres.

Methods: 3Winters-Ips is an investigator-initiated, non-interventional, retrospective/prospective clinical study on VWD3. The type of pd-VWFC was chosen by local investigators at EU and IR centres. A total of 108 patients who completed the 2-year prospective observation received pd-VWFC either on demand (OD) or under Secondary Long-Term Prophylaxis (SLTP). Efficacy/safety of pd-VWFC was assessed according to FDA-agreed objective criteria following regulatory procedures.

Results: Among pd-VWFC, HAEMATE-P/VONCENTO were administered in 93/108 (86%) VWD3 patients. 69/93(74%) received OD treatments to manage 629 bleeding episodes (mucosal [83%]—joint bleeds [17%]) with excellent/good efficacy in 96%. Moderate/poor responses were reported in 25 bleeds [menorrhagia ($n = 11$), GI bleeds ($n = 7$), joint bleeds ($n = 4$) and epistaxis ($n = 3$)]. 24/93(26%) VWD3 received SLTP. Annualised bleeding rates (ABR) during SLTP were significantly reduced by 66% in these individual patients when compared to their previous retrospective OD treatments. Only two patients showed recurrent GI bleeds under SLTP. No major side-effects were reported.

Discussion/Conclusion: pd-VWFC are confirmed to be effective and safe to treat or prevent mucosal and non-mucosal bleeds in the rarest and most severe form of VWD. VWD3 exposed to SLTP can reduce substantially their ABR.

Disclosure of Interest: A. Federici Consultant for: Csl-Behring, Grifols, Kedrion, Takeda, Speaker Bureau of: Csl-Behring, Grifols, Kedrion, Takeda.

PO211 | Management of heaving bleeding menstrual in patients with von Willebrand disease. experience of department of haematology of chu of constantine in Algeria

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Introduction: It is estimated that 5%–20% of women with heavy menstrual bleeding (HMB) have a von Willebrand disease (vWD), and 32%–100% of women with vWD have an HMB. Management of HMB. the ASH, ISTH, NHF, WFH 2021 recommendations suggesting using tranexamic acid over desmopressin to treat women who wish to conceive.

We describe the haemostatic management of HBM in our centre.

Methods: It is an observational, retrospective study of 17 women of reproductive age with vWD. The ISTH BAT score to quantify HBM were performed during the initial clinical exam and during treatment to manage them. It was high in four patients: three with vWD type 2; and one with vWD type 3. The mean of ISTH BAT was 7, and the mean of Higham score was 305.5. An iron deficiency was noticed among three patients.

Results: The therapeutic means prescribed are tranexamic acid given orally or through injections, etamsylate orally and through injections. The hormonotherapy based on oestroprogestatives in addition to a substitutive treatment based on plasmatic VWFactor concentrate and double concentrates of factor VIII (FVIII) plasmatic immunate type. Only three women had a prophylaxis of short duration during the menstrual bleeding. However, the fourth one evolved favourably with hormonotherapy. The iron deficiency treatment obliged us the use of blood transfusion for one patient and the martial treatment for the other two patients. For the first prescribed orally, and the other trough injections.

Six months later, the mean of ISTH BAT was 4 and the mean of Higham score was 38.5.

Discussion/Conclusion: The HBM treatment for the women suffering from vWD depending on age of the patient and her wish to conceive. The prophylaxis even if not codified in the case of vWD could be very fruitful in HBM treatment and decreases their abundance.

Disclosure of Interest: None declared.

PO212 | Association of von Willebrand disease type 2N and connective tissue abnormality resembling ehlers–danlos syndrome: A case report

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Introduction: The heterogeneity of the haemorrhagic phenotype observed in 2N Von Willebrand disease (VWD) presents challenges in diagnosis and management. The coexistence of congenital anomalies with this severe phenotype can further aggravate the bleeding tendency.

Methods: This case report describes the association between VWD Type 2N and a congenital connective tissue abnormality resembling Ehlers–Danlos syndrome (EDS). The patient, a 29-year-old individual from a consanguineous family, was referred for investigation of bleeding symptoms. The patient's sister was already diagnosed with RIN2 syndrome, an autosomal recessive connective tissue disorder characterised by facial dysmorphism, cranial hypertrophy, hypertrophy of the lips, café-au-lait spots and thoracolumbar scoliosis. The dermatological phenotype exhibited by this family aligns closely with EDS and was already described by Syx et al. in a 2010 article.[1]

Results: The significant bleeding phenotype ISTH-BAT > 6 and an APTT ratio within the normal limit prompted us to explore factor VIII (FVIII) and Von Willebrand factor (VWF). Laboratory tests included FVIII:C assay (chronometric method in a single step), FVW:Ag assay(ELISA), FVIII:Rco assay (freeze-dried platelet aggregation), VWF:VIIIB and VWF:CB assays (ELISA) were performed. The results revealed an FVIII level of 13%, VWF:CB level of 38% and an FVIII/VWF:Ag ratio of 0.2. Further exploration indicated a VWF:VIIIB level of 12%, consistent with a diagnosis of VWD Type 2N.

Discussion/Conclusion: The occurrence of dual genetic abnormalities, predisposing individuals to bleeding, is not uncommon in patients with EDS or other genodermatoses. Therefore, the exploration of platelet, VWF primary haemostasis and coagulation is crucial to detect any associated deficits. In our case, the diagnosis revealed VWD Type 2N associated with a syndrome closely resembling EDS.

Disclosure of Interest: None declared.

PO213 | Accumulation of factor VIII and von Willebrand factor during prophylaxis with a plasma-derived von Willebrand FACTOR/FACTOR VIII concentrate during the WIL-31 study

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Introduction: Prophylaxis with von Willebrand factor (VWF) is used for people with von Willebrand disease (VWD) with frequent and severe bleeds. The WIL-31 study demonstrated the efficacy of prophylaxis with a plasma-derived VWF/factor VIII (pdVWF/FVIII) concentrate containing VWF and FVIII in a 1:1 activity ratio (wilate®) in adults and children with VWD. As elevated levels of FVIII are associated with increased thrombosis risk, it is important to determine if repeated dosing with pdVWF/FVIII leads to FVIII accumulation.

Methods: WIL-31 (NCT04052698) was a prospective, non-controlled, international, phase 3 trial that enrolled patients aged ≥6 years with VWD type 1, type 2 (except 2N) or type 3. Prior to WIL-31, patients received on-demand treatment with VWF concentrates during a 6-month, prospective, observational, run-in study (WIL-29). During WIL-31, patients received pdVWF/FVIII prophylaxis 2–3× per week at 20–40 IU/kg for 12 months. VWF activity (VWF:RCo) and FVIII activity [chromogenic (Chr) and one-stage (OS) assays] were performed

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throughout the study. Full pharmacokinetic (PK) analyses were performed in patients aged 6–16 years. Samples were collected prior to injection of a single dose (60 ± 10 IU/kg), and then at multiple time points post-injection (1–72 h). Safety was monitored throughout.

Results: The study included 33 patients, with a median age of 18 years. Six patients had severe type 1 VWD, five had type 2, and 22 had type 3. Baseline FVIII and VWF activities were similar regardless of age group, and as expected were lower in patients with type 3 VWD compared with severe type 1 and type 2. There was a negative correlation of baseline FVIII and VWF activity with the number of spontaneous bleeding episodes during prophylaxis. Mean peak and trough FVIII and VWF activity levels remained consistent during the study and there was no accumulation of either factor over the 12-month prophylaxis period. Full PK assessments were performed according to protocol in 13 patients aged 6–16 years. The mean ± standard deviation in vivo half-life was 16 ± 7 (FVIII Chr), 16 ± 8 (FVIII OS) and 10 ± 8 (VWF:RCo) h. No thrombotic events were observed.

Discussion/Conclusion: No accumulation of FVIII or VWF was reported in 33 patients who received 12-month pdVWF/FVIII prophylaxis, regardless of VWD type and age.

Disclosure of Interest: V. Kateryna: None declared, V. Vdovin: None declared, M. Timofeeva: None declared, C. Khayat Speaker Bureau of: Octapharma, CSL Behring, A. Inati Grant/Research support from: Novartis, Bausch Health, Forma/Novo Nordisk, Agios, Octapharma, Vifor, Roche, GBT/Pfizer, Speaker Bureau of: Roche, Forma, Novartis, Takeda, Pfizer, Novo Nordisk, R. Sidonio Jr Grant/Research support from: Genentech, Octapharma, Takeda, Speaker Bureau of: Genentech, Takeda, Octapharma, Guardian Therapeutics, Bayer, Novo Nordisk, UniQure, Biomarin, Spark, Pfizer.

PO214 | Successful desensitisation protocol following anaphylaxis secondary to recombinant factor VIIa

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Introduction: Factor VII (FVIII) deficiency is a rare genetic bleeding disorder characterised by a deficiency or reduced activity of clotting FVII. Recombinant factor VIIa (rFVIIa) has been approved to treat bleeding episodes in individuals with congenital FVII deficiency. The most commonly reported adverse events are thrombolytic in nature. Allergy is very rare with rFVIIa.

Methods: We report the case of a 15 teenage girl with a history of gingival bleeding who was diagnosed with FVII deficiency (level 1%). It is during the third administration of rFVIIa that our patient presented an urticary. During the fourth administration, she presented dyspnoea, tachycardia and urticaria. Her symptoms resolved after administration of intramuscular adrenaline for this anaphylaxis.

She was referred to our clinic for the evaluation of the rFVIIa allergy.

Results: We performed a skin prick test which was negative and an intradermal skin test which was positive.

Since there was no other therapeutic alternative, we decided to start a desensitisation protocol.

A 16 steps desensitisation was successfully performed using an initial dose of 0.001 mg of rFVIIa intravenously and this dosage was increased every 20 min until the full dosage.

Our patient was monitored during this protocol, and no problem was noticed.

Now, she can receive rFVIIa without any allergy side effect, but she has always to do it according to this protocol.

Discussion/Conclusion: Drug hypersensitivity reaction with rFVIIa is very rare.

To our knowledge, this is the second report of a successful desensitisation protocol for rFVIIa.

In the absence of an alternative therapeutic, desensitisation should always be considered in the case of an allergy to rFVIIa.

Disclosure of Interest: None declared.

PO215 | Establishment of diagnostic facilities for the autosomal recessive bleeding disorders in Pakistan

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Introduction: Pakistan has 20 million population and 40% are living in the rural areas. Autosomal recessive bleeding disorders (ARBDs) are not so rare due to consanguinity. Only basic haemostatic testing was available before 2001. The diagnostic facility of haemophilia A and B was only available in 2–3 tertiary care hospital but do not have expertise to measure its inhibitors. The project was planned on the principle of build, operate and transfer in 2007.

Methods: The study was approved by the ethics committee of the National Institute of Blood Diseases and Bone Marrow Transplantation (NIBD), Karachi, Pakistan, in accordance with the declaration of Helsinki. It was a descriptive study with cross-sectional time prospect, conducted from March 2007 to December 2014. Study was divided in two phases. Patients were screened from only Karachi or Sindh in first phase. Patients were selected throughout Pakistan in phase 2. A general questionnaire, with basic demographic details, clinical and family histories, and the Tosetto bleeding score questionnaire were filled out for each patient by a doctor at the corresponding recruitment centre.

To identify the period prevalence for various ARBDs, record from the current study was merged with that from all the studies reported in the last 12 years.

Results: The study cohort consisted of 429 patients, 250 males and 179 females, with a male to female ratio of 1.3:1.

Median age of patients was 11 ± 5 years.

A history of consanguinity was present in 89% of cases.

The most common symptoms reported by the cohort of patients included gum bleeding (57%), and easy bruising (39%).

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Spontaneous epistaxis and gum bleeding were found in 6%, whereas menorrhagia was reported in 19% of the adult female patients.
Anaemia was found in 48% of the patients.
Life-threatening intracranial haemorrhage affected 4% of the patients.
Discussion/Conclusion: These data have shown that vWD type 3 has the highest incidence amongst the ARBDs in this study cohort, followed by fibrinogen deficiency. GT was found to be the third most common disorder. The incidence of ARBDs in this region is higher than previously thought.
Disclosure of Interest: None declared.

PO216 | Elevated soluble endoglin could play a role in bleeding by interfering with platelet aggregation and thrombus stability

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Introduction: The circulating form of human endoglin (sEng) is a cleavage product of endothelial transmembrane endoglin, which concentration dramatically increases in preeclampsia or during HELLP syndrome. Because sEng encompasses an RGD motif, known to be involved in integrin binding, we hypothesised that sEng would bind integrin αIIbβ3, thereby compromising fibrinogen binding to platelets and thrombus stability.
Methods: In vitro human platelet aggregation, thrombus retraction and secretion competition assays were performed in the presence of recombinant sEng. Surface plasmon resonance (SPR) binding and computational (docking) analyses were carried out to evaluate protein–protein interactions. A transgenic mouse overexpressing human sEng (hsEng+) was used to measure bleeding/rebleeding, prothrombin time (PT), blood stream and thrombus formation after FeCl3-induced carotid injury.
Results: Under flow conditions onto a collagen matrix, supplementation of human whole blood with sEng led to smaller thrombi. In washed platelets, sEng (1–5 μg/mL) inhibited platelet aggregation and thrombus retraction, therefore interfering with fibrinogen binding, but did not affect platelet activation. SPR binding studies and molecular modelling showed a good fitting for the interaction between αIIbβ3 and sEng, involving specifically the endoglin RGD motif, suggesting the formation of a highly stable αIIbβ3/sEng complex. hsEng+ mice showed increased bleeding time and a higher number of rebleedings compared to wild-type mice. No differences in PT were denoted between genotypes. After FeCl3 injury, the number of released emboli in hsEng+ mice was higher and the occlusion was slower compared to controls.
Discussion/Conclusion: We show that high sEng levels interfere with thrombus formation and consequentially could play at supraphysiological concentrations a role in bleeding diathesis, such as observed in postpartum haemorrhage secondary to preeclampsia or HELLP syndrome. These results are consistent with a specific interaction of high affinity between sEng-RGD motif and αIIbβ3.
Disclosure of Interest: None declared.

PO217 | Clinical presentation and management of factor XIII deficiency: Case study

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Introduction: Factor XIII (FXIII) deficiency is a rare congenital bleeding disorder. The first clinical report of FXIII deficiency was described in 1960; since then, more than 500 cases of FXIII deficiency have been identified worldwide with an incidence of one individual in 1–3 million It is characterised by severe delayed spontaneous bleeding with normal coagulation screening tests. In this study, we aim to report the clinical findings and treatment modalities of eight patients with FXIII deficiency at Çukurova University and Acibadem Adana Hospital, Adana, southern part of Turkey.
Methods: We retrospectively reviewed medical records of eight patients with FXIII deficiency.
Results: Eight patients with FXIII deficiency, age ranging from 9 to 28 years were included in the study. Three patients were female. Umbilical stump haemorrhage was observed in all patients during the neonatal period. Haematoma, soft tissue haemorrhage and poor wound healing are other manifestations of our patients. Intracranial haemorrhage (ICH) was seen in two patients. One of our patients had a history of miscarriage, one for 3 months and the other for 7 months. This patient was given FXIII prophylaxis when pregnancy was planned. The patient reached the 8th month of her pregnancy with FXIII prophylaxis without any problem. This patient's birth is expected. Fresh frozen plasma and FXIII concentrate were used for bleeding control and surgery in these patients.
Discussion/Conclusion: Clinical findings and management of rare coagulation factor deficiencies are limited due to its low prevalence. Increased evidence-based guidelines for the diagnosis and management of this patient population is required. In this study, we reported the cases and have encountered in management of FXIII deficiency.
Disclosure of Interest: None declared.

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PO218 | Coagulation factor FXII—is a rare coagulopathy or a common laboratory finding?

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Introduction: The study is dedicated to isolated prolonged activated partial thromboplastin time (APTT) syndrome (IP APTT S) and the frequency of factor XII (FXII) deficiency. Coagulation factor FXII is monitored by the APTT test. Deficiency of FXII is manifested by isolated IP APTT S, but does not lead to clinically significant bleeding and asymptomatic and the risk of perioperative bleeding in patients is low.
Methods: A total of 214 plasma samples from patients with IP APTT S were examined. Patients with liver pathology and patients taking anticoagulants were excluded. The distribution by sex and age: two children (boy and girl 6 and 4 year old), nine men (21–54 years, average age 37 years), 42 women (18–83 years, mean age 38 years). Screening tests [APTT sensitive to lupus anticoagulant (LA), test with Russell's viper venom, in case a positive result—a mix test and confirmatory tests; coagulation factors VIII, IX, XI, XII], von Willebrand factor (vWF) antigen and activity, %, clotting inhibitors (FVIII, FIX). A total of 396 studies of the FXII were conducted.
Results: IP APTT S were identified: LA $n = 118$ (55%); FXII deficiency $n = 53$ (25%); von Willebrand disease, $n = 14$ (7%); haemophilia A, $n = 11$ (5%); haemophilia B, $n = 11$ (5%) and FXI deficiency, $n = 7$ (3%). The severity of FXII deficiency: 0%–1% (severe) $n = 3$; 1%–5% (moderate) $n = 6$; and FXII 5%–50% (mild) $n = 44$.
Discussion/Conclusion: It was found that the second most common cause of IP APTT S was FXII deficiency (25%). Thus, in the absence of haemorrhagic syndrome, it is first of all advisable to examine plasma with IP APTT S for the presence of LA and FXII deficiency.
Disclosure of Interest: None declared.

PO219 | Heavy menstrual bleeding in an adolescent with platelet GP VI deficiency and thrombocytopenia: A challenge between hereditary or acquired

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Introduction: Platelet surface contains large number of receptors that when expose to their ligands result in platelet adhesion, activation and thrombus formation. Collagen is one of the most abundant components of the extracellular matrix serving as a substrate for platelet adhesion and activation. Platelets contain two receptors for collagen, integrin $\alpha 2\beta 1$ and glycoprotein VI. Without GPVI binding to collagen, platelets cannot form a clot leading to bleeding problems.
Methods: A 13-year-old female was transferred to haematology clinic for severe menorrhagia. Her past history was remarkable for an episode of gastrointestinal bleeding at the age of 8 attributed to infectious colitis. Laboratory tests showed moderate thrombocytopenia at that time. Later, she developed scattered petechia and ecchymoses which diagnosis of ITP was made for the patient. Upon presentation, she was severely anaemic for which she received blood transfusions. CBC showed mild thrombocytopenia which was not appropriate with degree of the menorrhagia.
Results: Coagulation tests including PT and aPTT were normal. BT was upper limit of normal (Ivy: 8:30 min). Von Willebrand factor activity and antigen along with coagulation factor VIII (FVIII) activity were assessed which were within normal ranges. Platelet aggregometry using a panel of agonists including ristocetin, ADP and collagen was performed on platelet-rich plasma. The patient's platelets failed to respond to collagen at 2 and 5 μg/mL concentrations but aggregated normally in response to ADP, arachidonic acid and ristocetin. Also, impaired ATP release was observed in response to collagen 2 μg/mL, ADP and arachidonic acid. GPVI quantification by flow cytometry evidenced a deficiency, but GPIb and IIb/IIIa integrins were expressed at normal levels on patient's platelets.
Discussion/Conclusion: Autosomal recessive defects of GPVI gene cause a mild bleeding disorder. GPVI deficiency has also been described in patients with ITP where autoantibodies are assumed to induce GPVI shedding. Here, we report an adolescent with bleeding manifestations and mild to moderate thrombocytopenia whose platelets failed to become activated in response to collagen. Considering both hereditary and acquired aetiologies in deficiency of platelet GPVI and history of thrombocytopenia in this case, the authors highly recommend genetic study to discriminate these two entities in this patient.
Disclosure of Interest: None declared.

PO220 | Leukocyte adhesion deficiency, type III in an infant presenting with intestinal obstruction: A case report from Iran

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Introduction: The kindlin family member 3 preferred name FERMT3 is a 'β-integrin protein' expressed mainly in hematopoietic cells. Deficiencies in FERMT3 have been linked to the autosomal recessive 'leukocyte adhesion deficiency, type III'.
Methods: A 20-month-old boy, first-born child to parents with consanguinity, was referred from department of paediatric immunology for investigation of a bleeding tendency. He was admitted with symptoms

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suggestive of intestinal obstruction at first to the surgical emergency. Non-enhanced CT scan showed a dilated proximal loop and a collapsed distal loop of small bowel. On laparotomy, he was diagnosed to have perforated small intestine without any previous history. Resection and anastomosing the bowel was performed. He had abnormal longstanding bleeding following the surgery. CBC showed marked leukocytosis repeatedly with normal platelets. Coagulation tests were remarkable for a prolonged bleeding time. He also developed recurrent respiratory symptoms in favour of pulmonary infections for which was admitted to paediatric immunology department.

Results: Due to abnormal bleeding phenotype, platelet function tests were performed which revealed severely impaired aggregations in response to all agonists, suggesting a defect in the inside-out activation of integrin aIIbβ3. Flowcytometry revealed a normal expression of the platelet receptors CD41 (integrin aIIb), CD61 (integrin β3), CD42a (GPIX) and CD42b (GPIb-α). The patient was diagnosed with a Glanzmann-like platelet disorder. Regarding the abnormal platelet function profile and marked leukocytosis, a diagnostic exome sequencing test was performed which showed homozygous mutation in exon 14 of FERMT3 gene (p.Arg573*). Flow cytometry revealed a normal expression of the leukocyte receptors. He was diagnosed with leukocyte adhesion deficiency, Type III, a moderate LAD-1-like syndrome and a severe Glanzmann-like bleeding tendency.

Discussion/Conclusion: Individuals with LAD-III (also called LAD-I variant) have Glanzmann's thrombasthenia like bleeding problems and LAD-I-like life-threatening infections. This was the first child with LAD III presenting with intestinal obstruction at diagnosis.

Disclosure of Interest: None declared.

PO221 | Pharmacological management of paroxysmal nocturnal haemoglobinuria in UK: A critical appraisal

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Introduction: Paroxysmal nocturnal haemoglobinuria is a chronic, multi-systemic, rare disease characterised by intravascular haemolysis, thrombosis and bone marrow failure. It is treated with eculizumab infusions every 2 weeks. However, in 2021, the NICE recommended ravulizumab. We evaluated the methodological quality of the UK clinical practice guideline (CPG).

Methods: Four independent reviewers used AGREE II and AGREE-REX tools to evaluate NICE CPG 2021. A score > 60% indicates high quality.

Results: The CPG achieved the following scores in Agree II: D1 Scope and Purpose 87.50%, D2 Stakeholder Involvement 68%, D3 Rigor of Development 53.13%, D4 Clarity of Presentation 91.67%, D5 Applicability 64.58% and D6 Editorial Independence 22.92%. In the Agree-REX: 75% in D1 Clinical Applicability, 57.29% in D2 Values and Preferences, and 68.75% in D3 Implementability.

Discussion/Conclusion: The CPG showed high ratings and methodological quality. The D3 and D6 of Agree-II and D2 of Agree-REX may be improved to give independent and context-specific guidance for clinicians.

The UK CPG highlights the patients' perspective and raises personal and social issues that directly affect the care process. The frequency of eculizumab infusions makes it difficult to work, socialise and participate in family life. Additionally, it is challenging to schedule the infusions, and frequent cannulations can lead to scarring of the veins. These patients would have similar clinical results with ravulizumab every 8 weeks. The CPG highlights the need for a new drug option to reduce the frequency of administration.

The document does not consider adjusting recommendations to tailor local adaptations. Economic factors, such as financial limitations, barriers in insurance coverage and indirect costs of obtaining healthcare, may affect the patient care process. The guidelines often fail to disclose the authors' competing interests. Thus, we suggest explicitly declaring the types of conflicts and mentioning if the funding source has influenced the document's content. The strengths, limitations and risk of evidence bias were not clearly described. However, providing practical and useful guidance for rare diseases in the absence of high-quality evidence may be a challenge.

The PNH CPG developed in England has significantly high-quality scores. It can be implemented in daily practice, and ravulizumab is a cost-effective use of NHS resources.

Disclosure of Interest: None declared.

PO222 | Complex thrombotic and haemorrhagic events in a patient with takayasu arteritis, FVII deficiency, FV leiden thrombophilia and multiple cardiovascular interventions: A case report

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Introduction: FV Leiden thrombophilia when coexisting with congenital bleeding disorders, individuals with these mutations may still exhibit thrombosis while experiencing alleviation of bleeding symptoms.

Methods: A case report.

Results: A 66-year-old woman presented with recurrent epistaxis 4 months after bilateral stenting and balloon angioplasty of the brachial, axillary and subclavian arteries for peripheral artery disease. Two months after stenting she experienced bilateral occlusion of stents despite anticoagulation with 1.25 mg warfarin for mechanical heart valves. Genetic testing confirmed FV Leiden homozygous, FI and FVII

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heterozygous mutations. The patient had a history of atrial fibrillation, arterial hypertension and prior cardiac surgeries (tricuspid valve annuloplasty, aortic dilation, and mitral and aortic valve replacement) in 2014, necessitating continuous warfarin therapy. Additionally, she had rheumatism in childhood.

At admission, coagulation studies revealed low FVII activity (10%), prolonged PT (29 s) and INR (2) with normal APTT, fibrinogen and lupus anticoagulant. ANA, anti-dsDNA, anticardiolipin IgM and anti-β-2-glycoprotein IgM were within normal limits. The patient was managed with cautious warfarin adjustment targeting an INR of 2–3.

Four months after the first presentation to our hospital, the patient presented with numbness and limitation of movement in her arms. Lab tests showed elevated APTT (47.6 s) and INR (3.26). The D-dimer level was 0.37 μ/mL, AT measured at 94%, and FVII was at 19%. Clopidogrel and hydroxychloroquine 200 mg twice a day were added to the treatment regimen. Three months after the last visit (INR 4.19, D-dimer 0.42 μ/mL) colchicine 1 g for 6 months was added to the treatment. Afterward, Takayasu arteritis was confirmed in the patient. Subsequent management will be adjusted in collaboration with related specialists to determine the appropriate treatment.

Discussion/Conclusion: This case presents a challenge due to inherited thrombotic and bleeding disorders, posing difficulties in management amidst prior cardiac interventions and Takayasu arteritis and the need for continuous anticoagulation. A multidisciplinary approach and regular adjustments in the treatment based on evolving clinical findings are essential in achieving optimal patient outcomes in such complex scenarios.

Disclosure of Interest: None declared.

PO223 | Rare acquired bleeding disorders: A challenge in diagnosis and management

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Introduction: Acquired bleeding disorders, including acquired haemophilia A (AHA) and acquired von Willebrand disease (AvWD), are rare. While AHA is an autoimmune disease caused by autoantibodies anti-factor VIII (FVIII), AvWD is associated with multiple mechanisms, which mostly increase the clearance of FvW, but can also decrease its production. Unlike AHA, which in 50% of cases is idiopathic, AvWD is almost always secondary to underlying diseases.

Objective: Characterisation of 24 patients with AHA or AvWD, and comparison between the two entities.

Methods: Retrospective evaluation of 14 patients with AHA and 10 with AvWD. Data collected included clinical presentation, aetiology, diagnosis and treatment.

Results: The 14 patients with AHA (8 M/6F) had a median age of 77 (32–86). Half of the cases were idiopathic, 21.4% were drug-related, 14.3% were associated with pregnancy, 7.1% with autoimmunity and 7.1% with lymphoproliferative diseases. The average inhibitor titre was 41 IUB (4–128). Thirteen patients presented moderate to severe bleeding, which in 64% of cases led to treatment with bypass agents and in all cases, led to the eradication of inhibitor, all with good response but relapse in five cases. One case related to clopidogrel, resolved with discontinuation of the drug. There was no bleeding mortality, but in three cases, mortality was associated with treatment complications.

The 10 patients with AvWD (5 M/5F) had a median age at diagnosis of 51 (8–75). All patients had vWF levels compatible with types 1 or 2 vWD, but only seven had bleeding symptoms. In 30% of patients, AvWD was associated with metabolic diseases (glycogenolysis and Gaucher disease), 20% essential thrombocythemia, 20% Waldstrom macroglobinemia, 10% multiple myeloma and 20% monoclonal gammopathy of uncertain significance. Two patients underwent treatment with intravenous immunoglobulins, and four with vWF concentrates. One patient died with a cerebral haemorrhage.

Discussion/Conclusion: Our cohort confirms that AHA is an autoimmune disease of the elderly, often idiopathic, associated with severe bleeding symptoms and therefore requiring inhibitor irradiation, while AvWD is a more heterogeneous disease, with varied age of presentation and varied bleeding symptoms (absent to severe haemorrhages), associated with multiple mechanisms and is therefore more difficult to eradicate. The identification of the two entities is fundamental as treatment is crucial for the favourable evolution of the diseases.

Disclosure of Interest: None declared.

PO224 | Factor XI deficiencies and deliveries—an observationnal study in Paris Saclay Hospitals

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Introduction: Factor XI (FXI) deficiency is a rare bleeding disorder. The incidence (about 1–10/million) is underestimated because of an important variability of the bleeding phenotype. The weak correlation between FXI level and bleeding manifestations complicates the establishment of a threshold allowing invasive procedures, in particular for neuraxial anaesthesia (NA) (epidural and spinal anaesthesia) in obstetrical context.

In our hospitals, we used the threshold of 40% without personal bleeding history to authorise NA for deliveries. To determine if this threshold could be lowered, we retrospectively studied women with FXI deficiency (FXI < 50%) admitted in two high risk obstetric services during 7 years.

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Methods: This study was conducted in two high-risk two high-risk obstetric departments (Bicêtre and Antoine Béclère hospitals, Paris Saclay, APHP). From 1 January 2014 to 31 January 2021, pregnant women with FXI level determination < 50% were retrospectively identified from the lab software and electronic medical records were evaluated.

Results: We could study 109 deliveries corresponding to 103 women.

Five women (six deliveries) were yet followed for FXI deficiency (21%–36%) with a bleeding symptomatology. None of them underwent neuraxial anaesthesia. One woman (two deliveries) was followed for familial thrombophilia and had an incidental discovery of FXI deficiency. She had epidural anaesthesia only for one delivery (FXI 40%).

For the remaining 101 deliveries (97 patients), FXI deficiency was discovered incidentally during pregnancy follow-up. Nineteen women reported bleeding symptomatology, only two with also family history. FXI level was <30% for six women. NA was realised in nine deliveries (seven epidural and two spinal anaesthesia).

The other women did not report bleeding symptoms and only four had a familial history of bleeding. FXI level was <30% for seven women. NA was realised in 59 deliveries (40 epidural and 19 spinal anaesthesia).

For all reported NA, FXI levels were >30% and we did not observe haemorrhagic complication, whatever the level of FXI.

Discussion/Conclusion: Results of this study are in agreement with previous data suggesting that, in the absence of a bleeding history, the threshold of FXI level ≥30% is sufficient to allow NA without excess bleeding risk (Trossaert, 2023). Published data even suggest that this practice could be extended to FXI < 30% according to clinical data, which requires further studies (Abulafia, 2020).

Disclosure of Interest: None declared.

PO225 | Genetic association of tissue factor pathway inhibitor (TFPIrs7586970 variant) with circulating tissue factor pathway inhibitor levels and ischemic coronary artery disease

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Introduction: Tissue factor pathway inhibitor (TFPI) inhibits the extrinsic pathway of pathway and significantly contributes to the pathogenesis of coronary artery diseases.

Methods: A descriptive case–control study that included 156 individuals; 78 ischemic coronary artery disease patients (ICAD) and 78 apparently healthy individuals as a control group. All participants were subjected to interview questionnaire, clinical and laboratory assessment, quantitative TFPI plasma level using sandwich ELISA and molecular genotyping of TFPI-rs7586970 genetic variant using Real-time PCR Eva-Green-based high resolution melting curve (HRM) analysis.

Results: A statistically significant increase in the mean TFPI plasma level in the ICAD patients group as opposed to control group (124.85 ± 69.51 ng/mL, 40.11 ± 10.46 ng/mL) which could be attributed to TFPI increased release from injured vascular endothelium, and might be a compensatory reaction to increased (TF) levels in myocardial infarction, as increased levels of TF can overwhelm the inhibitory capacity of TFPI, resulting in thrombosis. The ROC for the plasma TFPI level showed that the TFPI plasma level of more than 60.4 ng/mL as a cut-off value can detect the occurrence of MI [95% confidence interval (CI): 0.918–0.986], with a sensitivity of 80.77% and a specificity of 98.72%. Positive predictive value and negative predictive value of the TFPI were 98.40% and 83.70%, respectively, in diagnosing MI. The ICAD group recorded 26 allele copies of the TFPI-rs7586970 genetic variant whereas the control group recorded six copies. The binary logistic regression model for ICAD occurrence showed that the TFPI-rs7586970 genetic variant polymorphism is a significant predictor for the development of ICAD.

Discussion/Conclusion: TFPI plasma level was higher in ICAD patients; TFPI is a good diagnostic biomarker in ICAD, and an independent risk factor of this disease. Tissue Factor Pathway Inhibitor (TFPIrs7586970 variant) genetic basis and biological pathways could be responsible for circulating tissue factor pathway inhibitor levels and the development of ICAD.

Disclosure of Interest: None declared.

PO226 | Assessment of fibrinolytic status in bleeding disorders of unknown aetiology

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Introduction: Defects in fibrinolysis may be the cause of mild to moderate bleeding symptoms in patients undiagnosed after routine haemostatic testing, but the evaluation of fibrinolysis is not straightforward due to the lack of standardised methods for its assessment. Rotational thromboelastometry (ROTEM) in the presence of fibrinolytic activators such as tPA is one of the available approaches.

Our aim was to analyse the fibrinolytic profile by ROTEM-tPA in patients with bleeding of unknown cause.

Methods: Patients referred for bleeding diathesis were evaluated in this study, excluding those with thrombocytopenia, anaemia or hypofibrinogenaemia. Blood count, basic coagulation assays, aggregometry, PFA-100 and euglobulin lysis time were performed.

ROTEM tests were performed with NATEM, FIBTEM and EXTEM with and without the addition of 125 ng/mL tPA. ROTEM parameters to evaluate fibrinolysis were: lysis index (LI), lysis onset time (LOT) and lysis time (LT).

Results from ROTEM-tPA analysis of 20 healthy volunteers were used to calculate the normal reference ranges.

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Results: Alteration of the euglobulin lysis time (<120 s) was detected in 25% of the patients.

ROTEM values of NATEM, and EXTEM CT (clotting time) and FIBTEM MCF (maximum clot firmness) were within the normal reference range in all patients studied, suggesting the absence of coagulation defects or fibrinogen deficiencies.

The EXTEM-tPA parameters LI, LOT and LT were decreased in 55% of the patients compared to the control group, indicating a hyperfibrinolytic profile. In contrast, the EXTEM-tPA results of one patient showed LI, LOT and LT values above the control reference range, suggesting a hypofibrinolytic state.

Discussion/Conclusion: Due to the lack of validated laboratory assays, the diagnosis of fibrinolytic bleeding disorders continues to be a challenge.

In this study, the ROTEM-tPA analysis allowed the identification of a profile consistent with hyperfibrinolysis in several patients, which could be probably involved in their haemorrhagic symptoms. In these patients, it will be necessary to evaluate the levels of fibrinolytic regulators (TAFI, PAI, tPA, plasmin) to determine if any of them are involved in their bleeding symptoms.

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Disclosure of Interest: None declared.

PO227 | MAGT1 deficiency in XMEN disease is associated with impaired platelet function

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Introduction: The magnesium transporter 1 (MAGT1) is a Mg^{2+}-specific ion transport system involved in magnesium homeostasis in lymphocytes. XMEN disease is a rare immunodeficiency disorder caused by loss-of-function mutations in MAGT1 gene. MAGT1 deficiency is known to dysregulate platelet cation homeostasis. So, we aimed to assess platelet function in three brothers with XMEN disease.

Methods: Blood samples from three brothers genetically diagnosed of XMEN disease, from their mother and from healthy donors (HD, $n = 10$) were collected in citrate.

Intracellular Ca^{2+} fluxes were determined by flow cytometry in washed platelets loaded with 1 μM Fura Red in HEPES buffer, at 37°C for 20 min in a 5% CO_2 atmosphere and stained with mAb anti-CD61 PE. Basal intracellular Ca^{2+} levels were measured for 60 s, followed by stimulation with 10 μmol/L of ADP or 100 μmol/L thrombin receptor-activating peptide 6 (TRAP). Finally platelets were stimulated with 2 μg/mL ionomycin to measure maximum Ca^{2+} signalling.

Platelet activation markers and receptors were determined in diluted platelet rich plasma. Platelets were incubated with either buffer or 100 μmol/L TRAP or 10 μmol/L ADP and either FITC-PAC1 (an mAb that recognises activated conformation of fibrinogen receptors), or FITC-anti-P-selectin mAb or anti-CD63 mAb were added. To determine platelet content of fibrinogen receptors, PE-anti-CD41 mAb was added and its binding evaluated by flow cytometry.

Results: MAGT1 mutation caused a reduction of approximately 50% in Ca^{2+} fluxes induced by TRAP, but not by ADP. Accordingly, activation of fibrinogen receptor by TRAP was reduced in patients (HD: 74.61% ± 11.43%; XMEN: 41.60 ± 0.60, $p = .0044$), but no differences were observed when ADP was used as activator.

Similar results were obtained for TRAP-induced P-selectin exposure (HD: 81.57% ± 6.72%; XMEN: 54.83 ± 8.62, $p = .0044$) and CD63 exposure (HD: 51.71% ± 17.47%; XMEN: 25.03 ± 8.01, $p = .0088$). Diminution in TRAP-induced activation was not due to a reduction in the content of fibrinogen receptors on platelets from XMEN patients.

Discussion/Conclusion: These results suggest that deficiency or reduced functionality of MAGT1 induced an impairment in platelet function that could be a potential risk factor for bleeding in XMEN patients.

Disclosure of Interest: None declared.

PO228 | Thromboelastometry to evaluate coagulation in venous malformations

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Introduction: Venous malformations (VMs) are vascular low-flow lesions that present as a spongiform mass formed by dilated vascular channels. Many studies link VMs to coagulation abnormalities, characterised by an increase in D-dimer levels and the presence of phleboliths within the malformation. We aimed to clarify intralesional coagulation process using thromboelastometry (ROTEM) and endothelium condition in VM.

Methods: Thirty paediatric patients with focal VM were recruited. Platelet count, fibrinogen and D-dimer were evaluated by central lab.

Peripheral and intralesional blood samples were drawn in citrate and kinetics of clot formation was determined by ROTEM® triggering intrinsic (INTEM reagent) and extrinsic (EXTEM reagent) coagulation pathways. To evaluate fibrinolysis, ROTEM® EXTEM was performed with 125 nM tPA.

We recorded the clotting time (CT, time from the start of measurement to the start of clotting, in s); clot formation time (time from the start of clotting to 20 mm of amplitude, in s, which reflects the speed of the clotting process); α angle (tangent to the curve at 2 mm amplitude, in degrees, which reflects the rate of fibrin

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polymerisation); amplitude at time '*x*' (in mm); maximum clot firmness (MCF, in mm, which reflects the maximum tensile strength of the thrombus); and lysis at 60 min (LI60, in %; residual clot firmness 60 min after CT).

To test endothelium condition, Syndecan-1 was determined by ELISA. Data were analysed with GraphPrism 6.0.

Results: In patients with VM platelet count and fibrinogen were within the normal range but D-dimer was higher than the normal cut-off value (500 ng/mL). ROTEM® INTEM and EXTEM analyses showed that clot from intralesional blood had less strength than that from peripheral blood (lower A5, A10 and MCF values). This fact can be caused by an increased fibrinolysis in intralesional samples because when EXTEM was done in presence of tPA an extensive fibrinolysis was observed in these samples when compared to peripheral ones.

Syndecan-1 was higher in peripheral than in intralesional plasma (in ng/mL: 34.9 ± 21.1 vs.) and (30.6 ± 22.1 ng/mL, $p = .026$) indicating differences between peripheral and intralesional endothelium.

Discussion/Conclusion: We observed an intralesional hyperfibrinolytic profile in VM and differences in its endothelium condition when compared to peripheral one.

Disclosure of Interest: None declared.

PO229 | Silent convergence: Thrombocytopenia and severe factor X deficiency co-occurrence

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Introduction: Congenital factor X deficiency is a rare hereditary bleeding disorder that can manifest with symptoms ranging from asymptomatic patients to life-threatening bleeding episodes. Chronic thrombocytopenia is also associated with a bleeding risk starting from various aetiologies, with immune thrombocytopenia and congenital thrombocytopenia/thrombopathy being the most relevant in young adults.

Methods: We herein present the case of a 31-years old female patient referred to the coagulation consult for an incidental discovery of both thrombocytopenia and severe factor X deficiency. Platelet counts fluctuated between 26 G/L and 111 G/L, and the factor X level was 4.6%.

Results: No previously normal platelet count was found and the first diagnosis of thrombocytopenia was made during the patient's first pregnancy. Vaginal delivery was successfully performed without any postpartum haemorrhage. Thrombocytopenia workup did not reveal any secondary causes.

Surprisingly, with both a thrombocytopenia and a severe factor X deficiency, the patient never presented with bleeding symptoms, and there were no reports of heavy menstrual bleeding. Genetic analysis revealed a homozygous mutation of the FX gene [p.(Gly447Glu)]. The patient's son was also diagnosed with factor X deficiency with a 21% level and has undergone circumcision without any bleeding complication.

Discussion/Conclusion: Despite the severe factor X deficiency, thrombocytopenia and vitamin K deficiency, the patient did not present with any bleeding symptoms. This highlights the importance of a thorough medical history assessment rather than solely relying on factor levels to evaluate bleeding risk.

Disclosure of Interest: None declared.

PO230 | Hyperfibrinolysis as an undiagnosed cause of haemorrhage: Evaluation of 67 individuals with plasminogen activator inhibitor 1 (PAI1) deficiency

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Introduction: Hyperfibrinolysis is rarely evaluated as a cause of bleeding, although in clinical practice patients with bleeding disorders of unknown cause (BDUC) are common. The failure to investigate fibrinolysis is due to the scarcity of reports of patients with fibrinolysis disorders and the lack of well-established tests.

Objective: We aimed to review data from 67 individuals with decreased plasma levels of plasminogen activator inhibitor 1 (PAI1) identified in our Coagulopathies Centre.

Methods: Retrospective study of 67 patients with functional-PAI1 (PAI:Func) < 2 IU/mL from an initial cohort of 212 patients with PAI1 determinations, selected from laboratory records. Data collected included measurements of PAI:Func (Siemens Healthineers, Marburg) and antigenic PAI1 (PAI:Ag) (Technoclone, Vienna) and ISTH-BAT bleeding score (BS). Only patients with more than 2 low PAI:Func determinations and presence of personal and/or familial bleeding symptoms, and at the same time, absence of other identified bleeding disorders, were included. We consider low PAI:Func < 2IU/mL and low PAI:Ag < 25 ng/mL.

Results: The 67 patients included had median age of 37 years (min 6–max 84) and were predominantly female (78%). The majority of patients (77.6%) had haemorrhagic symptoms, and 15 had familial history ± personal history of bleedings. In 39 patients (58.2%), there was a functional and antigenic deficit of PAI1, and in the remaining patients ($n = 28$), only the PAI:Func was decreased. Average PAI:Func values were 0.39 IU/mL (min 0.41 ± 0.45; max 1.87 ± 1.24) and PAI:Ag values were 18.8 ng/mL (min 11.2 ± 12.9; max 28.6 ± 21.3). Among bleeding patients, BS was 6.94 ± 3.55 in men, 9.55 ± 6.00 in women and 4.78 ± 2.73 in children (<18 years). The most common bleeding observed was menorrhagia (63.5% of women), followed by post-surgical haemorrhage (56.7%) and epistaxis. Additionally, other fibrinolytic defects were excluded in 47 patients (normal α2-antiplasmin and FXIII levels).

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Discussion/Conclusion: PAI1 deficiency associated with bleeding is a challenging diagnostic due to its intrinsic variability, confirmed in this study. Despite being rare, it appears to be underdiagnosed, what is not observed in this study, partially justified by the investigation of fibrinolysis in all patients with BDUC followed at our Centre. Predictably, therapeutic use of antifibrinolytics in our patients improved bleeding symptoms.

Disclosure of Interest: None declared.

PO231 | Morbidity in factor XIII deficiency

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Introduction: Factor XIII (FXIII) is a tetramer made of FXIIIA and FXIIIB components, the deficiency of which leads to unstable clot formation that is easily dissolved by the fibrinolytic system. The instability in clot formation leads to clinical presentations such as brain haemorrhages, delayed bleeding, spontaneous abortions and delayed wound healing; all of which may lead to death. Thus in this study, we evaluate the morbidity of FXIIID, in our population in 2022.

Methods: In this study, the documents of 168 FXIIID patients from 2022 were selected. The cause of deaths was evaluated and those with an identified source of bleeding were enrolled. The demographics, presentation at the time of diagnosis, complications and histories were documented and ISTH bleeding assessment tool was utilised to assess the recorded bleeding episodes of the patients. Statistical analyses were done via SPSS Statistical Software Version 26.

Results: Our results show that the morbidity in FXIIID is slightly more common in men (53%) and occurring in ages between 1 months and 10 years of age (45.8%). The most common clinical presentations that led to diagnosis were seizures, and the least were hemarthrosis of the ankles and abdominal pain (0.6%). Most FXIIID patients experience placental bleeding (85.1%) at birth. Cerebral haemorrhage was the most common cause that led to morbidity (48.2%).

Discussion/Conclusion: FXIIID is a rare, yet severe bleeding disorder, which can lead to serious complications and death. Patient education regarding the signs and symptoms of complications as well as extra precautions regarding presentations in undiagnosed cases should be considered in regions where the prevalence is deemed higher.

Disclosure of Interest: None declared.

PO232 | Utility of activated partial thromboplastin time coagulation waveform analysis for patients with acquired haemophilia A

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Introduction: Activated partial thromboplastin time (aPTT) coagulation waveforms offer supplementary insights for assessing patients' coagulation systems. Certain attributes of aPTT coagulation waveforms can prove instrumental in the diagnosis and monitoring of factor VIII (FVIII) inhibitors. Our aim was to identify distinctive features within the aPTT coagulation waveforms that may provide valuable guidance for initiating early investigations in individuals with unexplained prolonged PTT, thereby facilitating the diagnostic process and the management of patients with FVIII inhibitors.

Methods: We conducted a retrospective analysis of aPTT waveforms generated at our institution in Toledo, Spain, utilising ACL TOP 700 CTS instruments and SynthASil aPTT reagents. We specifically examined the aPTT waveforms of three patients with acquired FVIII inhibitors and a control group of individuals with normal aPTT values.

We gathered data on aPTT values, FVIII levels, inhibitor titres, 1Dmax, 2Dmax and 2Dmin. In addition, we conducted a subjective assessment of the graphical waveforms to identify qualitative features that could potentially aid in the detection and monitoring of acquired factor inhibitors.

Results: From a quantitative perspective, significant differences were observed in the values of 1Dmax, 2Dmax and 2Dmin between patients with an FVIII inhibitor and normal controls (medians in mAbs/s^2 of 312, 1121 and −533 compared to 123, 182 and −33, respectively). Qualitatively, patients with a FVIII inhibitor exhibited a double peak in the first derivative, even when TTPa values were within the normal range. This feature was not observed in any of the healthy controls.

Furthermore, a strong positive correlation was identified between the values of 2Dmin and FVIII levels ($r = 0.844$).

Discussion/Conclusion: The quantitative and qualitative analysis of aPTT coagulation waveforms generated by coagulation analysers employing optical detection methods can prove invaluable in the identification and monitoring of acquired FVIII inhibitors in patients with unexplained prolonged PTT. This approach holds the potential to expedite the confirmation of this condition, thus enabling the prompt identification of patients at risk of severe bleeding if not promptly treated.

Disclosure of Interest: None declared.

PO233 | A novel homozygous variant disrupting splicing site of VPS33B causing bleeding of unknown cause

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Introduction: Bleeding of unknown cause (BUC) is a diagnosis of exclusion after extensive investigation and remains challenging. Congenital platelet function disorders (CPFD) are commonly seen among these patients. Moreover, in cases of syndromic manifestations whole exome sequencing (WES) may be useful to achieve an accurate diagnosis.

Methods: Two patients with BUC, from a consanguinity family, were enrolled in our Spanish Project of Inherited Platelet Disorders. Bleeding score (BS) was recorded by ISTH-BAT. Platelet phenotyping included full blood count, blood film, coagulation test, light transmission aggregometry (LTA), flow cytometry (FC) analysis of major surface glycoproteins, and agonist-induced granule secretion and western blotting (WB). Genetic analysis consisted of WES and transcript analysis by PCR and Sanger sequencing.

Results: Index cases (II.1 and II.2) were referred due to moderate–severe bleeding (BS = 11 and 3, respectively), short stature, learning difficulties, mild impaired renal function and cholestasis. Blood count, coagulation factors test and LTA were normal. Blood film showed large and hypogranular platelets. FC exhibited severely reduced alpha (P-selectin) secretion with different agonists (II. 1.: 44.5% and 41.9%; II. 2.: 51.3% and 34.4% vs. 88.2% and 97.1% of the control after its activation with ADP 10 μM and TRAP6 25 μM, respectively). WES analysis revealed a homozygous variant within the exon 16 in *VPS33B* gene (c.1225 + 5G > C). In silico analysis suggested that this variant interrupt the canonical splicing donor site and that 114 base pairs of intron 16 could be introduced into the gene transcript. WB analysis unveiled there were a lower expression of VPS33B and von Willebrand factor (II.1.: 12% and II.2.: 8.03%; (II.1.: 23.7% and II.2.: 36.3%) to control. These findings confirmed the diagnosis of arthrogryposis, renal dysfunction and cholestasis (ARC) syndrome in our patients.

Discussion/Conclusion: We identified a homozygous variant in *VPS33B* gene which led a platelet dysfunction and syndromic manifestations. This study reinforces the value of integrated diagnosis, including WES, for patients with BUC, and expands our knowledge on the ARC syndrome.

Disclosure of Interest: None declared.

PO234 | Clot waveform analysis for intrinsic pathway factors abnormalities

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Introduction: Clot waveform analysis (CWA) is a recent global coagulation assessment allowing to observe fibrin formation kinetics during routine clotting tests.

Activated partial thromboplastin time (aPTT) CWA is shown to be useful for diagnosing deficiencies in intrinsic pathway coagulation factors.

The aim is to evaluate the utility of aPTT-based CWA in patients with deficiencies in coagulation factors VIII (FVIII), IX (FIX), XI (FXI) and XII (FXII).

Methods: A retrospective study carried out over a 22-month period (January2022-October2023) including samples from patients with FVIII, FIX, FXI or FXII deficiencies and normal control samples

APTT was performed on ACLTOP® analyser and CWA data were retrieved using an automated photo-optical detection system. The fibrin formation curve was studied along with its two derivatives: the first derivative D1 (coagulation velocity) and the second derivative D2 (coagulation acceleration).

We studied five parameters: Max1(maximum velocity), Max2(maximum acceleration), Min2(maximum deceleration), tMax1(peak time of velocity) and tMax2 (peak time of acceleration).

Intrinsic pathway factor activity was measured using a one-stage assay.

Results: A total of 164 patient samples were included belonging to patients with HA($n = 133$), HB($n = 15$), FXI deficiency($n = 14$) and FXII deficiency($n = 2$) along with 50 normal controls.

Patients with intrinsic pathway factors deficiencies showed visibly impaired thrombin formation compared to normal controls with significantly longer peak times of velocity and acceleration and lower heights of velocity (Max1) and acceleration (Max2, Min2) ($p < .0001$). They often presented with a particular aspect of the curve with a biphasic pattern of acceleration and velocity.

There was a good correlation between FVIII levels and CWA parameters Max1($r = 0.768$), Max2($r = 0.834$) and Min2($r = 0.899$) in HA patients ($p < .0001$) also demonstrating better differentiation at very low FVIII levels when compared to FVIII assay.

Study of HB samples showed a good correlation between FIX levels and Max1($r = 0.785$), Max2($r = 0.878$) and Min2($r = 0.954$) ($p < .0001$).

The same observation was found in patients with FXI deficiency as FXI levels correlated well with Max1($r = 0.719$), Max2($r = 0.680$) and Min2($r = 0.651$) ($p < .001$).

Discussion/Conclusion: APTT-based CWA through its good correlation with intrinsic coagulation pathway factor levels and increased sensitivity in the lower values appears to be a fast cheap and useful tool to assess bleeding risk and examine haemostatic abnormalities.

Disclosure of Interest: None declared.

PO235 | Evaluation of the causes of deaths in families with factor XIIIL deficiency

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Introduction: Factor XIII deficiency disrupts the final stage of the coagulation cascade that inflicts 1 in every 2 million individuals. As an autosomal recessive condition, it is far more common in populations with high rates of familial marriages. The unstable clot formation predisposes patients to bleeding complications such cerebral haemorrhages, placental bleeding, delayed wound healing and prolonged and recurrent bleeding, all which can vary from mild to severe and deadly events.

Methods: In this cross-sectional, descriptive study, the documents of 68 expired patients from families known for FXIIID in our repository were selected. The genders and causes of death were gathered and possible associations were identified, and the sources of bleeding along with presentations at the diagnosis along with complications were recorded. Then the statistical data were analysed using SPSS Statistics Software Version 26.

Results: Of the 68 selected documents, 51.5% were women and 48.5% were men. Forty-six patient (67.6%) were below 24 months old, and in 50% of the families were at least one death, while ≥3 deaths were only seen in 8.8% of the families. In families with FXIIID as the likely cause of death, 79.4% were the result of familial marriages. The clinical presentation of 105 patients who were the first individuals diagnosed with FXIIID in their family, are shown in the table with the highest number being due to placental bleeding (30.55%). Complications that led to death were mostly due to cerebral haemorrhage and placental bleeding (36.8% and 63.2%, respectively).

Discussion/Conclusion: In conclusion, we recommend a prenatal screening program for regions with high rates of familial marriages, as well as protocols for follow-ups with families registered with FXIIID. Emphasis should be made on the presentations and complications specifically in both the likely cases and suspicious presentations.

Disclosure of Interest: None declared.

PO236 | Three case reports of afibrinogenaemia: Different phenotypes and different clinical evolutions—an open issue

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Introduction: Congenital afibrinogenaemia is a hereditary disorder characterised by absence of fibrinogen leading to a broad range of symptoms from life-threatening bleedings to thrombosis. At the moment neither guidelines are available for treatment nor risk factors have been identified to predict thrombotic complications. Here, we describe three cases with different evolution of phenotype and treatment.

Methods:

Results: Case report 1: V.A. is a 35 year-old woman, diagnosed at 1 year old for gums bleeding. She started prophylaxis treatment but with a poor compliance. After repeated episodes of haemoperitoneum due to corpus luteus rupture, combined hormonal contraceptive was begun at the age of 20. At the age of 30 she was accepted to emergency department (ED) for abdominal pain and hematoma of abdominal wall. A Budd–Chiari syndrome was diagnosed. She was selected for orthotopic liver transplantation (OLT). During pre-transplantation work up a left subdural hematoma was diagnosed. OLT and, months later, evacuation of subdural hematoma were performed. At the moment, 5 years after OLT, first pregnancy is ongoing with normal coagulation parameters.

Case report 2: C.G. is a 23 year-old man, diagnosed at 1 year old for gingival frenulum bleeding; no major bleedings were referred. He continued with fibrinogen infusions once/twice a month for minor bleedings such as recurrent epistaxis or hematoma. In October 2022, he was admitted to ED for abdominal pain due to a venous thrombosis of porto-spleno-mesenteric confluence; he started anticoagulant therapy with low molecular weight heparin together with regular prophylaxis with fibrinogen concentrate, maintaining a trough level of 70 mg/dL; no bleedings have been reported so far. Liver transplantation is at the moment not feasible because of scarce recanalisation.

Case report 3: E.G. is a 41 year-old man on prophylaxis with fibrinogen concentrate since the age of 30 because of recurrent hemarthrosis. Further, he suffers from Bardet–Biedl syndrome and he is currently on follow up for HCV related liver disease and mild kidney failure. He has not experienced any bleeding or thrombotic complications so far.

Discussion/Conclusion: Here, we report three different phenotypes of afibrinogenaemia. So far, neither clinical nor biological data can predict clinical evolution; further evidences are needed to improve treatment in this difficult setting.

Disclosure of Interest: None declared.

PO237 | ADAMTS-13 activity and its implications in paediatric sepsis: A synthesis of key findings from a decade of research

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Introduction: ADAMTS-13 is a crucial enzyme responsible for modulating the size of von Willebrand factor (VWF) in plasma, playing a pivotal role in haemostasis and thrombotic processes. Its deficiency can lead to excessive platelet adhesion, thereby promoting clot formation. Paediatric sepsis is a severe and potentially life-threatening response to infection that can escalate rapidly, leading to organ damage or failure. The intersection of ADAMTS-13 activity and sepsis in children may shed light on disease severity and potential therapeutic avenues.

Methods: An analysis of the relationship between ADAMTS-13 activity and sepsis in children was conducted using the PubMed and Scopus databases with the keyword 'ADAMTS-13 Sepsis Children', yielding five publications from 2007 to 2019. No publications on this topic published after 2019 were identified.

Results: Studies between 2007 and 2019 consistently found altered ADAMTS-13 activity in paediatric patients with severe sepsis. Nguyen

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et al. (2007) and Karim et al. (2013) reported high percentages of patients with this deficiency, correlating to illness severity. Lin et al. (2016) and Bongers et al. (2010) observed noticeable reductions in ADAMTS-13 levels, especially in severe cases such as septic shock or meningococcal sepsis. However, Rautiainen et al. (2019) found its reliability as a prognostic indicator inconclusive.

Discussion/Conclusion: Alterations in ADAMTS-13 activity in paediatric sepsis patients can greatly influence the disease's severity and outcomes. The consistent findings across various studies underscore its potential role in the pathophysiology of sepsis and its viability as a prognostic marker. Early detection of ADAMTS-13 deficiency permits the prompt initiation of targeted treatments, including the administration of fresh frozen plasma and recombinant ADAMTS-13. This can potentially reduce severe health issues associated with this deficiency. Given these findings, there is a pressing need to develop a diagnostic-therapeutic algorithm for paediatric sepsis that incorporates ADAMTS-13 level assessments and addresses its deficiencies in the treatment strategy.

Disclosure of Interest: None declared.

PO238 | From severe sepsis to amputation: The pivotal role of ADAMTS13 deficiency in paediatric outcomes

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Introduction: Thrombotic thrombocytopenic purpura (TTP) is a haematological disorder characterised by microangiopathic haemolytic anaemia and thrombocytopenia. Central to TTP's pathophysiology is the metalloproteinase enzyme ADAMTS13, which cleaves ultra-large von Willebrand factor (vWF) multimers. A deficiency in ADAMTS13 activity allows the accumulation of vWF multimers, leading to platelet aggregation and microthrombi formation. Sepsis-induced endothelial dysfunction can perturb the ADAMTS13-vWF axis. The resultant endothelial activation potentially promotes proteolytic degradation of ADAMTS13 and inhibits its synthesis. We present a case of a 3.5-year-old girl, who was admitted with severe sepsis leading to cardiopulmonary arrest, multiorgan failure and limb ischemia necessitating bilateral below-knee amputations.

Methods: A retrospective analysis was conducted on a paediatric patient's medical records from the Paediatric Intensive Care Unit, followed by consultations at the Clinic for Blood Coagulation Disorders. The authors of this publication are also the attending physicians of the child.

Results: The girl was initially admitted due to a septic shock resulting from a *Streptococcus pyogenes* infection. Rapid deterioration led to signs of septicaemia including a rash and purpura. She underwent fasciotomy and then bilateral amputation of the lower limb due to progressive tissue necrosis. Significant laboratory findings included reduced ADAMTS-13 activity (min. 13.3%) during sepsis, with subsequent improvement after administration of fresh frozen plasma (FFP). Further tests including antibodies against beta-2 glycoprotein, cardiolipin and lupus anticoagulant returned negative. The coagulation profile was within normal limits. Currently, the young patient has fully recovered from sepsis, with her ADAMTS-13 levels registering at 116%. Following her recovery, the child has undergone three procedures related to the stumps of her lower limbs.

Discussion/Conclusion: By presenting this case, we aim to shed light on the importance of monitoring ADAMTS13 levels during sepsis, not solely for the risk of TTP but also to comprehend the mechanisms potentially leading to vascular complications in sepsis. Given these findings, there is a pressing need to develop a diagnostic-therapeutic algorithm for paediatric sepsis that incorporates ADAMTS-13 level assessments and addresses its deficiencies in the treatment strategy.

Disclosure of Interest: None declared.

PO239 | Management of glanzmann thrombasthenia: A European survey on current clinical practice

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Introduction: Glanzmann thrombasthenia (GT) is a rare and complex bleeding disorder, of which diagnosis and management is particularly challenging. Expert opinions and registry data have informed some existing guidelines and recommendations, but there remains a lack of consensus on optimal approaches in clinical practice. This initiative aimed to explore current European clinical practice via a physician survey.

Methods: European haematologists were invited to an online 57-question questionnaire covering various aspects of GT diagnosis and management. Survey data were tallied using simple descriptive statistics.

Results: Ninety-four participants from 16 countries participated in the survey. On average, most centres followed up <10 patients. Participants reported similar approaches to several issues. Almost all participants perform light transmission aggregometry, flow cytometry and genetic analysis to diagnose patients with GT. About 90%

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screened for anti-HLA antibodies and almost three quarters would use HLA-identical apheresis platelet concentrates if available. When asked how many days of therapy (platelet transfusions or rFVIIa) they would propose in case of minor surgery, about 80% replied 'less than 2 days'. 87% used the recommended dose of rFVIIa (80–120 μg/kg body weight every 2–3 h). Finally, three quarters of participants prescribed chronic oral iron supplementation to their patients. Dissimilar approaches were reported on other aspects including (i) circumstances in which to use HLA-matched platelet concentrates, as only one third of practitioners used them systematically; (ii) the number of units and days of platelet concentrates or rFVIIa generally administered in case of major surgery; (iii) more than 50% recognised that they did not regularly screen anti-$\alpha_{IIb}\beta_3$ antibodies and finally, (iv) almost two thirds did not use pharmacological thromboprophylaxis in surgical settings.

Discussion/Conclusion: Much of the variation in practice reflects the lack of evidence-based recommendations in the management of GT. International consensus and guidance may facilitate better care and improved outcomes for these patients.

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PO240 | Targeting tissue factor pathway inhibitor with concizumab to improve haemostasis in patients with glanzmann thrombasthenia: An in vitro study

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Introduction: Glanzmann thrombasthenia (GT) is a rare bleeding disorder caused by inherited defects of the platelet $\alpha_{IIb}\beta_3$ integrin. Platelet transfusions and/or recombinant activated factor VIIa (FVIIa) are used to control life-threatening blood loss. However, these therapies have short lifespan, requiring repeated intravenous administrations, rending them not adapted for prophylaxis. Concizumab is a monoclonal humanised antibody specific for the second Kunitz domain of tissue factor pathway inhibitor (TFPI), abolishing its anticoagulant effect. Thus, it facilitates the production of thrombin and might have potential as subcutaneous prophylaxis in GT. We aimed to evaluate the in vitro effect of concizumab to improve haemostasis in GT.

Methods: We used thrombin generation assay (TGA), microchip flow-chamber assay (T-TAS), rotational thromboelastometry and global fibrinolytic capacity to investigate and compare the effects of mixing concizumab (200, 1000 and 4000 ng/mL) with the main bleed treatment options for persons with GT: platelets concentrates (fresh washed platelets-WP from healthy donors at 50 and 100 G/L) and 20 nM of recombinant activated FVIIa.

Results: Patients with GT ($n = 9$) displayed a significantly prolonged lag time of TGA ($\Delta = +85\%$; $p < .05$) compared with controls ($n = 9$). In contrast, WP (50 and 100 G/L), rFVIIa or concizumab (200, 1000 and 4000 ng/mL) normalised thrombin peaks. In flow conditions, 10 min after starting, occlusive thrombi were present in all healthy subjects ($n = 6$), whereas in GT ($n = 6$), results showed no platelet-fibrin depositions. In contrast, whole blood samples from patients with GT spiked with 100 G/L of WP, rFVIIa or concizumab (1000 and 4000 ng/mL) allowed the formation of subocclusive or occlusive thrombi. The median ROTEM clotting time (CT) from patients (677 s; $n = 10$) was significantly prolonged compared to controls (523; $n = 10$) and clots from GT patients displayed excessive susceptibility to fibrinolysis. When WP (50 and 100 G/L), rFVIIa or concizumab (200, 1000 or 4000 ng/mL) were spiked in samples of patients with GT, CT and time of lysis were improved.

Discussion/Conclusion: We showed that concizumab enhanced thrombin generation, improved thrombus formation under flow condition, reduced clotting time and limited clot lysis. These results suggest that concizumab might be a novel approach for future clinical evaluation in GT.

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PO241 | Prospective examination of acquired von Willebrand syndrome co-occurrence in patients with BCR-ABL1-negative myeloproliferative neoplasms

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Introduction: BCR-ABL1 negative myeloproliferative neoplasms (MPN) represent a group of disorders characterised by a clonal proliferation of one or more myeloid cell lineages. An intriguing, yet often overlooked, complication of MPN is the development of acquired von Willebrand syndrome (AVWS), likely triggered by high platelet counts, which increases shear stress and von Willebrand factor (VWF) multimer adsorption onto platelets, leading to increased VWF proteolysis.

Aim: We explored the co-occurrence of AVWS in MPN patients, and examined the relationship between VWF activity and various haematological parameters.

Methods: We prospectively examined 299 patients (174 females, 125 males) diagnosed with MPN (157 patients with essential thrombocythemia, 88 with polycythemia vera and 54 with myelofibrosis) since 2003 according to WHO diagnostic criteria. Alongside a complete blood count, and taking into consideration blood group, we assessed AVWS presence at MPN diagnosis by measuring VWF antigen (VWF:Ag), FVIII activity and VWF activity (VWF:Ac) utilising the functional assay VWF:GP1bM.

Results: At diagnosis of MPN and after excluding three patients with congenital deficiency of VWF, 75 (25.1%) patients were diagnosed with AVWS defined as VWF activity/antigen <0.7. In our cohort, 43 (13.7%) patients had bleeding complications at MPN diagnosis, of those 12 (27.9%) patients had AVWS. Compared with patients with normal VWF:Ac, patients with VWF:Ac < 50% had significantly higher leukocyte count ($p = .001$), erythrocyte count ($p < .001$), platelet count ($p < .001$), haemoglobin levels ($p < .001$) and haematocrit values ($p < .001$). We evaluated two platelet count cut-offs for predicting VWF:Ac less than 50%. For a cut-off of 600x109/L, specificity and sensitivity were estimated at 77% and 67%, respectively; conversely, at 1000 x 109/L, although specificity dropped to 30%, sensitivity reached 95%.

Discussion/Conclusion: AVWS can be present at diagnosis in a significant number of newly diagnosed MPN patients. Decisions regarding AVWS testing based on platelet count often pose challenges; thus, the diagnostic workup should be grounded in a comprehensive understanding of laboratory and clinical indicators. The management of MPN, as the root cause of AVWS, and patient preparation before procedures are essential to avert bleeding complications.

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Disclosure of Interest: None declared.

PO242 | Haemorrhagic phenotype of factor VII de ficiency between biology and clinical

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Introduction: Hereditary factor VII (FVII) deficiency is clinically and biologically heterogeneous. The severity of haemorrhagic signs is variable and poorly correlated with plasma FVII:C levels. The majority of studies note discrepancies between the factor level and the importance of haemorrhagic signs; moreover, common haemostasis tests are poorly predictive in terms of haemorrhagic risk. In addition, a proportion of patients remain asymptomatic, which can make the prediction of bleeding risk and its management difficult. Two severity scales are currently available (Peyvandi, Jain).

Our objective is to analyse the relationship between the haemorrhagic phenotype and the plasma level of FVII.

Methods: This is a retrospective study, which includes all patients with FVII deficiency followed at the Haemophilia Centre (CTH) of the Beni Messous University Hospital. The various data were collected from patient files. Patients: age; history (ATCDS) of bleeding; the level of FVII. We classified the severity of the deficit according to two scales: Peyvandi:A, Jain:B.

Results: A total of 149 patients with FVII deficiency are followed at the CTH. Their average age is 36.9 years (18–89), including 46 men and 103 women. The sex ratio is 2.2.

Scale A: for a severe deficit 23.8% of patients were asymptomatic, for moderate and minor 65.42% presented a haemorrhagic syndrome and 4.67% observed postoperatively.

Scale B: For a severe rate, 100% of our patients presented with haemorrhagic ATCDS; for moderate and minor rates 66.9% presented haemorrhagic ATCDS and 4.22% observed in postoperative.

Discussion/Conclusion: In the case of a severe deficit according to scale B; a correlation exists between the rate and the phenotype, but for higher rates, the bleeding risk is poorly predictive.

Furthermore, according to scale A, a discordance is found for all FVII levels, and we observed that some patients presented a haemorrhagic syndrome postoperatively despite high levels and the absence of all haemorrhagic ATCD.

Conclusion: The direct relationship between the plasma level of FVII and the haemorrhagic phenotype remains unproven. It is necessary to establish a score including parameters which can better guide therapeutic indications (haemorrhagic ATCD, the site of the intervention, comorbidities, the age of symptomatological presentation).

Disclosure of Interest: None declared.

PO243 | Assessment of bleeding among paediatric patients at a tertiary care centre unveiled low vitamin K levels

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Introduction: Vitamin K has a pivotal role in haemostasis as it is a cofactor of coagulation factors II (FII), VII (FVII), IX (FIX) and X (FX), anticoagulation proteins C and S. This study was conducted in a Government Hospital which serves mainly the poor and rural population from all around the province of Sinsh. Limited data are available on the relative frequencies of early, classic and late vitamin k deficiency bleeding locally and plasma level of vitamin K has not been assessed before in the population of Sindh.

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Objectives: To assess vitamin K level presenting with bleeding.
To determine demographic profile of VKDB patients.
Methods: This descriptive cross-sectional study was conducted at the Department of Pathology and Department of Paediatrics LUMHS. Patients who met the criteria were selected from Paediatrics Department.
Detailed bleeding history and clinical examination of the patient was done. All patients underwent primary screening for bleeding including PT and APTT that was performed on coagulation analyser. All the samples were analysed for levels of vitamin K1 (ELISA).
Results: Sample size was total 114 patients, with age ranging from day of birth i-e day 1 up to day 180 (up to 6 months) out of which 56 were males and 58 were females. The mean age of was 44.01 days. Though the CBC profile was normal except anaemia in some patients, PT, aPTT, were prolonged in most of the cases. Classical VKDB was found to be the prevalent pattern of presentation. Bleeding sites commonly found were skin/bruises, umbilical stump, per-rectal followed by other sites including multiple sites.
Discussion/Conclusion: In developing countries like Pakistan, the vitamin K deficiency still remains a significant cause of concern among the newborn and infant visiting Emergencies & Outpatient setting due to bleeding. It presents with variable bleeding pattern depending on the level of vitamin K as well as its time of onset. It was found to be more frequent among males and in preterm neonates.
Keywords: Vitamin K deficiency bleeding, haemorrhagic disease of newborn, coagulation factors.
Disclosure of Interest: None declared.

PO244 | Factor VII deficiency: Monocentric experience

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Introduction: Factor VII (FVII) deficiency is very rare bleeding disorder, but like all autosomal recessive diseases it is more frequent in highly consanguineous communities. The severity of the bleeding syndrome is heterogeneous with no correlation to residual FVII levels.
Methods: We retrospectively evaluated seven cases of FVII deficiency diagnosed and followed over 10 years from 2013 to 2023 in the Clinical Haematology Department of the Farhat Hached Hospital in Sousse-Tunisia.
Results: Seven patients with FVII deficiency, three males and four females. The mean age at diagnosis was 32 years (11–63 years). Haemorrhage was the mean symptoms at the diagnosis, abnormal postoperative bleeding in three cases (C/S section, teeth innervation, bladder intervention), continuous bleeding (genital + gum) in two cases and fortuitous discovery in 2 cases while they were hospitalised for acute leukaemia. Four patients had had a history of familial consanguinity, second degree in two patients and third degree in one patient. One patient had a family history of bleeding in both his sister and his maternal grandmother. Initial haemostasis tests showed no thrombocytopenia in five cases and the two acute leukaemia case CBC showed thrombocytopenia and blasts in blood smear. Low prothrombin levels and normal activated partial thromboplastin time in all patients. FVII assay confirmed the deficiency, revealing low rates. Novo seven treatment was given to four patients with PFC infusions, and one patient was treated with PPSB associated to tranexamic acid and dicynone. For the two leukaemia cases, one had not presented a severe bleeding disorder that required the use of Novo seven while the other case had undergone a spine surgery so he had received factor V supplementation for 3 days. The evolution was marked by the cessation of bleeding in all patients, and a family investigation was carried out in four patients.
Discussion/Conclusion: There are two types of FVII deficiency: congenital and acquired deficiency. Three levels of severity have been identified; the positive diagnosis is based on biological elements, notably an elongated TQ suggesting an abnormality in the exogenous pathway. Confirmation is provided by assay of coagulation factors. Administration of FVII concentrate is effective, given that 0.5 U/kg increases proconvertin levels by 1%.
FVII deficiency is a rare hereditary bleeding disorder. However, in several forms, it can be a functionally life-threatening accident.
Disclosure of Interest: None declared.

PO245 | Bleeding disorders in heavy menstrual bleeding; debunking myths and revealing facts

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Introduction: Individuals with bleeding disorders experience bleeding symptoms such as mucocutaneus and orifical bleeding after trauma or spontaneously. Females with bleeding disorders face additional haemostatic challenges such as heavy menstrual bleeding (HMB) and estimated to be 15 to 30%.[1] Most females are ashamed to talk to their family about the issue of HMB and avoid seeking medical advice. We aimed in this study to determine how bleeding disorders can be a contributing factor in heavy menstruated females.
Methods: This study was cross sectional on females in reproductive age [14–45]. One-hundred females documented to have HMB by using pictorial bleeding assessment chart score [PBAC ≥100]. Thrombocytopenia, systemic illness and local causes, for example, uterine fibroids were excluded. Bleeding assessment tool ISTH-BAT was used to quantify the bleeding score. We assessed haemoglobin level (CBC), activated partial thromboplastin time (aPTT), prothrombin time (PT) and levels of factors V (FV), VII (FVII), VIII (FVIII), IX (FIX), ristocetin cofactor activity, VWF antigen assay, platelet aggregation tests (ADP, ristocetin).
Results: The mean of PBAC score was 234 [100–950]. The bleeding score mean was 9 [4–22]. Mean of haemoglobin level was 9.8 ± 1.2.

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Seventy-eight [78%] females out of 100 had bleeding disorders. The bleeding disorders were: 30 cases VWD, 24 cases clotting factor deficiencies [nine FVII deficiency, eight FVIII deficiency, five FV deficiency, two FIX deficiency], 24 cases platelet disorders (20 Glanzmann thrombasthenia, three platelet storage pool disease and one Bernard–Soulier syndrome). Other mucocutaneus bleeding symptoms were epistaxis, bleeding after dental procedures and ecchymosis.

Discussion/Conclusion: Early recognition of bleeding disorders in females is essential for management and avoidance of complications which has negative impact on quality of life. Because of perception of bleeding disorders, particularly haemophilia, causing bleeding in males and females are only carriers, so those females are often unrecognised and remain undiagnosed. Awareness through campaigns for girls in secondary schools and their mothers about HMB by PBAC score to recognise the difference between normal and abnormal bleeding. It is crucial to alert the general practitioners, physicians and gynaecologists about bleeding disorders as a cause of HMB. Moreover, such cases should be referred to a haematologist for proper management.

Disclosure of Interest: None declared.

PO246 | Shedding light on the intersection of rare bleeding disorders and heavy menstrual bleeding

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Introduction: Inherited platelet disorders are rare genetic conditions that affect platelet functions. Clinical presentations of inherited platelet disorders are mucocutaneus bleeding: epistaxis, easy bruising and heavy menstrual bleeding]HMB]. HMB is a symptom often presented to obstetrician-gynaecologist. It was shown that 15%–30% of those with HMB have an underlying inherited bleeding disorder.[1]

Methods: To highlight the contribution of inherited rare platelet disorders in unexplained HMB. A 20 year old female patient presented to ER by fatigue, dizziness, light headedness and syncopal attack 1 day earlier. Her laboratory investigations showed haemoglobin 6.5 g/dL (microcytic hypochromic anaemia), normal platelet count, normal prothrombin time and partial thromboplastin time with no source of bleeding as patient claimed. By taking a detailed history there was history of iron deficiency anaemia for which she received oral iron supplements. She also had a history of mild skin bruising, gum bleeding and bleeding after dental procedures since childhood which were controlled at home. To assess menstrual blood loss, we used pictorial bleeding assessment chart (PBAC): PBAC score was 255 (PBAC > 100 denotes HMB).[2] She considered that it was normal because it is similar to her mother and sister. Local causes of HMB, for example, polyps, adenomyosis and leiomyoma were excluded. The next step in evaluation of the patient was to assess Von Willebrand antigen, ristocetin cofactor and factor VIII (FVIII), their results were normal. Platelet aggregation tests revealed lack of aggregation with ADP agonist and normal aggregation with ristocetin.

Results: Diagnosis of Glanzmann thrombasthenia was established. Platelet function disorders can be challenging to diagnose, as platelet function tests are not requested through screening assessments, costly and rather not widely available.

Discussion/Conclusion: Assessment of menstrual blood loss should be objective to elicit HMB. A PBAC score can be used to achieve this goal. HMB may be the only significant symptom that receives medical attention as it can unravel a bleeding disorder. After excluding local causes for HMB meticulous investigations for hereditary platelet disorders must be included. This presented case can show challenges in suspecting and diagnosing a bleeding disorder. It should be managed by a multidisciplinary team.

Disclosure of Interest: None declared.

PO247 | A novel heterozygous variant in COL3A1 related to vascular ehlers-danlos syndrome found in study of bleeding of unknown cause

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Introduction: Bleeding of unknown cause (BUC) is a heterogeneous group of rare disorders which remain challenging to diagnose. Personal and family medical history and several laboratory assays, even molecular techniques, like next generation sequencing (NGS) are needed. However, in most of patients, an accurate diagnosis is not achieved.

Methods: A patient with hematoma in perineal region after delivery was evaluated. Bleeding tendency was evaluated by ISTH-BAT, and Beighton scale and Brighton criteria were used to assess possible joint hypermobility. Phenotype consisted of full blood count, basic biochemistry, basic coagulation test, von Willebrand assays and levels of other coagulation factors, including FXIII, while genotype was performed by whole-exome sequencing (WES).

Results: Index case was admitted to the gynaecology department for fever and extense dissecting hematoma in perineal region 8 days after her first delivery, requiring surgery, blood transfusion and antibiotic therapy. Due to the exclusion of gynaecological causes, haematology assessment was requested. She had superficial hematomas easily since

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childhood and metrorrhagia since menarche. Bleeding score was 6. Although there was no family history of bleeding, she reported paternal family history of several surgical and cardiac vascular complications at a young age.

Additionally, she suffered sprains after minimal trauma and rupture of lateral meniscus. Beighton scale (4 points) and the Brighton criteria meeting the following items: hyperextension of the elbows > 10°, active hyperextension of the knees > 10°, passive dorsiflexion of the fifth finger > 90° and subluxation in more than one joint.

All laboratory tests performed were normal. No specific platelet function studies were performed, given the high suspicion of disorder of connective tissue. So, WES unveiled a novel heterozygous and likely pathogenic variant in exon 27 of *COL3A1* (NM_000090.3: c.1889G > A p.Gly630Glu), related to vascular Ehlers-Danlos syndrome (vEDS) with autosomal dominant inheritance.

Brain MRI detected a 2.6 mm arterial aneurysm which is under surveillance. She receives antihypertensive treatment with Celiprolol.

Discussion/Conclusion: Disorders of connective tissues should be excluded in patients with BUC. We identified a novel variant which cause a vEDS by WES. Suspicion is essential to guide laboratory and genetic tests algorithm in these patients.

Disclosure of Interest: None declared.

PO248 | Glanzmann thrombasthenia and total thyroidectomy: A haemostatic challenge

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Introduction: Glanzmann thrombasthenia (GT) is a rare autosomal recessive disorder due to abnormalities of platelet integrin αIIbβ3. These patients often present with easy bruising and mucocutaneous bleeding and risk of severe bleeding when submitted to surgery, which reveals to be a haemostatic challenge.

So, our aim with this case report is to describe the treatment plan of a GT patient who was successfully submitted to total thyroidectomy.

Methods: A 53-year-old woman with GT diagnosed at birth, with personal history of gingival bleeding, epistaxis and menorrhagia, submitted to thyroidectomy. She has history of tooth extractions under aminocaproic acid without haemorrhagic complications. Although, in the past, she needed multiple transfusions of erythrocyte and platelet concentrates due to uncontrolled epistaxis, menorrhagia and a bleeding peptic ulcer.

Results: This patient underwent total thyroidectomy for non-toxic multinodular goiter and in the immediate perioperative received an apheresis platelet unit, 9 mg of recombinant activated FVII (rFVIIa, 90 μg/kg) and 1 g of tranexamic acid (TXA). An infusion of TXA 2 mg/kg/h for 8 h was started.

In the first 24 h after surgery, it was administered another apheresis platelet unit, 9 mg of rFVIIa every 3 h and 1 g of TXA every 8 h.

In the following days, the patient continued treatment with TXA and rFVIIa with gradually increased intervals between administrations. TXA was suspended on D4 and rFVIIa on D7. On D9, the patient was discharged without further care.

Discussion/Conclusion: Following the therapeutic plan the patient underwent total thyroidectomy without haemoglobin drop or bleeding complications.

So, despite the haemorrhagic risk associated with GT and the delicate location of the surgery, the administration of rFVIIa and antifibrinolytic proved to be effective and reduced the need for platelet transfusion.

Disclosure of Interest: None declared.

PO249 | Screening of inherited bleeding disorders in a large French cohort of women with abnormal uterine bleeding (AUB): analysis of a 'lived' experience

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Introduction: Among the multidisciplinary management of AUB, guidelines recommend screening of inherited bleeding disorders in all women suffering of AUB, bleeding which are the first cause of consultation in women between 30 and 50 years old, and the main bleeding symptom in adolescents with inherited bleeding disorders. The aim of the study is to report the results of the screening of bleeding disorders in a large French cohort.

Methods: All women visited our care centre specifically dedicated to AUB in Lyon from January 2022 to June 2023 were included. Clinical demographics, pictorial blood assessment chart, transvaginal or pelvic ultrasound, Laboratory tests included, aPTT, PT, fibrinogen, factors VIII (FVIII), IX (FIX), XI (FXI), WF:Act, VWF:Ag, platelet counts. Haemoglobin, ferritin, TSH tests were also collected.

Results: During the study period, 303 women have been followed. In the total population, the median (range) of age was 29 years (10–57), of BMI was 22.3 (15.8–56.0), of the Higham score was 315 (60–2750). Twenty eight percent of women presented an anaemia (Hb < 120 g/L) but 62% presented an iron deficiency (ferritin < 20 μg/L). Ultrasound was normal in 60%, and the main gynaecologyc aetiology was adenomyosis (14%), then fibroids (4%) or polyps (4%). Regarding coagulation factors deficiency, PT was normal in all women and no FIX, FXI deficiency or thrombocytopenia was highlighted. Concerning the screening of Von Willebrand disease (VWD), VWF :Act < 50% was found in 31 (10%) of women (71% of group O). In this group, the median (range) of VWF:Act, VWF:Ag and FVIII:C were 40 (2%–50%), 62 (2%–79%) and 77 (2%–132%), respectively. The median (range) of ISTH BAT was equal to 3 (1–7) and was not higher than in global population [3 (1–9)]. In this group, 20% had previously received iron infusion. On the other hand, only 4 (1%) had VWF: Act < 30% (50% of group O). The ISTH BAT was no higher and only one woman received iron infusion.

Discussion/Conclusion: As recommended, a targeted screening of coagulation factors could detect moderate forms of bleeding disorders in all women suffering of AUB regardless the age. If 10% of women

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presented low VWF (VWF:Act < 50%), only 1% have more severe VWD. In the majority of these women, the AUB are the main bleeding symptoms (ISTH BAT < 5).

Disclosure of Interest: None declared.

PO250 | Gynaecological and obstetrical manifestations in women with congenital fibrinogen deficiencies

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Introduction: Women with congenital fibrinogen disorders (CFD) are more likely to experience bleeding throughout their lives due to the natural to natural haemostatic challenges during menstruation, pregnancy and childbirth. Nevertheless, there are currently insufficient studies addressing gynaecological problems in women with CFD. We aimed to determine the gyanecological and obstetrical complications in women with CFD.

Methods: Data were collected from 36 centres in 16 countries from 2013 to 2020 using the Prospective Rare Bleeding Disorders Database (PRO-RBDD). Clinical data, routine and specific coagulation assays including fibrinogen activity (Fg:C) and its antigen (Fg:Ag) were recorded for patients and they were classified based on the Fg:C/Fg:Ag ratio.

Results: Of 123 well-characterised CFD cases, 56 (46%) were adult women. Thirty-two (57%) of them had 68 pregnancies (1 afibrinogenaemia, 16 hypofibrinogenaemia, 49 dysfibrinogenaemia and 2 hypodysfibrinogenaemia) resulting in 47 live births (one afibrinogenaemia, 13 hypofibrinogenaemia, 31 dysfibrinogenaemia and two hypodysfibrinogenaemia). Spontaneous abortion in dysfibrinogenaemic (55%) and menorrhagia in hypofibrinogenaemic (43%) cases were the most prevalent manifestations. Post-partum haemorrhage was observed in 10 cases of which 70% were dysfibrinogenaemic and 30% were hypofibrinogenaemic. There was a high rate of spontaneous abortions (n = 21, 31%), including 18 (86%) in dysfibrinogenaemia and 3 (14%) in hypofibrinogenaemia; 86% of spontaneous abortions occurred in the first-trimester of gestation. Two pregnancies in women with dysfibrinogenaemia and hypofibrinogenaemia ended in spontaneous abortions despite receiving prophylaxis. Bleeding complication during pregnancies was observed in two dysfibrinogenaemic cases (4%). No thrombosis events were observed following pregnancy in our cohort.

Discussion/Conclusion: This multicentre study provided an epidemiological picture of obstetric complications in women with CFD. Our findings indicate that women with dysfibrinogenaemia more often experience obstetric events. Menorrhagia was identified as a highlighted gynaecological manifestation in all CFD groups.

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PO251 | Management of an ovarian cyst rupture in an adolescent with glanzmann's thrombasthenia

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Introduction: Glanzmann's thrombasthenia (GT) is an autosomal recessively inherited platelet disorder caused by deficiency or abnormality of the platelet membrane glycoprotein IIb and/or IIIa. Control and prevention of bleeding among patients with GT remains challenging and treatment options include use of local measures, anti-fibrinolytic therapy, platelet transfusion (PT) and recombinant activated factor VII (rFVIIa). We present the case of a severe intra-abdominal bleeding, in an adolescent with GT, secondary to the rupture of an ovarian cyst, that was successfully controlled with recombinant activated FVII (rFVIIa).

Methods: Retrospective review of the clinical data of the patient.

Results: A 13-year-old girl with GT presented to the emergency of a Regional Hospital with an 8 h history of abdominal pain, syncope episodes and malaise. In the initial evaluation haemoglobin (Hb) was 11 g/dL, and the CT scan revealed the presence of intraperitoneal free fluid suggesting hematoma collection. After 16 h of initiation of the symptoms, the girl was finally transferred to our hospital and on arrival, Hb showed a significant drop to 9.1 g/dL. Decision was to start rFVIIa (100 μg/kg) every 2 h associated with tranexamic acid (TXA). The ultrasonography (US), performed some hours later, confirmed a haemorrhagic cyst of the left ovary. Administration of rFVIIa was maintained every 2 h for 36 h, and although at that moment, Hb was just 7.1 g/dL, the US did not show acute/active haemorrhage. Subsequently, rFVIIa dosing was decreased to every 3 h on days 2 and 3; to every 4 h on days 4 and 5; and finally to every 8 h till the day of discharge. No platelet transfusion was done and there was no need for red blood cells transfusion, although 1 g Iron EV was administered. She was discharged at D + 8, with an Hb of 10.4 g/dL and referenced to a gynaecologist to schedule an US control and to start hormonal treatment.

Discussion/Conclusion: As we show in this case, in GT the severity of symptoms quickly evolves, therefore rapid and efficient bleeding control is mandatory although still remains a real challenge. As our patient was very young, we decided to postponed platelet transfusion hoping to minimise refractoriness to platelets. In this particular case, rFVIIa alone showed efficacy in the control of the bleeding.

Disclosure of Interest: None declared.

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PO252 | Struma nodosa prevalence in european factor XI deficiency patients

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Introduction: Factor XI deficiency (FXI def) is an exceptionally rare coagulation disorder, with a prevalence of 1:106 in the general population. However, within communities characterised by segregated religious practices and intermarriage, such as Ashkenazi Jews and Israeli Arabs, the prevalence increases dramatically to 1:450.[1] Prior research has primarily centred on these specific communities, resulting in a knowledge gap regarding the broader implications of this disorder. Factor deficiencies have a direct link to thyroid function, with hypothyroidism often correlating with bleeding tendencies and hyperthyroidism associated with thromboembolic events.[2] An earlier study of 43 FXI def patients, mainly Ashkenazim, found a 9% prevalence of Struma nodosa.[3]

Methods: Our comprehensive study involved the assessment of 212 FXI def patients. We conducted detailed anamnesis, genetic and blood testing, FXI activity evaluation and ISTH-Bleeding Score assessments. We explored statistical correlations to gain a deeper understanding of the condition.

Results: In our cohort, 51 patients exhibited Struma nodosa, indicating a prevalence of 24%. Notably, both hemi- and homozygote patients displayed significantly lower FXI activity and higher ISTH Bleeding Scores when compared to heterozygote patients.

Discussion/Conclusion: Prior research by Rosen et al. 2006[3] hinted at a potential shared genetic origin between FXI def and Struma nodosa in a limited cohort of four patients, but resource limitations hindered further testing. Our ongoing research seeks to bridge this gap by conducting extensive genetic and laboratory analyses on our cohort of 51 patients with Struma nodosa and FXI deficiency.

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Disclosure of Interest: None declared.

PO253 | Proteomic screening in bleeding disorders of unknown cause

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Introduction: A variety of laboratory tests are needed to define the pathology underlying a bleeding disorder. Despite the diagnostic tools available, the aetiology of the disorder remains unexplained in most patients with a mild clinical phenotype, a so-called Bleeding Disorder with Unknown Cause (BDUC). We here determine plasma proteins involved in coagulation and fibrinolysis for diagnosis of exclusion and dissect protein signatures underlying bleeding phenotypes.

Methods: A coagulation and fibrinolysis protein panel was composed based on the Tier 1 diagnostic gene list (ISTH2023), supplemented with common inhibitors and regulators of fibrinolysis and coagulation. Targeted mass spectrometry was conducted to determine the plasma concentration of 30 target proteins in a single assay. The proteomic strategy was piloted in citrated plasma samples from BDUC cases and individuals from the general population and results were discussed with clinical and biochemistry experts.

Results: VWF, VWPpp, ADAMTS13, PF4 PPBP and coagulation factors fibrinogen (α,β,γ), FII, FV, FVII, FVIII, FIX, FX, FXI, FXII and FXIIIA/B could be quantified from plasma. AT, HCII, protC, protS, protZ, KIN-1, A2AP, PAI-I, HRGP, TAFI, TFPI and plasminogen were measured as representative inhibitors and regulations of coagulation and fibrinolysis. As a-proof-of-concept we first applied the proteomic strategy to differential coagulation protein deficient plasma's and the proteomic screening approach accurately identified partial and complete protein deficiencies. Next, we identified protein signatures representing the haemostatic imbalance directed by proteoforms of altered function, such as FV Amsterdam or VWF variants, in well-studied medical cases with inherited bleeding disorders. Finally, we piloted the proteomic methodology in patients with a BDUC. Overall, the typical coagulation and fibrinolysis signature was normal for most BDUC patients, although we identified altered levels in inhibitors and regulators of coagulation and fibrinolysis, including HCII and protZ, in the minority of BDUC patients.

Discussion/Conclusion: Multiplex quantitation of coagulation and fibrinolysis markers provided individualised protein signatures of haemostasis. Collaboration initiatives between clinical, laboratory specialist and biochemical scientist are ongoing to address the unmet clinical need for improved diagnostics in BDUC.

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PO254 | Evaluation of ADAMTS13 and von Willebrand factor antigen in Covid-19 patient

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Introduction: COVID-19 pandemic continues to pose a global health threat caused by the novel RNA beta coronavirus, SARS-CoV-2. Disease severity varies from asymptomatic to critical pneumonia and death. Identifying biomarkers for disease severity is crucial. COVID-19 is characterised by hypercoagulability, endothelial dysfunction, leading to a high incidence of venous thromboembolism in critically ill patients. Von Willebrand factor (VWF) being released extensively after inflammation-induced vascular damage. ADAMTS13, a metalloprotease responsible for regulating the size of VWF multimers, has been associated with increased thrombotic risk. Aim of the study is to investigate the coagulation and inflammatory changes in patients with COVID-19, focussing on ADAMTS13 and Von Willebrand factor antigen (VWF-AG), and their relationships to disease severity.

Methods: This is cross sectional purposive study on 110 Laboratory confirmed positive COVID-19 PCR Patients held in Department of Pathology at Liaquat University of Medical and Health Sciences Jamshoro, Pakistan. All Data was collected between November 2021 and April 2022.

Results: Mean age of the patients was 43.35 + 15.32 years. Males were 55.5% and females were 44.5%. VWF-AG was deranged in 91.8% of the cases, VWF RISTOCETIN-COFACTOR (VWF: RCo) deranged in 32.7%, factor VIII (FVIII) raised in 58.2%, D dimer was deranged in 84.5% of the cases. Alterations in ADAMTS13 was found to be low in 88.2% of cases, suggesting a deficiency in this enzyme. This indicates disruptions in the balance between VWF and ADAMTS13, contributing to abnormal clotting tendencies. On the other hand, the study found that the variations in the levels of the haemostatic markers were statistically significant when analysed according to the severity of the disease. Severity of the disease had a notable influence on the levels of VWF-AG, VWF: RCo, FVIII and ADAMTS13 in the study participants.

Discussion/Conclusion: In conclusion, the VWF antigen, VWF:RCo and FVIII levels were significantly elevated in COVID-19 patients suggests that these biomarkers can serve as independent risk factors for the severity of the disease and the development of thromboembolism. The severity of the disease had a notable influence on the levels of VWF-AG, VWF:RCo, FVIII and ADAMTS13 in the study participants. Monitoring these biomarkers may aid in identifying patients at high risk for severe disease and developing effective treatment strategies.

Disclosure of Interest: None declared.

PO255 | A first genetically proven case of factor VII deficiency in latvian family

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Introduction: Factor VII (FVII) deficiency is the most common rare inherited autosomal recessive bleeding disorders with different clinical manifestations. Only small amounts of FVIIa are needed to trigger coagulation. FVII deficiency is characterised by a wide spectrum of clinical phenotypes from asymptomatic condition to severe life-threatening bleedings.

Methods: *F7* gene was sequenced by private laboratory using the Illumina's sequencing-by-synthesis method with paired-end sequencing. This test targeted protein-coding exons, exon-intron boundaries (± 20 bps) and selected non-coding, deep intronic variants in the mother and daughter.

Results: We started genetic investigation in a 3-month-old child due to mother's FVII deficiency diagnosed during pregnancy. During pregnancy the mother complained about minimal bleeding from mamilla bruise, was diagnosed with FVII 29%, received replacement therapy with FVII peripartum. Before pregnancy the patient had nose bleedings, minor bruising, severe menstrual bleeding, bleeding after apendectomy and during ectopic pregnancy in the age of 21 years. Diagnosis was established during pregnancy in the age of 23 years.

The child was born by caesarean section due to gluteal position of foetus, no bleedings during perinatal period were noticed. In the age of 3 months skin haemorrhages were noticed, bleeding tests were performed, prolonged prothrombin time was detected, the FVIIc was 34%. Clinical manifestations during childhood were mild, more prominent bleedings were detected during dental manipulations. Until age of 6 years only one hospitalisation occurred due to head trauma with large frontal haematoma, no intracranial haemorrhage was detected. Until age of 6.5 years the child received only few FVII injections.

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DNA diagnostics identified homozygous pathogenic variant NM_000131.4 c.1061C > T, p.(Ala354Val), alias A294V, in *F7* gene in the mother, and heterozygous variant c.1061C > T, p.(Ala354Val) in the daughter.

Discussion/Conclusion: Variant NM_000131.4 c.1061C > T, p.(Ala354Val) in *F7* gene has previously been described as pathogenic in Factor VII Gene variant database. The highest allelic frequency recorded in Estonian population is 0.23% (gnomAd). All in silico tools predict damaging effect, CADD score is 23. Decreased FVIIc was observed (PMID: 15735798). The precise frequency in Latvian population is unknown, needs additional investigation.

Disclosure of Interest: None declared.

PO256 | Characteristics of patients with hereditary combined factor V and factor VIII deficiency in Russia

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Introduction: Combined factor V and factor VIII deficiency (F5F8D) is a rare bleeding disorder (RBD) that accounts for about 3%–5% of all RBDs. In this regard, data on the disease in different countries and populations are limited. The aim of the study is to analyse the clinical and laboratory features of patients with F5F8D in Russia.

Methods: The study group consisted of six patients with F5F8D.

Results: The average age at the time of contacting National Medical Research Center for Hematology, where the diagnosis was carried out, was 41 years (21–61 years). All patients are women. Of the six patients, there were two sisters of Tatar origin, and two other sisters of Chuvash origin. Before contacting our centre, patients had been diagnosed with von Willebrand's disease or haemophilia A or unspecified coagulopathy. In all patients, haemorrhagic syndrome debuted in childhood. Clinical manifestations are represented by nosebleeds (50%), gingival bleeding (67%), ecchymosis (83%), rupture of ovarian cyst (67%) and gastrointestinal bleeding (17%). Postoperative bleeding occurred in two out of six patients, abnormal bleeding after tooth extraction happened in five out of six patients. All women suffered from menorrhagia, massive postpartum bleeding occurred in one woman who gave birth. According to laboratory data, the average values of APTT was 94 s; INR was 1.81; factor V activity was 7.5%, factor VIII activity was 13%. A genetic analysis was performed in three out of six patients. A genetic study of two Tatars sisters revealed a full-scale homozygous deletion of the *MCFD2* gene. Another patient was found to have a homozygous deletion c.1464_1468del (p.Gln488Hisfs*10) in the *LMAN1* gene.

Discussion/Conclusion: The clinical manifestation of F5F8D is similar to the most common coagulopathies: von Willebrand's disease and haemophilia. Laboratory diagnostics are not available in all regions of Russia. Diagnosis is often delayed.

Disclosure of Interest: None declared.

PO257 | Enhanced thrombin and plasmin generation profiles in alpha-2-antiplasmin deficient patients: Data from the RBiN study

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Introduction: Fibrinolysis regulation involves various serine protease inhibitors, including the plasmin-inhibiting protein alpha-2-antiplasmin (A2AP). Alpha-2-antiplasmin deficiency (A2AD) is a rare and relatively unidentified bleeding disorder characterised by increased fibrinolysis and subsequent bleeding. Global haemostatic assays may provide more insight into the malfunctioning of coagulation and fibrinolysis in A2AD patients. Therefore, this study explores thrombin and plasmin generation profiles in A2AD patients and corresponding A2AP activity levels and bleeding phenotype.

Methods: The Nijmegen Haemostasis Assay (NHA) was used to assess thrombin and plasmin generation in 23 A2AD patients from the RBiN study (inclusion 2017–2019). The median age of the patients was 50 years and 70% of them were women. Analysed parameters included thrombin peak height, thrombin potential, fibrin lysis time, plasmin peak height and plasmin potential. These parameters were expressed as percentages of a reference obtained from 53 healthy controls (median age 46 years, 57% women). The NHA data were correlated with the A2AP activity levels and ISTH-BAT scores of the A2AD patients using Pearson correlation coefficients.

Results: A2AD patients displayed significantly shorter fibrin lysis times (74%), higher plasmin potentials (156%) and increased plasmin peak heights (219%) compared to healthy controls. Moreover, significantly higher thrombin potentials (146%) and thrombin peak heights (151%) were observed. Patients' A2AP activity levels ranged from 23% to 83%. Lower A2AP activity levels were correlated with shorter fibrin lysis times ($R = 0.70$), higher plasmin peak heights ($R = -0.68$), higher thrombin potentials ($R = -0.50$) and higher thrombin peak heights ($R = -0.49$). Higher ISTH-BAT scores were correlated with lower A2AP

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activity levels ($R = -0.72$), shorter fibrin lysis times ($R = -0.58$) and higher plasmin peak heights ($R = 0.50$).

Discussion/Conclusion: A2AD patients exhibit enhanced plasmin generation profiles that correlate strongly with both the A2AP activity level and the bleeding phenotype. Interestingly, a significantly increased thrombin generation profile was found as well, probably due to a physiological compensation mechanism to restore the haemostatic balance. These findings provide valuable insights into the haemostatic capacity of A2AD patients and their relationship with A2AP activity levels and bleeding phenotype.

Disclosure of Interest: None declared.

PO258 | Management of surgical intervention in a patient with congenital factor XIII deficiency: A case study

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Introduction: Congenital factor XIII (FXIII) deficiency, a rare bleeding disorder with an incidence of 1 in about 2 million people worldwide, poses a significant clinical challenge due to the potential for severe haemorrhagic complications. This case study examines the clinical management of a 66-year-old female patient with congenital FXIII deficiency, emphasising on the challenges faced and the efficacy of prophylactic treatment in preparation for hip arthroplasty.

Methods: A 66-year-old female was diagnosed with FXIII deficiency at the age of 17. Bleeding manifestations prior to diagnosis included haematomas, menorrhagia and intracranial haemorrhage. Since diagnosis, she has been receiving a prophylactic regimen involving monthly infusions of plasma-derived FXIII (250 IU).In March 2023, the patient underwent hip replacement surgery. Her treatment strategy was adjusted for this surgical intervention by administering an increased dose of plasma-derived FXIII (Cluvot 1250 IU) one day before the surgery. Throughout the perioperative phase, close monitoring of the patient's FXIII levels and routine laboratory values was conducted.

Results: The study's focus revolved around monitoring FXIII levels throughout the critical perioperative period. Prior to surgery, patient's plasma FXIII levels were 99% after Cluvot administration. The patient successfully underwent total hip replacement (Anterior Minimally Invasive Surgery), and post-surgery, her FXIII levels were monitored at intervals. These assessments revealed FXIII levels of 96% on day 2, 71% on day 3, 69% on day 6 and 36% at 9 days post-surgery. Additional 1250 IU doses were administered 1 day and 10 days post-surgery, enabling the patient to transition back to her monthly replacement therapy. Moreover, the patient received prophylactic doses of low molecular weight heparin.

Discussion/Conclusion: Congenital FXIII deficiency is associated with a heightened risk of severe and life-threatening haemorrhages, underscoring the imperative need for prophylactic intervention. This case study highlights the effectiveness of human plasma coagulation FXIII products in successfully elevating and sustaining FXIII levels within the medically recommended range (70%–140%) during the perioperative period of major surgery. The successful outcome of this surgical intervention offers valuable insights into the clinical management of this rare bleeding disorder and the significance of personalised therapeutic strategies.

Disclosure of Interest: None declared.

PO259 | No added value of testing for factor XIII and A2-antiplasmin deficiency in patients with a mucocutaneous bleeding disorder of unknown cause

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Introduction: In patients with an increased mucocutaneous bleeding tendency, extensive diagnostic blood testing is often done. When results of tier 1 assays of primary haemostasis are normal, protocols recommend additional testing to rule out rare disorders including coagulation factor XIII (FXIII) and α2-antiplasmin (α2AP) deficiency. This study aims to evaluate the diagnostic value of FXIII and α2AP levels in patients with a mucocutaneous bleeding disorder of unknown cause (BDUC).

Methods: A retrospective cohort study was performed in patients with a (mucocutaneous) bleeding tendency (defined by an increased ISTH-BAT) who visited our centre between August 2013 and August 2023. In all patients, routine tier 1 diagnostic assays for complete blood count, von Willebrand factor activity and platelet function (light transmission aggregometry and nucleotides) were normal and FXIII and α2AP activity levels were measured. The prevalence of FXIII and AP deficiency was investigated and the association of FXIII and AP levels with ISTH-BAT scores was assessed using linear regression.

Results: We included a total of 158 patients with a mucocutaneous BDUC and an elevated ISTH-BAT score. The median age at inclusion was 37 (range 5–79) years and 88.6% of patients were female. Mean ISTH-BAT scores were 8.2 (SD $\pm$ 3.7) in children, 6.2 (SD $\pm$ 2.1) in men and 10.6 (SD $\pm$ 3.3) in women. Patients displayed median FXIII levels of 111% (IQR = 97–131) and median α2AP levels of 112% (IQR = 103–119). Three (1.9%) patients had FXIII levels below 50%, respectively, 43%, 45% and 46%. Corresponding ISTH-BAT scores were 7, 12 and 14. We did not observe α2AP levels below 60%.

No significant association was found between FXIII levels and ISTH-BAT scores (beta coefficient = −0.006, 95% CI −0.031–0.018; $p = .615$).

Discussion/Conclusion: In our retrospective study we detected a mild FXIII deficiency in 1.9% of patients, with absolute values well above the 30% cutoff considered adequate for normal haemostasis. No patients with an α2AP deficiency were detected. These data suggest that

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in patients with an unexplained mucocutaneous bleeding tendency, measuring FXIII or AP levels is not indicated.

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PO260 | Current practice regarding bleeding disorder of unknown cause (BDUC) in the Netherlands: A national survey

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Introduction: In the majority of individuals who are referred to haemostasis experts with a clinically relevant bleeding tendency, no diagnosis can be made after extensive laboratory testing. These individuals are classified as having a 'bleeding disorder of unknown cause' (BDUC). There is a wide variation in BDUC definitions and performed laboratory haemostasis tests to rule out established bleeding disorders. Clear guidelines for BDUC diagnosis, treatment and follow-up are lacking. This study aims to investigate current practices regarding BDUC in The Netherlands as a foundation for guideline development.

Methods: From 8 June to 6 October 2023, an online survey was sent to 54 haematologists (paediatric and adult), internists vascular medicine, nurse practitioners and clinical chemists, working in Dutch haemophilia treatment centres. Questions comprised the essentials of a BDUC definition, the observed bleeding phenotype, as well as usual diagnostic process, treatment and follow-up. A cut-off of > 70% agreement was defined.

Results: Forty four (81%) healthcare professionals completed the survey including 28 haematologists and internists vascular medicine, nine nurse practitioners and seven clinical chemists. Nineteen percent of respondents indicates no formal registration of BDUC patients in their clinic. A definition for BDUC should entail the presence of (1) an increased bleeding tendency, (2) an elevated bleeding assessment tool (BAT) score, (3) exclusion of other (haemostatic) causes and (4) the absence of abnormal laboratory test results. To score bleeding symptoms, 92% of physicians applies a BAT, predominantly the ISTH-BAT (86%). In general, a stepwise approach, guided by the BAT-score, is used to determine the extent and type of laboratory testing. Significant heterogeneity is observed in the performed laboratory tests and the sequence of execution. Most frequently prescribed treatment options are tranexamic acid and desmopressin. Follow-up depends on bleeding phenotype and bleeding history.

Discussion/Conclusion: Based on preliminary results, four important elements of the definition for BDUC were identified. Furthermore, there is a need for agreement on a standard set of performed laboratory tests to diagnose a patient with BDUC. National consensus resulting in a national guideline will be achieved through panel expert discussion within the BDUC study group which represents all Dutch haemophilia treatment centres.

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and Octapharma and reimbursement for consultation for Received Uniqure. All payments go to the institute, Speaker Bureau of: Karina Meijer has received speaker fees from Alexion, Bayer and CSL Behring (all to institution), P. den Exter: None declared, L. Nieuwenhuizen: None declared, I. van Moort Grant/Research support from: Iris van Moort has received research funding from the Professor Heimburger Award (CSL Behring). Payment does to Erasmus MC as an institution, M. Cnossen Grant/Research support from: Marjon Cnossen has received researcher-initiated research and travel grants from the Dutch Research Council (NWO), the Netherlands Organization for Health Research and Development (ZonMw), the Dutch Healthcare Insurers Innovation Fund, Pfizer, Baxter/Baxalta/Shire/Takeda, Bayer Schering Pharma, CSL Behring, Sobi, Novo Nordisk, Novartis, Nordic Pharma, Roche and Octapharma and has served as a board member for Roche and Bayer. All scholarships, prizes and reimbursements go to Erasmus MC as an institution, F. Heubel-Moenen Grant/Research support from: Floor Heubel-Moenen has received a research grant from Octapharma.

PO261 | Experience in the treatment of ITP with fostamatinib

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Introduction: Idiopathic thrombocytopenic purpura (ITP) is a hematologic disorder characterised by a low platelet count and an increased risk of bleeding. Fostamatinib is a novel therapeutic option that has shown promise in the treatment of ITP. This study aims to share our experience with the use of fostamatinib in managing ITP.

Methods: We conducted a retrospective analysis of a cohort of eight ITP patients who were treated with fostamatinib at 100/12 h. Data were collected on prior treatment history, platelet counts before fostamatinib initiation, dosing adjustments and response to treatment. Adverse events and changes in blood pressure were also monitored.

Results: Our cohort was patients, with a median age of 58.5 years, and a slight majority being 37.5% females. Patients had previously received two prior lines of therapy (37.5%) and three prior lines (62.5%), with high-dose corticosteroids being the initial treatment, and at least were treated with TPO receptor agonist. None of the patients had achieved stable platelet counts or a complete response.

The median platelet count before initiating fostamatinib was 58.3 x 10e9/L (1–149). In 75% of cases, a dose escalation to 150 mg/12 h was required, as per the drug's technical specifications. After 1 month of fostamatinib treatment, the mean platelet count was 98 x 10e9/L (22–257). Notably, 50% of the patients maintained stable platelet counts with fostamatinib as monotherapy, while 12.5% required combination therapy with another TPO receptor agonist, and 37.2% needed corticosteroids in combination.

Importantly, no severe adverse reactions were reported, and all patients maintained normal blood pressure levels. Of the patients, 25% experienced relapse during the follow-up period, and only one patient discontinued treatment due to side effects.

With a median follow-up of 4 months, 37.5% of the patients achieved a complete response, and the mean platelet count at present stands at 89 x 10e9/L.

Discussion/Conclusion: In our experience, fostamatinib has shown promise as a therapeutic option for patients with chronic ITP who have failed to respond to other treatments. It has been effective in achieving stable platelet counts, both as a monotherapy and in combination with other agents, and has demonstrated a favourable safety profile. Further studies with larger sample sizes and longer follow-up periods are warranted to confirm these findings and better evaluate the real-world effectiveness of fostamatinib in the treatment of ITP.

Disclosure of Interest: None declared.

PO262 | Sexuality and reproductive choices in rare bleeding disorders: Data from the RBiN study

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Introduction: Living with a rare bleeding disorder (RBD) may influence sexuality and reproductive choices due to concerns about bleeding risk and RBD heritability. Knowledge about sexual health and reproductive choices in patients with RBDs is scarce, while these are major determinants of quality of life, with similar impact as mental and physical health.

Methods: The Rare Bleeding Disorders in The Netherlands (RBiN) study is a cross-sectional, nationwide study conducted from 2017 to 2019. Patients were included if they were previously diagnosed with a rare coagulation deficiency or disorder of fibrinolysis based on factor activity levels or a pathogenic genetic variant in an RBD gene. Data on sexuality and reproductive choices were retrospectively collected using self-administered questionnaires in patients > 16 years.

Results: Out of 210 RBiN participants aged 16 and older, 99 women and 54 men answered questionnaires about sexuality or reproductive

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choices. In total, 23/70 (33%) women experienced vaginal blood loss after intercourse, and 6/45 (13%) men experienced haematospermia ever in life. However, RBD-related sexual restriction was reported by only 9/120 (7%) participants, with six patients harbouring mild deficiencies. Discussions about sexuality were rarely initiated by healthcare providers (2/130; 2%). A minority of RBD patients (10/128; 8%) would appreciate sexuality being addressed in the consultation room, while 30% (39/128) does not know or would rather not say.

Four men and 23 women (27/123; 22%) with severe (38%) and mild factor deficiencies (6%) reported that reproductive choices were influenced by their RBD. Fear for passing on disease played an important role in men (4/4) and women (7/23). In women, reproductive choices were mainly influenced by fear of bleeding (30%), medical advice from health care providers (13%), fear of intensive treatment during pregnancy (9%), heavy menstrual bleeding (9%) and/or other reasons (13%).

Discussion/Conclusion: Sexual health in RBD patients remains largely unaddressed in the consultation room. Providing an entry point for conversation about sexuality may support recognition of RBD related sexual restriction and would allow discussion for possible solutions for a selection of RBD patients. Family reproductive choice is influenced by their disease in 22% of RBD patients from the Dutch RBiN study, mainly through fear of bleeding during pregnancy and delivery, as well as heritability.

Disclosure of Interest: None declared.

PO263 | Clinical value of laboratory diagnostics for bleeding disorders in general practice

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Introduction: The Dutch national guidelines on laboratory diagnostics in primary care (Landelijke Eerstelijns Afspraak, LESA) advise activated partial thromboplastin time (aPTT), prothrombin time (PT) and thrombocyte count as screening laboratory tests in case of analysis of an increased bleeding tendency in primary care. Since 2018, the Central Diagnostic Laboratory (CDL) in MUMC+ uses a more extensive assortment of tests, including haemoglobin (Hb), leukocyte differentiation and platelet function analyser (PFA, ADP and EPI). The aim of this study is the clinical evaluation of bleeding tendency diagnostics in primary care.

Methods: Data from primary care patients who were screened for an increased bleeding tendency from 2018 to 2022 were analysed. Test results, referral to secondary care services and diagnostic outcomes were analysed.

Results: A total of 304 patients (234 women, 70 men, mean age 54 years old) were screened for a bleeding tendency in primary care. In 25% of these patients (n = 80/304), a laboratory abnormality was found. In 78% of these patients (n = 63/80), only the PFA was prolonged (one or both agonists). Thirty-two patients with abnormal test results were referred to a haematologist for further analysis. In 17/32 patients, a diagnosis was found [platelet function disorder (n = 10), von Willebrand's disease (n = 4), bleeding disorder of unknown cause (n = 2) and thrombopenia (n = 2)]. In the majority of these patients (16/17), only the PFA was prolonged. Out of the 224 patients with normal laboratory test results, 13 patients were referred to a haematologist for further analysis. None of these patients were eventually diagnosed with a bleeding disorder.

Discussion/Conclusion: Adding PFA to the diagnostic screening tests for bleeding disorders in primary care leads to more referrals to secondary care. In referred patients with an increased bleeding tendency and test abnormalities, the chance of having a bleeding disorder is rather high. A part of the patients with abnormalities in the screening laboratory tests are not referred to the haematologist, which is a remarkable observation. The complexity of the bleeding history and interpretation of haemostasis laboratory tests in primary care might (partly) explain this. This could be solved by a customised (phone) consult from the laboratory specialist, instead of a generic consult. This service will be offered by the Central Diagnostic Laboratory from the MUMC+.

Disclosure of Interest: None declared.

PO264 | Fibrinolysis assessment with tPA-ROTEM in patients with bleeding disorders of unknown cause (BDUC)

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Introduction: In the majority of patients referred to a haematologist for evaluation of bleeding symptoms, no diagnosis can be made after extensive laboratory testing. These patients are classified as having a bleeding disorder of unknown cause (BDUC). The lack of clear guidelines on diagnosis, treatment and follow-up is challenging for patients and physicians. Several haemostasis assays have been investigated in BDUC-patients, but little is known about the role of the fibrinolytic pathway. The lack of standardised fibrinolysis tests and their limited availability could explain this. We aimed to investigate the capacity of the tPA-ROTEM assay to detect fibrinolytic abnormalities in BDUC-patients and to correlate these findings with fibrinolytic protein activity levels.

Methods: Data from patients referred to the haematologist for bleeding evaluation were used. BDUC-patients were identified based on an increased bleeding tendency and no abnormalities in extensive

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laboratory testing. tPA-ROTEM assay was done according to the in 2016 validated and published method on the ROTEM device. Fibrinolysis protein plasma levels are measured using ELISA assays. Pre-specified definitions of hyper- and hypofibrinolysis as measured by tPA-ROTEM were applied.

Results: tPA-ROTEM identified a hyperfibrinolytic profile in 15/73 (20%) of BDUC-patients, a hypofibrinolytic profile in 16/73 (22%) of BDUC-patients and a normal profile in 42 BDUC-patients (58%). Plasminogen activity inhibitor 1 (PAI-1) activity and antigen levels and α2-antiplasmin levels were lower in BDUC-patients with a hyperfibrinolytic profile compared to BDUC-patients with a hypofibrinolytic profile. No statistically significant correlations between tPA-ROTEM parameters and fibrinolysis protein plasma levels were identified using multivariate regression analysis.

Discussion/Conclusion: tPA-ROTEM identified a hyperfibrinolytic profile in 20% of BDUC-patients. In this group, the lower PAI-1 activity and antigen levels and lower α2-antiplasmin levels are in concordance with the expected changes in case of hyperfibrinolysis. These findings indicate that these fibrinolysis protein plasma levels are within the lower functional range of their distribution, shifting the balance towards increased clot lysis leading to an increased bleeding tendency. These findings might deliver evidence to the use of antifibrinolytic therapies in BDUC-patients in case of bleeding or interventions.

Disclosure of Interest: None declared.

PO265 | Evaluation of innovative laboratory tests to predict a thrombotic phenotype in a family with dysfibrinogenaemia and a novel FGG mutation

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Introduction: Hypodysfibrinogenaemia is a rare hereditary fibrinogen disorder characterised by quantitative and qualitative fibrinogen defects. These fibrinogen defects can cause thrombotic and haemorrhagic phenotypes. Predicting the phenotype in a specific patient is often not possible with routine coagulation tests. The aim was to characterise the phenotype and the genetic profile of a family with hypodysfibrinogenaemia and to investigate the ability of innovative tests to predict bleeding and/or thrombotic phenotypes in asymptomatic family members.

Methods: The proband, a 60-year-old woman with both bleeding and thrombotic complications, currently on DOAC treatment, and two asymptomatic daughters were referred to our Haemophilia Treatment Centre (HTC) for phenotypical and genotypical analysis of a congenital fibrinogen disorder (CFD). Extensive laboratory testing was done, as well as DNA-sequence analysis and molecular modelling. Thrombin generation and microfluidic testing were also performed to investigate their ability in phenotype prediction.

Results: Fibrinogen activity and antigen levels led to the diagnosis of dysfibrinogenaemia in the proband and hypodysfibrinogenaemia in both daughters. In all three cases, the same heterozygous missense mutation in the *FGG* gene was uncovered. This likely pathogenic mutation leads to the p.(Tyr375Cys) amino acid change. Molecular modelling predicted possible conformational changes or covalent dimerisation of the fibrinogen molecule. Thrombin generation was elevated in one daughter. Microfluidic testing showed enhanced fibrin formation in both daughters, regardless of the coagulation trigger.

Discussion/Conclusion: We described a family with hypodysfibrinogenaemia in whom a novel heterozygous missense mutation in the *FGG* gene was found, possibly leading to conformational changes or covalent dimerisation of the fibrinogen molecule. Microfluidic testing and thrombin generation indicated a thrombotic phenotype in these patients, not detected with routine coagulation tests.

Disclosure of Interest: None declared.

PO266 | Participation in sports in Dutch children and adults with inherited platelet function disorders is similar to the general population: Not afraid to participate

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Introduction: Comprehensive information concerning sports participation in patients with inherited platelet function disorders (IPFDs) is lacking. The primary aim of this study is to assess sport participation in Dutch IFPD patients of different ages in comparison to sport participation with the general population. Secondary, we evaluate the reasons for avoiding sport participation.

Methods: This concerns a sub-analysis of the Trombocytopathy in The Netherlands (TiN) study. Dutch children and adults with IPFD were included between 2016 and 2023 and were asked to fill in questionnaires containing questions about sport participation and measuring the quality of life domains involving anxiety concerning sports and injuries by using the RAND 36-items health survey in adults and a modified version of the Kids ITP Tool and the Child Health Questionnaire (CHQ) in children. Relevant data from the general population were

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collected by the Dutch Central Bureau of Statistics. The general population and patients with IFPD were compared using the Chi-square test.

Results: A total of 130 patients with IFPD (Bernard-Soulier, Glanzman, storage pool disease or other) of 6 years and older were included in this sub-study. Analysis was done on 121 patients (28 paediatric patients and 93 adult patients) who completed the questionnaires. In adults, sports participation was significantly higher (77.4%) in patients with IPFD compared with the general population (49.1%) ($p < .001$). In children with IPFD sports participation was similar to the general population (74.3% vs. 60.7%, respectively). Both paediatric and adult patients did not report fear for accidents or bleeds as a primary reason for not partaking in sports.

Discussion/Conclusion: The results of this study indicate that sports involvement in patients with IPFDs is comparable to the general population. Fear for injury and/or bleeds does not seem to be the primary reason for patients not to participate in sport activities. Follow-up studies are needed to formulate guidelines for sport participation in patients with IPFDs.

Disclosure of Interest: None declared.

PO267 | Thrombin-mediated cleavage of membrane endoglin: Implications in endothelial dysfunction

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Introduction: Increased levels of circulating endoglin, known as soluble endoglin (sEng), have been reported in serum, plasma and urine from preeclampsia (PE) women. In vitro studies have shown that sEng is released from membrane-bound endoglin upon the proteolytic activity of metalloproteases-14/12. However, sEng from PE patients is heterogeneous with different protein lengths, suggesting the involvement of additional proteases. As thrombin (Thr) and sEng have been postulated to be involved in the disease mechanism of PE, we have investigated whether Thr can target membrane bound-endoglin.

Methods: We conducted alignments of the amino acid sequence of human endoglin (Eng) with those of ten other mammal species using Clustal-O. Then, we searched for potential cleavage sites on the Eng sequence by Thr through a Profile Specific Scoring Matrix analysis. Additionally, we performed docking studies on Eng and Thr using the ClusPro program and Western blot (WB) analysis on plasma and serum samples from women with preeclampsia. Purified recombinant Eng was treated with Thr, and the samples were then subjected to electrophoresis on a Nu-PAGE® gradient gel. This was followed by Coomassie blue staining, WB and the Simple Western technique. The spots of interest were excised from the Coomassie blue gels to perform C- and N-terminal sequencing using nanoLC–MSMS and Edman degradation, respectively. Finally, we treated endothelial cells and mesenchymal stromal cells, which express endoglin on their surface, with Thr. The supernatant was then tested using an ELISA assay.

Results: First, amino acid sequence analysis of endoglin revealed the presence of a conserved peptide that is a known thrombin cleavage site present in the protease activated receptor (PAR)-1. WB analysis of plasma and serum from PE women demonstrated the existence of small Eng fragments compatible with Eng proteolysis by Thr. Incubation of purified recombinant Eng with Thr resulted in several fragments, whose C- and N-terminal sequencing confirmed the predicted cleavage sites. Finally, Thr treatment of Eng-expressing cells, release sEng while a decrease of Eng on the cell surface was observed.

Discussion/Conclusion: These findings could account for the existence of sEng with different lengths and the presence of multiple cleavage sites, whose sequential targeting may have a prognostic value during PE development, as well as being a marker of endothelial dysfunction.

Disclosure of Interest: None declared.

PO268 | Impact of semantic interoperability and usability-based optimisations on a clinical decision support (CDS) tool to reduce bleeding risk in patients with bleeding disorders

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Introduction: Irish patients with haemophilia and related bleeding disorders have their ambulatory care managed using a national electronic patient record (EPR). Inpatient care, however, is documented in a local hospital EPR. An interruptive Clinical Decision Support alert, triggered by manual documentation of the SNOMED 'Bleeding Disorder' term in the hospital EPR, is available to warn hospital prescribers if they select medications for these patients which increase bleeding risk.

An interface was introduced between the national and hospital EPRs which facilitated the automated transfer of SNOMED coagulation diagnoses (including bleeding disorders) between the systems.

Methods: The usability of the CDS alert was assessed and optimised using a validated assessment tool and the logic was updated to include the SNOMED bleeding diagnoses terms transferred across the interface.

The study was a retrospective service evaluation of the effectiveness of the CDS alert. A report was generated from the EPR listing all of the occasions when the CDS alert was triggered over a four-month period

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pre- and post-optimisation in response to an attempt to prescribe a medication with a high bleeding risk to a patient with a documented SNOMED bleeding disorder diagnosis.

Results: Alert Burden: A total of 30 alerts on 16 patient's pre-optimisation and 91 alerts on 30 patient's post-optimisation were generated.

Acceptance rate (number of medications not prescribed): Pre-optimisation 13% (two medications) of the alerts were accepted compared to post-optimisation where 26% of alerts were accepted (11 medications).

Discussion/Conclusion: In optimising the alert, the alert burden increased 50% however it was hypothesised this was due to the automatic transfer of the SNOMED bleeding diagnoses and requirement for manual data entry in only one system. Despite the increase in burden, the alerts presented were of greater clinical relevance due to the removal of alerts generated by task reminders, COX-2 inhibitors and visibility of the documented bleeding disorder within the alert window. Overall, directed optimisations can increase effectiveness of CDS and using information transferred automatically across an interface (i.e. semantic interoperability) to drive CDS is a novel concept that can support optimisation of other CDS.

Disclosure of Interest: None declared.

PO269 | Implementation of single factor X replacement treatment in adults with inherited severe factor X deficiency

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Introduction: Inherited factor X deficiency (FXD), an extremely rare autosomal recessive coagulation disorder has an increased prevalence in Ireland due to a founder mutation. Severe deficiency is associated with a high risk of spontaneous bleeding, highlighting the need for effective prophylaxis. Prothromplex, a plasma-derived prothrombin complex concentrate (PCC), is widely used but associated with thrombotic complications. Coagadex, a plasma-derived, single factor X concentrate may provide safer and less burdensome treatment. The aim of this study is to evaluate treatment outcomes before and after an en-masse switch of FX replacement to Coagadex.

Methods: A retrospective study of all patients registered in the National Coagulation Centre with severe FXD evaluated treatment outcomes for 14 months pre and post-switch. This included FX:C levels, bleed rates, FX consumption, management of gynaecological bleeding and procedures. Bleeds were documented as traumatic or spontaneous and interval from last prophylaxis was recorded where available. A qualitative analysis was conducted based on patient reports of differences between treatments.

Results: Five patients (three male, two female, 21–34 years) were prescribed prophylaxis with FX replacement, initially with PCC and since 2022, with Coagadex. Median (range) of prescribed prophylaxis dose was 19 IU/kg (17–24) twice weekly for PCC and 25 IU/kg (24–30) once or twice weekly for Coagadex. Median (range) for annual consumption was 1988 IU/kg/year (921–2457) for PCC and 1907 IU/kg/year (1466–2984) for Coagadex. Median annualised bleeding rates were less than 2 for both products; 0.9 (range 0–2.6) on PCC and 1.7 (range 0–3.4) on Coagadex. Menorrhagia was an ongoing issue for menstruating patients illustrating that gynaecological bleeding may not respond to FX prophylaxis alone. Socioeconomic factors (literacy, accommodation) impeded patient adherence. Qualitative data showed patient satisfaction improved with Coagadex, with reduced infusion volume making self-administration 'much easier'.

Discussion/Conclusion: Comprehensive data collection in a small complete adult patient cohort confirms that Coagadex provides equivalent bleed protection to PCC, with reduced administration burden. Menorrhagia poses a management challenge, even with prophylaxis. Adherence is essential for successful prophylaxis and is affected by socioeconomic factors. Further analysis is needed on long-term treatment outcomes.

Disclosure of Interest: None declared.

PO270 | Mutation spectrum of MYH9 gene in Russian population

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Introduction: Immune thrombocytopenia (ITP) is the most common cause of thrombocytopenia. However, before its establishing other causes of thrombocytopenia should be excluded, such as inherited thrombocytopenias (IT). One of the most common genetic abnormalities is MYH9-related disease (MYH9-RD) with worldwide prevalence 1:25,000. Differentiation between MYH9-RD and ITP is challenging, and misdiagnosis leads to ineffective and even harmful treatment.

MYH9-RD is characterised by macrothrombocytopenia, Döhle-like bodies and MYH9 aggregates in the neutrophil cytoplasm from birth. Most affected individuals develop one or more additional manifestations over their lifetime, including sensorineural hearing loss, renal disease, cataracts and/or elevation of liver enzymes. MYH9-RD resulted from mutations in *MYH9* gene, has autosomal dominant inheritance, but 35% of cases are sporadic. The aim of this work was to describe a mutation spectrum of *MYH9* gene in Russian population.

Methods: This study was a part of our research devoted to IT in Russian population. We conducted genetic analysis of patients suspected for specific type of IT, with thrombocytopenia since childhood or family history with it, platelet abnormalities to exclude ITP.

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Six unrelated patients were included for verification of MYH9-RD using single-gene testing. Mutation in *MYH9* of another patient was found during target multigene panel sequencing.

Results: In seven unrelated patients we found three known pathogenic variants: p.Arg702His ($N = 1$), p.Arg1165Cys ($N = 3$) and p.Glu1841Lys ($N = 3$). All of them were located in worldwide hot spots. Sensorineural hearing loss was associated only with p.Arg702His.

Discussion/Conclusion: Mutations revealed in Russian MYH9-RD patients are identical to the world population. p.Arg702His is known to rapidly lead to the most severe phenotype manifesting in different ways (severe thrombocytopenia, nephropathy, hearing loss). The only patient in our sample with this variant displayed hearing loss as well. p.Arg1165Cys is associated with a high risk for hearing loss before age of 60 and p.Glu1841Lys usually does not lead to non-haematological manifestations. In our sample patients with those two variants had only macrothrombocytopenia.

MYH9-RD is a common cause of inherited thrombocytopenia and it is essential to differentiate it from ITP to prescribe an appropriate therapy. Genetic testing allows this differentiation and to assess the need of other medical specialists involvement.

Disclosure of Interest: None declared.

PO271 | Clinical management of A patient with bernard–soulier syndrome misdiagnosed with von Willebrand disease

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Introduction: Bernard–Soulier syndrome (BSS) is an extremely rare (1:1,000,000) autosomal recessive blood clotting disorder characterised by excessive bleedings, giant platelet cells, thrombocytopenia and prolonged bleeding time. It resulted from mutations in *GPIBA*, *GPIBB* or *GP9* genes encoding subunits of GPIb-IX-V complex, which binds with von Willebrand factor (vWF) and initiates platelet aggregation. Because of underrecognition or misdiagnosis of BSS its prevalence may be higher than estimated. Here, we present a clinical case of confusion with von Willebrand disease (vWD).

Methods: This is clinical case of a 22-years-old female.

Results: At 2.5 years old she was examined due to ecchymosis after taking aspirin. Inherited coagulopathy with platelet dysfunction was diagnosed based on reduced RIPA, prolonged APTT, platelet count 113–117 x 10^9/L, vWF 56% and later changed to chronic thrombocytopenic purpura.

At the age of 4 the diagnosis was changed to vWD after episode of tonsil and mucosal bleeding with reduced RIPA, platelet count 80 x 10^9/L, vWF 72%. In-demand treatment with FVIII/vWF concentrate was prescribed.

Since age of 13 patient experienced menorrhagia, tonsil and uterine bleeding on the background of FVIII/ vWF concentrate therapy and combined oral contraceptives.

At the age of 21 there was threat of a premature birth at the 27nd week of her first pregnancy with decrease of platelet count to 46 x 10^9/L. She was consulted with haematologists, but verification of vWD was not possible during pregnancy. In the early postpartum period platelet transfusion and intravenous iron were administrated with a positive effect.

A year later during her second pregnancy (21−-22 weeks) based on laboratory phenotype (platelet count 44 x 10^9/L, marked reduction of CD42b) haematologists suspected BSS. Genetic study resulted in no mutations in *VWF* but a homozygous deletion in *GP1BA* gene (p.Tyr534CysfsTer82) which confirmed the diagnosis of BSS. Patient was recommended planned hospitalisation in perinatal centre specialising in haemostasis problems on 36–38 weeks of gestation and administration of eptacog alfa (activated), tranexamic acid according to the indications.

Discussion/Conclusion: Our aim was to describe a clinical case of misdiagnosis to emphasise the importance of clinical awareness for platelet disorders. An accurate diagnosis has important implications for prevention, patient care and improvement of patient's life quality.

Disclosure of Interest: None declared.

PO272 | Severe anaemia and red blood cell transfusions in patients with rendu-osler-weber disease—a retrospective study based on single centre experience

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Introduction: Osler–Weber–Rendu disease (ORW) is a rare hereditary phakomatosis characterised by alterations in vascular walls, leading to formation of abnormal vessels and increased susceptibility to damage of the altered blood vessels. The most frequent manifestation of ORW are telangiectasia and nosebleeds. The bleedings can be of diverse severity but there is not much data of the factors influencing bleeding burden in this disease. In this study, we analyse the patients with severe course of ORW resulting in anaemia with HGB < 8 g/dL and patients who received red blood cell (RBC) transfusions.

Methods: Retrospective analysis of patients records from years 2007 to 2023 diagnosed with ORW in Hematology Clinic in Krakow.

Results: There were 65 patients with ORW at our clinic in years 2007–2023. The mean age at diagnosis was 43.7 years. From this group, 18 patients received red blood cell transfusions. Two patients had severe anaemia with haemoglobin < 8 g/dL but refused transfusions. The main reasons for severe anaemisation or red blood cell concentrate demand were gastrointestinal bleedings (seven patients, 35%), recurrent nose bleedings (six pts, 30%), peripartum haemorrhages (three pts, 15%) and hysterectomy (two pts, 6.7%). All the patients who needed RBC concentrates were initially treated with haemostatic medication (tranexamic acid or etamsylate). In five patients (25%) unsatisfactory

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response to that treatment was observed and bevacizumab was initiated, resulting in a good response and bleeding resolution in two patients.

Discussion/Conclusion: Standard haemostatic medications are effective in most patients with ORW. In patients with more severe disease phenotype bevacizumab is an option. Our research has limitations due to a small study group. Further investigation is needed to establish the possible correlation of ORW severity with individual factors and genetic background.

Disclosure of Interest: None declared.

PO273 | Diagnosis of patients with bleeding of unknown cause

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Introduction: Bleeding of unknown cause (BUC) has been defined as an elevated bleeding tendency with normal results of the standard tests of haemostasis. Diagnostic evaluation of patients with BUC is a challenging process. Routine coagulation tests and platelet function testing are not able to detect the dysfunction, suggesting an impaired interplay between several haemostatic mechanisms. We hypothesise that a global test such as thrombin generation test (TGT) could be sensitive to detect this defect in BUC. So, we aimed to investigate the diagnostic value of TGT for BUC patients.

Methods: Patients with bleeding symptoms (evaluated with ISTH-BAT score) were studied with routine coagulation tests (aPTT and PT), factor XIII (FXIII) and platelet function testing: PFA-100, flow cytometry, aggregometry and T-TAS.

In those patients without platelet dysfunction and/or abnormal coagulation test, TGT was performed by Calibrated automated thrombography (CAT) in citrate without and with corn trypsin inhibitor (CTI, an inhibitor of contact activation phase) platelet poor plasma. A low amount of tissue factor (1 pM TF and 4 μM phospholipids) was used as a trigger. Lagtime (time when 10 nmol/L thrombin is formed); peak (maximum thrombin concentration reached) and endogenous thrombin potential (ETP, area under the thrombin-concentration-vs.-time curve) were calculated with the Thrombinoscope software package.

A healthy control group ($n = 10$) was also included.

Results: Twenty five patients (10 male and 15 female, with BATH scores 4.8 ± 1.0 and 6.6 ± 2.4, respectively) who met the inclusion criteria were studied. In samples of citrated plasma, TGT parameters of BUC patients were similar to those from healthy controls [control vs. BUC: LT (min): 4.8 ± 0.9 vs. 4.1 ± 0.7; ETP (nmol/lxmin): 1335 ± 215 vs. 1418 ± 200 and peak (nM): 225 ± 48 vs. 214 ± 46]. On the contrary, differences were observed between BUC and healthy controls when TGT was performed in plasma with CTI [control vs. BUC: LT (min): 5.6 ± 1.4 vs. 6.3 ± 2.9, $p = .462$; ETP (nmol/lxmin): 749 ± 215cvs. 643 ± 274, $p < .0001$ and peak (nM): 76 ± 54 vs. 49 ± 66, $p = .037$].

Discussion/Conclusion: TGT was useful in the diagnostic process of patients with BUC when contact phase activation is blocked at sampling to allow the evaluation of the TF-dependent pathway.

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Disclosure of Interest: None declared.

PO274 | Non-invasive diagnosis of anaemia using conjunctival photos

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Introduction: Our study seeks to enable individuals at risk of anaemia to monitor their haemoglobin levels without the need for hospital visits or medical consultations. Anaemia, a widespread health concern affecting one-third of the global population, disproportionately affects individuals with bleeding disorders, children, women of reproductive age and the elderly. Inadequate monitoring of anaemia-prone individuals can lead to its progression, resulting in a decline in their quality of life and imposing a financial burden on the government. To address this issue, we focussed on the development of a cost-effective and non-invasive method for the early prediction of low haemoglobin levels. Our objective in this study is to devise a methodology to prevent anaemia complications by enabling early detection and intervention while maintaining cost-effectiveness.

Methods: We devised a mobile application to capture conjunctival images and simultaneously record haemoglobin values from a cohort of 54 patients. The 94 conjunctival images were randomly divided into an 84-sample training set and a 10-sample test set. Haemoglobin values were associated with segmented images, and values falling below 12 g/dL were classified as indicative of low haemoglobin levels. Utilising colour histograms from the segmented images, we constructed a Support Vector Classifier (SVC) model to classify individuals based on their colour histograms and predict haemoglobin levels.

Results: The performance of the developed SVC model was assessed utilising an independent test dataset consisting of 10 samples. Within this dataset, five samples indicated low haemoglobin levels, while the remaining five demonstrated normal haemoglobin levels. The model accurately classified nine out of 10 samples, achieving a 90% accuracy rate (AUC: 90%, F1-Score: 89%).

Discussion/Conclusion: Numerous non-invasive techniques for anaemia screening exist, each with its distinct advantages and disadvantages. Our straightforward and non-invasive conjunctival haemoglobin level estimation approach holds the potential to facilitate early detection and intervention, thus reducing both the health risks and the economic burdens associated with undiagnosed anaemia. However, while our study shows promise in simplifying haemoglobin level estimation, further research involving larger datasets and the exploration of alternative image processing methods is warranted to enhance its efficacy.

Disclosure of Interest: None declared.

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PO275 | Constitutional haemorrhagic diseases and surgery, experience in the hematology department bordjbouarreridj, Algeria

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Introduction: The surgical aspect of the management of constitutional haemorrhagic diseases is very delicate, given the exacerbated haemorrhagic risk, which may affect the patient's vital prognosis, requiring proper packaging and appropriate therapeutic weapons to avoid complications.

Methods: From 2015 to 2022, 10 surgeries were identified in our unit:

_Willebrand: five surgeries (two caesarean sections and three ruptures of ovarian cysts), high haemorrhagic risk (type 3), substitution protocol: factor 8,wilfactin 80 μ/kg, 1 h before the intervention, then 10 h after 60 μ/kg then 40 μ/kg/10 h until the output. Tranexamic acid 1 g X3/day, hospitalisation time 5 days for caesarean sections and 7 days for ruptures of ovarian cysts, no complications.

_ Factor 7 deficiency: three surgeries, two appendectomies and one nasal septum deviation, moderate haemorrhagic profiles, protocol: 30 mg/kg factor 7, 2 h before the intervention and 2 h after, then every 4 h for 24 h and every 6 h for 36 h, 3 days trt time for nasal septum deviation, 5 days for appendicectomies, 0 complications.

_ Severe haemophilia A: one circumcision in adulthood, protocol: 50 μ/kg factor 8.1 h before the intervention, then 30 μ/kg 8 h for 48 h, then 20 μ/kg/8 h for 3 days, duration of hospitalisation 6 days, 0 complications.

_Factor 13 deficiency: one appendectomy, substitution by PFC 20 mL/kg 1 h 30 min before intervention. Ultrasound control at 3rd day, hospitalisation duration 5 days.

Results: Ten surgeries conducted over a period of 8 years: Willebrand (50%), deficit in 7 (30%), then haemophilia A (10%) and deficit in 13 (10%).

_All patients were already known and followed.

_60% emergency surgeries, 40% programmed.

_The average age of 28 years.

_Sex ratio 1, with gynaecological predominance in women, and digestive in men.

_Substitution protocols have been established according to the haemorrhagic risk based on: the degree of the deficit, patient's haemorrhagic profile and the type of the surgery.

_Adjuvant treatments: all patients received analgesics and antibiotic therapy.

_Antithrombotic prophylaxis has not been discussed (low risk).

_No complications, the average length of hospitalisation is 5 days.

Discussion/Conclusion: Surgery in constitutional haemorrhagic diseases requires multidisciplinary cooperation, good evaluation of haemorrhagic risk, availability of substitution treatment, with good supervision allowing the smooth running of the operative act.

Disclosure of Interest: None declared.

PO276 | Rare bleeding disorders in the obstetric patients: An egyptian centre experience

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Introduction: Inherited bleeding disorders increase the risk of bleeding in obstetric patients, there is a severe shortage of data to conclusively support an evidence-based strategy for the management of these rare disorders especially in pregnancy and during delivery.

Methods: We described our experience in peripartum management of 3 rare bleeding disorder cases [Von Willebrand disease, Glanzmann thrombasthenia, and factor VII (FVIII) deficiency] including the management during pregnancy, at delivery, and management of postpartum complications.

Results: Three pregnant cases of rare bleeding disorders were presented to our adult haematology clinic for follow-up during pregnancy and to prepare for delivery, 1st case was a 20-year-old pregnant lady known to have von Willebrand disease type (3). She received VWF/FVIII concentrate with the 1st phase of delivery. Phases of vaginal delivery ended by episiotomy under complete haemostatic cover and resulted in a normal living baby and normal vaginal spotting then she was discharged to home, after 1-week the patient presented to ER with severe vaginal bleeding, and hypovolemic shock. The patient was admitted to ICU with massive vaginal bleeding for 4 days in spite of all the haemostatic measures, all gynaecological causes, sepsis and DIC were excluded. Vaginal bleeding did not stop except after the insertion of a Bakri balloon by the gynaecology team. The patient became vitally stable and was discharged home safely. 2nd case was a 22-year-old pregnant lady with Glanzmann thrombasthenia, the mode of delivery was co-decided by the obstetric team and the haematology team to be a caesarean section to shorten the phases of the delivery and for fear that the neonate inherited the same disorder. She received recombinant FVII and platelet transfusion 2 h before her surgery and maintained with lower doses for 2 days. Her delivery passed smoothly without complications. The 3rd case was a 27-year-old pregnant lady with a background of FVII deficiency, she received recombinant FVII with the 1st phase of delivery and maintained with lower doses for 2 days. Phases of vaginal delivery ended by episiotomy under complete haemostatic cover and resulted in a normal living baby and normal vaginal spotting.

Discussion/Conclusion: Further exploration of obstetric management of rare bleeding disorders is needed and requires extensive collaboration to collect large, organised data sets.

Disclosure of Interest: None declared.

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PO277 | Inherited FVII deficiency in egyptian children: A 17 year retrospective study with high incidence of cerebral bleeding

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Introduction: Inherited factor VII (FVII) deficiency is the most common of the rare autosomal recessive bleeding disorders and the prevalence is higher in those countries where consanguineous marriages are frequent, especially with respect to the severe forms of the disease. It is second in distribution amongst our Egyptian paediatric cohort with rare coagulation disorders following up in Haematology Clinic, Cairo University Paediatric Hospital. Patients have a wide phenotypic variability ranging from asymptomatic to life-threatening bleeding, including intracranial haemorrhage (ICH) with significant mortality and morbidity.

Methods: We studied the clinical spectrum of our cohort to see if their bleeding phenotype behave differently in a population with multiethnic historical background. We correlated FVII activity with the severity of the bleeding phenotype. FVII deficiency was diagnosed when factor assay was below normal (n = 70%−120%) and patients were classified into asymptomatic, minor and major bleeders.

Results: 50/170(29.4%) of our rare coagulation disorders paediatric cohort were diagnosed with inherited FVII Deficiency with equal sex prevalence and were usually of a consanguineous marriage. 48% are major (cerebral bleeding, hemarthrosis, gastro-intestinal) bleeders, 40% minor bleeders and 12% asymptomatic diagnosed after a haemostatic screen prior to surgery. The bleeding phenotype showed wide variability and mostly correlated with FVII activity. Cerebral bleeding was reported in 24% of patients and they were all major bleeders (FVII activity <5%) and mortality was high, 58.3%. Four patients are on prophylaxis and one developed postnatal hydrocephalus secondary to intrauterine cerebral haemorrhage.

Discussion/Conclusion: Nearly 50% of our paediatric cohort diagnosed with inherited FVII deficiency are severe bleeders. Cerebral bleeding is usually severe with an early onset and poor prognosis.

Disclosure of Interest: None declared.

PO278 | Initiatives of the EAHAD Glanzmann Working Group

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Introduction: Glanzmann's disease (GD) is an ultra-rare inherited platelet disorder, with an estimated prevalence of 1:10,000,000 with an autosomal recessive mode of inheritance. Patients with GD have phenotypic variability in bleeding and other manifestations. To date, several attempts have been made to gain more insight into bleeding severity and treatment outcomes in GD. Still, many clinical relevant questions are unanswered and current clinical practice is still not optimal. These include basic management of surgery and bleeding, pregnancy management, prophylactic treatment in the context of anti-platelet antibodies and cardiovascular comorbidities.

Methods: The EAHAD Glanzmann Working Group was established in December 2022. It consists out of at least four members from at least three different European countries (with a maximum of 10 members) and one member from the European Haemophilia Consortium. The first goal of the working group is to share and disseminate knowledge among European health care providers on management of GD. The second goal is to define and execute a European research pipeline for GD.

Results: To date, two deliverables have been achieved. First, a pan-European survey on current diagnosis and management of GD has been finished. This survey serves as a cross-sectional observation of current clinical practice and helps in identifying knowledge gaps. Second, the implementation of a digital instant messaging platform using Siilo (www.Siilo.com), a free safe messaging app for health care professionals, to provide real time advice and guidance in individual cases has been set up. The ambition is to expand this platform to caregivers of patients with GD in Europe. Next, a Glanzmann Natural History Study will begin where 200 patients with GD will be prospectively followed for at least 2 years. This will be a longitudinal cohort with retrospective, baseline and annual collection of data from routine care visits including laboratory data, physical exam findings, questionnaires, results of standard-of-care procedures, medical diagnoses, hospitalisations, transfusion regimen, clotting factor therapy and other treatments for GD and its complications.

Discussion/Conclusion: With the initiation of the EAHAD Glanzmann Working Group, we are connecting health care providers and fill in the knowledge gaps on this ultrarare inherited platelet function disorder. This could be a model for other rare disorders next.

Disclosure of Interest: None declared.

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PO279 | Predictors of health-related quality of life in children with rare bleeding disorders at a single centre

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Introduction: In developing countries, health-related quality of life (HRQOoL) is not very well investigated among children with rare bleeding disorders (RBDs). This age group might present with severe bleeding phenotype, which poses a significant impact on HRQoL. In addition, modern recombinant replacement therapies might not be always readily available. The aim of this work is to assess HRQoL in children with RBDs and explore their potential predictors.

Methods: A cross-sectional study done on all children aged up to 16 years, attending the haematology clinic in our centre throughout a duration of 1 year (July 2022–June 2023). 36-Item Short Form Survey (SF-36) was utilised to assess HRQol. Informed consents were obtained from patients and/or their guardians, and ethical approval was made.

Results: Out of 65 patients recruited, 54 completed the questionnaire [18 cases with FVII deficiency (FVIID), 14 with FXD, nine with hypo/dysfibrinogenaemia, eight with FVD, three with combined FV/FVIIID and two with FXIIID] HRQoL score was significantly lower in studied patients, compared to controls (62.3 ± 11.1 vs. 73.5 ± 14.6) (p-value $< .0001$). Multiple regression analysis revealed that the most significant predictor of total HRQoL score was adherence to prophylactic therapy (if indicated) [$B = 0.59$, 95% confidence interval (CI) 0.12–1.04, $p = .008$], outweighing other parameters. In addition, negative history of intracranial haemorrhage, adherence to prophylactic therapy (if indicated), proximity to a specialised healthcare centre and higher socioeconomic status were significantly correlated with better HRQoL (p-values: .02, .032, .04 and .05, respectively). On the other hand, type of replacement product (either recombinant or plasma-derived) and family history of bleeding diathesis were not significantly correlated to HRQoL.

Discussion/Conclusion: Overall, HRQoL is significantly lower in children with RBDs. Factors denoting optimum control of bleeding episodes are significantly correlated with better HRQoL. Recognition of these factors could help healthcare professionals develop effective management strategies. Establishing a National Bleeding Registry is mandatory to offer better care.

Disclosure of Interest: None declared.

PO280 | Comprehensive haemophilia care model [CHCM] for haemophilia patients in resource poor settings

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Introduction: Issues: People having haemophilia needs price-discounted-drugs and proper-nursing-care in Asian region. Appropriate public-health-program for supportive-care needed in rural/tribal areas of Asia.

Description: Treatment-cost of haemophilia is very high for rural/tribal population. Over 74% patients in rural-Asia cannot afford drug therapies. NGO's need to facilitate development of sound/sustainable nursing-care-programs in marginalised Asian communities. There is need to Establish Uniform public-health-policy to develop of sound/sustainable health care-programs.

Methods: This is a public health policy paper. The suggestions of this NGO project were reccomended by five physicians, four patient advocates, two governmental officers and six nurses from different rural hospitals in Asian set up.

Results: Long-term therapy of haemophilia is out of reach for >90% Indian-patients. Rehabilitation/palliative care plans non-existent. Concrete proposals done only by two NGOs. Seven such projects currently running in Asia. Of these none supported by WHO, two NGOs, four government and one private entities and none by corporate/pharma sector initiatives. Psychosocial support services and nursing care in rural/tribal areas is abysmal.

Discussion/Conclusion: Lessons learned: Community participation of NGO in administration of nursing-care/therapeutic RX of haemophilia is very effective in terms of cost-management, better-compliance. Community mass intervention and low-cost drug-supply-projects have proven useful in rural communities of resource poor-nations. EAHAD participants can collaborate with NGO-activist to address this burning allied-health-issue. Uniform government public-health-policy needed to implement supportive-care-services.

Recommendations: Promoting dialogue between health-services and nurses accelerates health-care-efforts. nurses participation increases more Rx-compliance and improves treatment outcomes in haemophilia patients. Nurses have direct-communication with patients. Hence nurses must be involved in such public-health-policy issues. This would reduce difficulties faced by patients from resource-poor-southern-countries. This being policy paper, we advocate that WHO, EAHAD should form common-guideline-manual on this issue affecting developing-countries.

This complex issue needs indepth discussion at EAHAD-forums for better outcome in management of haemophilia.

Disclosure of Interest: None declared.

PO281 | Alternative system of medicine and joint pain control in haemophilia patients

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Introduction: Issues: Joint pain is very-common in haemophilia patients. Do not have access to palliative and rehabilitation services. No specific-centre in Asia for haemophilia-patients-rehabilitation. Hence our Our-NGO used locally available complementary-alternative-medicines (CAM) for providing home-based-care of joint pain.

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Aims: To provide CAM in collaboration with traditional-faith-hearers (TFH). Evaluate cost-efficacy/responses of CAM in haemophilia pain of haemophilia-patients-on-ARV-drugs.

Methods: Twenty-eight patients [$n = 28$], age 34–65 years enrolled. 40% females, 60% males. 55% complained of severe joint-pain.

We used Mud therapy 20%, Bach-flower remedy 30%, acupressure/acupuncture 10%, hydrotherapy 40%, hypnotherapy 70%, ayurvedic-therapy 10% unani medicines, 80% homeopathic-medicines, 50% on herbal-oil-TFH massage-therapy, 30% aromatherapy. Nine sessions CAM oner 5 weeks.

Feedback performa responses evaluated. Our NGO functioning shown graphically to EAHAD-conference-participants. Pain recorded scale of 1–10. Mean score pain fell from 8.2 (SD 1.4) to 3.8 (SD 2.7) point ($p < .001$).

Results: Group-1 NSAIDs + corticosteroids [$n = 8$], Group-2 CAM [$n = 8$], Group-3 [$n = 12$] NSAIDs + corticosteroids + CAM [$n = 32$]. GROUP-4 NSAIDS + OPIOIDS.

Symptom wise relief in joint pain best seen in Group 3. Group 2,3 preferred CAM compared to standard pain-killers. CAM 52% cheaper compared to allopathic medicines. CAM-available locally/high-acceptance.

Discussion/Conclusion: Twenty-eight of haemophilia-patients used/preferred CAM. CAM needs further evaluation. We shall form group with researchers from USA/Europe to develop this policy to exchange experiences/knowledge.

Limitations: Due to lack of expertise/resources/technical-assistance sample size was small.

Disclosure of Interest: None declared.

PO282 | Evaluation/analysis of nurses in haemophilia care: What we need to do?

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Introduction: (1) To assess knowledge, perception and attitudes of nurses about nursing care of haemophilia patients.

Methods: This is questionnaires based study: consisted (1) information about respondents. (2) Methods to elicit nurses' knowledge perception and attitudes in care of haemophilia patients. (3) Impact of nurses counselling on QOL of haemophilia patients.

All questionnaires were returned and analysed using simple statistical method. We also designed framework for orientation/CME that would novices to experts in providing nursing care for haemophilia patients. This presentation outlines role of nurses in counselling, impact on patient outcomes and education required for competent practice.

Results: $N = 22$ nurses aged between 20 and 35 years enrolled from district hospital and rural catholic mission in rural/tribal area. Eighteen females, four males, knowledge, perception and attitudes of nurses towards cancer care is minimal with only five showing special skill, perception and good attitudes towards caring for haemophilia patients as opposed to 16 with little knowledge and low perception to caring for patients and the remaining with no specific knowledge and perception towards nursing care of cancer patients.

Discussion/Conclusion: Nursing is an important specialty but neglected filed in developing nations. Resources are scarce for such initiatives on training of nurses. Trained nurses can improve QOL of haemophilia patients. This presentation will pictorially show role of nurses, impact on patient QOL and education required for competent nursing care of haemophilia patients.

Disclosure of Interest: None declared.

PO283 | When is epistaxis just a nosebleed? Type 1 von Willebrand disease diagnosed through a Nurse Led Service

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Introduction: A 58-year-old woman of Chinese origin was referred for investigation of nose bleeding. She presented with epistaxis after migrating to the United Kingdom (UK).

Methods: She admitted to minor epistaxis and mild gum bleeding in childhood with no recurrent episodes after puberty. On arrival to the UK from Hong Kong, severe recurrent epistaxis was noted, and medical advice was sought. Ear, nose and throat (ENT) intervention included several unsuccessful cautery treatments leading to specialist haematologist referral. A bleeding state work up was undertaken to investigate the bleeding complaint.

Results: Initial investigations at a local District General Hospital (DGH) revealed an increased APTT ratio of 1.55 and a low factor VIII clotting activity (FVIII:C) of 17.5 IU/dL; a presumed diagnosis of mild haemophilia A resulted in referral to the haemophilia centre (HC). Initial consultation at the HC highlighted a lack of family bleeding history and a personal bleeding score (ISTH BAT) of 6. Blood results confirmed an APTT ratio of 1.51 and a FVIII:C of 25.2 IU/dL. Additional blood tests revealed abnormal von Willebrand factor (vWF) antigen of 12.8 IU/dL and activity of 10.1 IU/dL; factor IX (FIX), factor XI (FXI) and factor XII (FXII) were normal. Additional tests included protein electrophoresis, thyroid function tests, blood film, lactate dehydrogenase, genetics [heterozygous for a c.3614G > A, p.(Arg1205His)] and echocardiography.

Discussion/Conclusion: Following consultation and MDT discussion, acquired von Willebrand syndrome was excluded and a diagnosis of Type 1 von Willebrand disease (vWD) was made. The patient was registered on the National Haemophilia Database, a bleeding disorder card was issued, appropriate follow up arranged and patient diagnosis education and treatment plan were initiated. In addition ENT and dental referrals were made for further support. Points for further discussion include: DGH medical knowledge and education needs for bleeding disorders; patient's own cultural barriers plus additional lack of gynaecology and obstetrics history; changes in climate resulting in exacerbation of symptoms; and family screening to ascertain whether other family members are affected.

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PO284 | Nursing role as coordinator in a multidisciplinary team in patients with congenital coagulopathy during elective surgeries

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Introduction: In recent decades, the clinical follow-up of patients with coagulopathies has become more complex as a consequence of the introduction of new treatment therapies. These people often require surgery and invasive procedures with a high risk of bleeding. Furthermore, there is great variability in perioperative management guidelines depending on the type of coagulopathy, the surgery or procedure to be performed and the treatment required. For this reason, it is essential to manage these situations by a specialised and experienced multidisciplinary team (MDT) in a reference centre.

Within the MDT the nurse can assume a leadership role as a coordinator. The coordinator is responsible for ensuring that all steps associated with surgical preparation, the management and patient follow-up are executed efficiently and thoroughly.

Methods: Retrospective, observational study including patients with bleeding disorder who undergoing elective surgery or invasive procedures in a centre in Spain.

Definition of the role of the nurse coordinator during the surgical process through multidisciplinary sessions carried out during the first quarter of 2022.

Results: Review of minor and major surgeries and invasive procedures performed during the period from September 2022 to August 2023 at reference hospital.

The median age is 45.79 (range 0.64–84.34). The 51.63% were patients diagnosed of haemophilia and the 25% were patients with von Willebrand disease.

We have carried out 89 surgeries: 49 major surgeries (39.52%), 40 (32.26%) minor surgeries and 35 (28.23%) invasive procedures. Highlighting orthopaedic surgeries (27.42%) as the most common.

Discussion/Conclusion: The nurse is the link between all the services involved and coordinates all the services involved in the care process, from the coordination of admission and preparation prior to surgery to the discharge of the PWBD.

The role of the nurse coordinator highlights the importance of interdisciplinary management and specific guidelines for each procedure, achieving quality of care and safety in the care of the patient and family.

Disclosure of Interest: None declared.

PO285 | The role of the study nurse in congenital coagulation disorders

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Introduction: In recent decades, the clinical follow-up of patients with haemophilia has become more complex because of the introduction of new treatment strategies, the presence of comorbidities related to haemophilia or aging, as well as the appearance of new tools to evaluate the medical and social consequences of haemophilia.

In recent years, it has been especially productive in the research and development of new treatments that currently offer better control and prevention of bleeding. The most of them were based on strategies aimed at replacing the coagulation factor or developing gene therapy for curative purposes. However, the arrival of new drugs based on the use of bi-specific antibodies has meant a paradigm change and a revolution in the treatment.

This is why the multidisciplinary teams of the haemophilia units have had to adapt to these new challenges and establish new roles from the point of view of nurses trained and qualified in the field of clinical trials.

Methods: Observational study of the inclusion of clinical trials in the unit on new treatments and tools.

Training sessions for nursing staff involved in participating in clinical trials.

Presence of a haemophilia nurse at site initiation visit.

Results: The functions of the clinical trials nurse are:

Health education for the patient on treatment administration, prevent and manage side effects.

Perform procedures rigorously outlined by the protocol: electrocardiogram, samples extraction and processing, pharmacokinetics, vital signs, weight and height.

Registration of the clinical trial-nursing visit in the medical history.

Treatment adherence monitoring: patient diary or digital application.

Emotional and psychological support for the patient and family.

Discussion/Conclusion: The role of the nurse in clinical trials is essential to guarantee quality and rigor in clinical trials. The nurse becomes the link between the patient, the principal investigator, the sponsor and the rest of the team, minimising mistakes and increasing adherence to treatment.

In addition, the nurse is who carry out the procedures correctly to ensure quality results. We achieve this with an ongoing training in each new clinical trial and new therapy. Nurses become the person of trust and reference for the patient, achieving quality care and safety in care.

To overcome the barriers to engaging in research and publishing, nurses require dedicated research time, mentorship and collaboration with more experienced nurses researchers.

Disclosure of Interest: None declared.

PO286 | Effectiveness of myofascial therapy (MFT) and conventional physiotherapy (CPT) with intermittent prophylaxis on joint health in haemophilic arthropathy—a proof of concept randomised control trial

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Introduction: Haemophilic arthropathy is a debilitating condition characterised by joint damage and chronic pain due to recurrent bleeding in people with haemophilia. Myofascial therapy (MFT) and conventional physiotherapy (CPT) with intermittent prophylaxis have been suggested as potential interventions to improve joint health in HA. This Proof of Concept Randomised Control Trial aimed to investigate the effectiveness of these interventions on joint health in male participants with haemophilia A.

Methods: The study enrolled 31 male participants with haemophilia A, aged 28 ± 9 years, who were randomly assigned to either Group A (MFT and CPT with intermittent prophylaxis) or Group B (CPT with intermittent prophylaxis alone). The intervention was administered over a 3-week period, comprising 12 physiotherapy sessions. The HJHS, Gilbert score, ROM and FISH were assessed at baseline and after the intervention.

Results: The study revealed significant improvements in HJHS and knee joint scores for Group A compared to Group B ($p = .016$ and $p = .007$). Both groups showed enhanced ROM, notably in the knee (18.97% in Group A vs. 9.49% in Group B) and elbow (10.10% in Group A vs. 1.25% in Group B). While functional outcomes improved in both groups, Group B showed a slightly greater enhancement (13.68% vs. 11.08%), although not statistically significant.

Discussion/Conclusion: The results of this Proof of Concept Randomised Control Trial suggest that MFT and CPT with intermittent prophylaxis effectively improve joint health, as indicated by reduced HJHS scores and increased ROM.

Our study results support the study hypothesis with a significant improvement in joint health by HJHS scoring in the MFT group participants (MFT + CPT and intermittent prophylaxis) relative to control group participants (CPT and intermittent prophylaxis).

There was a reduction in bleeding frequency for Group A participants despite higher baseline bleeding rates.

There was a significant improvement in both knee and elbow range of motion (ROM) also but not in the overall functional score.

Disclosure of Interest: None declared.

PO287 | Developing a novel low-cost orthotic intervention to reduce bleed incidences in haemarthropathy in the global south

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Introduction: According to the world federation of haemophilia annual global survey, low income and lower-middle-income population make up around 70% of the global haemophilia population. However, account for less than 10% of the pharmaceutical usage to treat haemophilia.

In the UK, alongside pharmaceutical treatment, patients who suffer musculoskeletal (MSK) bleeds may be offered podiatry services and/or physiotherapy. Individually, or in combination, these services can improve biomechanics to reduce joint stresses, which have been linked to joint bleed events. The success of these has prompted the design of a novel low-cost orthotic intervention for use in developing countries to reduce MSK bleed prevalence in these patients.

Methods: Eight orthotic device designs have been developed based on sandals being the preferred footwear choice in much of the global south. Each was modelled in Solidworks, and 3D printed in polyurethane. Combinations of components that have proven valuable in podiatric care in PwH, such as forefoot rockers and SACH heels, were included. Four of the designs have integrated the orthotic components into a footwear, and four have been designed as an attachment to a standard flip-flop.

Elements of the 3D printed prototypes, such as the attachment between the straps and footbed, have been tested for mechanical strength and potential failure mechanisms. Each design will be assessed using motion capture on a health control population ($N = 12$) under local research ethics. Walking biomechanics for the full lower limb kinetic chain will be assessed for the eight concepts, and contrasted with barefoot walking, and flip-flop only walking biomechanics. This allows the biomechanical influence of each component, and the efficacy of the attachment, rather than whole device, to be assessed.

Results: Eight designs were successfully tested to assess for the influence of the forefoot rocker, SACH heel or combination. Whether the device needs to be one complete device, or components affixed to a standard flip-flop was also assessed.

Discussion/Conclusion: The results of the biomechanics and mechanical testing will contribute to a final design selection for future efficacy testing on a patient population. The outcome of testing on a patient population will lead to a design that can potentially be distributed to patient populations in the global south.

Disclosure of Interest: None declared.

PO288 | Posturology in patients with severe haemophilia a in the province of Salta, Argentina

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Introduction: Haemophilic arthropathy is the leading cause of disability in severe haemophilia. Haemarthrosis generates capsular distension with inhibition of the myotendinous reflex, dysfunction of the postural tonic system generating instability, joint stress, increased risk of bleeding, greater predisposition to generate target joints (joint with three or more hemarthrosis in a period of 6 months). What leads to a sedentary life generating a vicious circle of muscle weakness, proprioceptive alterations, deficiency of postural control, joint stress and increased risk of bleeding. Early identification of postural alterations can help to understand biomechanical alterations, which is important for planning preventive interventions in patients with haemophilia.

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In 2022, postural evaluations of patients attending the Haemophilia Foundation of Salta began to be carried out.

Objective: To evaluate postural alterations in patients with haemophilia who attend the Haemophilia Foundation of Salta.

Methods: A static postural evaluation sheet was prepared based on Bernard Bricot's Postural Reprogramming, in anterior, posterior and sagittal plane. A total of 30 patients with haemophilia A, aged 5–51 years, were evaluated to determine the most frequent postural alterations.

Results: The following postural alterations were found: navel laterality: 18 (60%), left 6 (33.4%) and right 12 (66.6%). Achilles tendon: 19 (63.3%), varus: 1 (5.3%) and valgus: 18 (94.7%), left valgus: 8 (42.1%) and right valgus 11 (57.8%).

Anterior projection of the head: 19 (63.3%). Abdominal protrusion: 15 (50%).

Target joint: elbow: 2 (6.6%): left: 1 (50%) and right: 1 (50%). Knee: 16 (33.3%): left: 5 (31.3%) and right 11 (68.7%), ankle: 16 (53.3%): left: 7 (43.7%) and right: 9 (56.3%).

Discussion/Conclusion: It was observed that the most frequent biomechanical alterations are: first, the deviation to valgus of the Achilles tendon manifested by an ankle valgus that coincides with the target joint of the patients, second the anterior projection of the head, third place the navel laterality and fourth the abdominal protrusion. We believe it is important to continue evaluating postural alterations to initiate early treatment of them in order to reduce joint stress and prevent future hemarthrosis.

Disclosure of Interest: None declared.

PO289 | Physical activity and heavy menstrual bleeding amongst women with inherited bleeding disorders in ireland

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Introduction: Women and men with inherited bleeding disorders may experience abnormal bleeding tendencies which significantly impact health and quality of life. This may include spontaneous and/or traumatic mucocutaneous, musculoskeletal and visceral bleeding. Women with bleeding disorders (WBD) can additionally experience heavy menstrual bleeding (HMB), which may significantly impact physical activity (PA) participation. For substantial health benefits, adults should aim to do at least 150 min of moderate-intensity or 75 min of vigorous-intensity aerobic PA per week, or an equivalent combination of both.

Methods: In September 2023, data collection commenced for the Women's Opinions and experiences of Menstrual health on Exercise and physical activity Nationally (WOMEN) survey. The aim of the WOMEN survey is to explore bleeding experiences, PA and menstrual health amongst WBD in Ireland. The survey is also collecting responses from the general population in Ireland who do not have a diagnosed bleeding disorder. Women and people with the potential to menstruate over the age of 18 years are invited to participate in a short, anonymous survey, which comprises 24 questions, typically taking 15 min to complete. The survey collects information on basic demographics, bleeding disorder history, PA, bleeding experiences, menstrual health and quality of life. A full analysis will be carried out when data collection has been maximised. Survey responses will be compared between WBD and the general population. Basic descriptive findings for demographics, PA and HMB amongst WBD are presented, which should be interpreted with caution considering data collection is ongoing at present.

Results: To date, 22 WBD have responded to the survey: 11 haemophilia carriers, eight with Von Willebrand disease, two with mixed factor deficiencies and one with a platelet function disorder. The majority of respondents are aged 18–45 years. HMB has been reported by 95% of WBD, and 77% have reported < 150 min of combined moderate-vigorous PA per week.

Discussion/Conclusion: HMB experienced by WBD may impact PA participation. The WOMEN survey aims to explore bleeding experiences, PA and menstrual health in WBD, and survey responses will be compared with the general population. Data collection is ongoing. Further details of survey methods and overall results will be disseminated upon study completion.

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PO290 | Comparison of outcome assessment in prophylaxis versus on demand treatment: A research support program of WFH World Bleeding Disorders Registry

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Introduction: With the grant from 2020 Research Support Program of the World Federation of Heamophilia's World Bleeding Disorders Registry (WBDR), Aluva Heamophilia Treatment Centre in India conducted the study comparing outcomes of people with heamophilia (PWH) who received prophylaxis versus on demand treatment. The aim of the study was to assess outcomes of PWH who receive prophylaxis compared to on demand treatment in the resource constraint environment.

Methods: A total of 100 PWH with heamophilia A or B <18 years old, without inhibitors, were included in this comparative study. Fifty PWH were on prophylaxis, defined as any dosage of ongoing regular replacement therapy for at least 6 months. Using age matched controls, another 50 PWH who received on demand treatment were selected

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for comparison. Baseline and final data were collected from both study groups on January 2021 and on December 2021 consecutively.

We measured outcomes of treatment of 100 PWH using three assessments tools: Heamophilia Joint Health Score (HJHS), Functional Independence Score in Heamophilia (FISH) and EQ-5D-5L. We also compared annualised bleeding rate (ABR) between both study groups. We applied Wilcoxon signed rank test to find out whether or not there is a significant difference between the baseline and final values of prophylaxis and on demand treatment. All data are entered in the WBDR.

Results: In prophylaxis study group, statistically significant changes between baseline and final values were found as follows: HJHS (2.28 ± 4.238 vs. 0.92 ± 2.498, $p < .001$), FISH (31.66 ± 2.264 vs. 31.86 ± 0.99, $p = .180$), EQ-5D-5L (92.12 ± 4.457 vs. 95.42 ± 2.673, $p < .001$) and ABR 6.18 ± 7.148 vs. 2.88 ± 4.906, $p < .001$).

For the on-demand study group, a statistically significant change between baseline and final values were found as follows: HJHS (3.5 ± 7.192 vs. 4.12 ± 7.816, $p = .027$), FISH (30.86 ± 3.807 vs. 30.42 ± 4.399, $p = .026$), EQ-5D-5L (90.76 ± 9.05 vs. 87.8 ± 9.196, $p < .001$) and ABR (10.26 ± 7.505 vs. 12.54 ± 7.885, $p < .001$).

Discussion/Conclusion: Prophylaxis coupled with physiotherapy appears to be an effective and sustainable step to improve joint and functional activity. We also see the reduction ABR. The overall quality of life of PWH have also shown improvement.

Disclosure of Interest: None declared.

PO291 | Comparitive study of joint status of haemophilia A severe patients with inhibitor positive and inhibitor negative

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Introduction: Haemophilia is an X linked congenital bleeding disorder caused by a deficiency of coagulation factor VIII (FVIII) or coagulation factor IX (FIX). They are divided into three groups depending on the factor level. Mild haemophilia means factor level of 5%–40%, moderate means 1%–5%, severe means <1%.This is a retrospective analysis of joint status haemophilia A severe, patients with or without inhibitors who was on ON DEMAND treatment.

Methods: Twenty patients with haemophilia A severe were taken for the study, for comparing the joint status ON DEMAND treatment, with inhibitor positive and inhibitor negative. They were divided into two groups of 10 patients each with inhibitor positive and inhibitor negative. The assessment scales used were HJHS and FISH. HJHS depicts joint health score of haemophilia patients while FISH depicts functional independence of haemophilia patients.

Results: The study was to compare the joint status of haemophilia A severe patients, who was on ON DEMAND treatment, with inhibitor positive and inhibitor negative using HJHS and FISH. The result showed that mean value HJHS of inhibitor positive was 29.20 and inhibitor negative was 22.80. The mean value FISH of inhibitor positive was 21.80 and inhibitor negative was 26.

Discussion/Conclusion: The compliance of patient under study for prescribed physiotherapy was poor. The result showed that joint health status and functional independence with inhibitor negative showed better score than inhibitor positive patients on assessment scales HJHS AND FISH.

Disclosure of Interest: None declared.

PO292 | Development of an evidence-based, expert-driven, practical statement for primary care physiotherapists in the management of persons with bleeding disorders

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Introduction: Physiotherapy is recommended alongside clotting factor in the management of acute bleeding and haemophilic arthropathy. Treatment is often provided by a primary care physiotherapist

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because of the distance to the haemophilia treatment centre (HTC). However, given the rare nature of haemophilia primary care physiotherapists generally have no experience with haemophilia. A previous study showed that a written guideline is the top priority to improve the care for persons with haemophilia in primary care. Current study aims to formulate evidence based practical recommendations for primary care physiotherapists treating persons haemophilia.

Methods: Following a survey of primary care physiotherapists, HTC physiotherapists and persons with haemophilia 13 questions were identified that required answering to formulate the recommendations. A systematic literature review was carried out, all available literature was summarised and consensus meetings were held with expert physiotherapists in the field of haemophilia. Finally, feedback on draft recommendations was collected from all relevant stakeholders, including representatives from the patient's association, physiotherapy association and haemophilia treaters association. Consensus for agreement was set at ≥80%.

Results: Results from 69 studies on physiotherapy in haemophilic arthropathy, joint bleed, muscle bleed, synovitis and the pre- and post-operative phase after orthopaedic surgery were included. Findings from the literature were discussed with 12 international expert physiotherapists. The research team compiled a comprehensive list of more than 30 recommendations on therapy for joint- and muscle bleeding, synovitis, haemophilic arthropathy, pre- and post-surgery and for non-bleeding related complaints. Additionally, recommendations on indications to start primary care physiotherapy and when to contact the HTC were drafted. Initial recommendations based on the literature and consensus meetings were further adjusted based on feedback from experts and stakeholders.

Discussion/Conclusion: This comprehensive process has resulted in a list of evidence-based practical recommendations for primary care physiotherapists treating persons with haemophilia. The current list of recommendations will support inexperienced physiotherapists to provide more adequate care for all persons with haemophilia.

Disclosure of Interest: None declared.

PO293 | The impact of musculoskeletal assessment on physical activity choices and prophylaxis decisions: A case study of monozygous twins with severe haemophilia A

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Introduction: Physical activity (PA) improves health outcomes. The World Health Organisation (WHO) recommended at least 150 min moderate or 75 min vigorous exercise per week. PA is safe for patients with haemophilia (PwH) and the WHO recommendations regarding amount and intensity apply.

Methods: We report a case of 24-year-old monozygous twin males, with severe haemophilia A (SHA) on primary prophylaxis who requested support regarding choices about PA and prophylaxis treatment. Both attended a multidisciplinary team (MDT) review utilising a Shared Decision Making (SDM) approach that included; HJHS, HEAD-US and education to support their PA goals and treatment options. This case will showcase the benefit of person-centred care in PA and prophylaxis decisions.

Results: Patient F; HJHS 0, HEAD-US 0, ABR 0. Meets WHO PA guidelines. Key goal: to increase PA. Remained on efmoroctocog alfa. Patient H: HJHS 1, HEAD-US 0, ABR 0. Below WHO PA guidelines. Key goal: to reduce treatment burden. Switched to emicizumab. Six months data on bleed rates, joint health, PA levels and patient experience will be presented.

Discussion/Conclusion: MSK assessment, with a person-centred approach, influences PA choices in patients with SHA, which influences prophylaxis treatment decisions. PA in PwH should be assessed on an individual basis. PwH should be reviewed by an MDT and should include musculoskeletal (MSK) assessment by a Specialist Haemophilia Physiotherapist.

Disclosure of Interest: None declared.

PO294 | Barriers to home based prophylaxis therapy in persons with haemophilia (PwH)

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Introduction: World Hemophilia Federation recommends home based prophylaxis therapy in all persons with haemophilia (PwH) to lead a near normal life. In developing country like India, this is not always implemented.

Aim: To investigate the barriers to home-based prophylaxis in PwH.

Methods: This is a descriptive-qualitative study where data was collected by a semi-structured interview with PwH, parents or guardians of PwH, health care workers and volunteers involved with haemophilia treatment in our centre. Data was analysed by accumulating all the interview proforma and recall by interviewer.

Results: Data analysis let to the identification of four major categories of barriers that included technical expertise (difficulty in finding vein and fear of injecting improperly), logistic challenges (collecting and storing factors, syringes at home, keeping it safe from other children), motivation (inertia in initiation of home-based therapy by parents and guardians) and inadequate advocacy (lack of enough numbers of workshops or patient education programs). This led us to focus on the problems at hand and try to find out the key areas to work on finding problem-based solutions. The technical and logistic challenges could be addressed by education, workshops and training modules. The motivation and advocacy will require more involvement of the health care

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providers in the form of one-to-one interactions and patient group meeting.

Discussion/Conclusion: We identified the key barriers to home-based prophylaxis therapy in PwH which included technical, logistic, motivational and advocacy related issues, giving us the focused areas to work on the solution for overcoming them.

Disclosure of Interest: None declared.

PO295 | A cross-sectional study to estimate socio-economic costs in patients with haemophilia in North-Western india

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Introduction: In India, haemophilia, a rare genetic bleeding disorder, affects around 18,353 individuals, but only 1% of those under 18 receive preventive treatment. In 2022, the average India's per-capita income was Rs. 1.27 lakhs, yet there is a lack of data on haemophilia's economic impact in the North Western region.

Objectives: To determine the economic burden from a societal perspective including both direct medical and non-medical costs, loss due to labour productivity losses.

To assess the health-related quality of life (HRQOL) of persons with haemophilia (PwH).

Methods: This design of study was cross-sectional investigation involving individuals who had been diagnosed with haemophilia and were residing in Punjab, India. These individuals were receiving both inpatient and outpatient medical care. The participants were then given a six-page questionnaire containing 100 closed-ended questions. Prior to administration, the questionnaire underwent face validation for both content and construct. The questions primarily covered topics related to income, as well as direct and indirect medical expenses.

Results: We analysed the data of 54 participants data in this study. Most families had an annual income between Rs 30,831–46,128. The median distance to the Haemophilia Treatment Centre (HTC) was 50 km. The median annual bleeding rate was 18 (ranging from 1 to 70), with an average of 29 factor infusions per year. Seventy two percent patients required only one factor infusion, while 28% required more. Monthly HTC visits varied: 27% once, 40% twice and 33% more than twice. The average yearly non-factor medical cost was Rs. 28,223 (range: Rs. 2200–Rs. 486,750), totalling Rs. 206,507.88 including indirect costs. The cost per bleed without considering donated factors was Rs. 19,864.6.

Discussion/Conclusion: The study reveals that haemophilia patients, primarily from low to moderate-income families, face a considerable economic burden due to frequent bleeding episodes and the associated medical costs. Access to haemophilia treatment centres varies, and while many patients require only single-factor infusions, the costs per bleed are substantial. Addressing the financial challenges and improving accessibility to care are essential for enhancing the well-being of individuals with haemophilia.

Disclosure of Interest: None declared.

PO296 | Substance abuse disorder in haemophilia patients

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Introduction: Haemophilia is a plasma coagulation disorder that in its most common forms there is a deficiency in factors VIII (FVIII) and IX (FIX). The physical toll in addition to its effect on mental health leads to depression and low self-esteem, which causes those afflicted with the disease to turn to substance abuse and even overdose. The resort to addictive medications is a known issue in haemophiliacs, and the reasoning behind this has always been associated with pain. Therefore we decided to study the scale of pain-scores haemophiliacs report in those with substance abuse and those without.

Methods: This cross-sectional, descriptive-analytical study was performed on the haemophilia patients 12 years and older, who were registered in the Ali-Asghar Pediatrics Hospital, Hemophilia registry. Patients use regarding substance abuse, that is, cigarettes, alcohol and other addictive drugs (opium, morphine, etc.) were recorded and analysed using SPSS Statistics Software Version 26.

Results: Of the 80 enrolled, 24 were female and 56 were males. Twenty-eight (35%) had substance abuse disorders and 46 (57.5%) scored their pain intensity at 8.21 ± 2.12. This score was 8.53 ± 1.71 in those with substance abuse disorders and 7.77 ± 2.54 in those without substance abuse disorder the difference of which was not significant (p-value = .212). This most likely indicates that patients resort to drugs for reasons beyond pain, possibly psychosocial ones.

Discussion/Conclusion: Given that the pain-scores in haemophiliac are not significantly correlated with the abuse of addictive substances, psychosocial reasons leading to addiction come to mind. Therefore, we suggest a more careful approach in addition to routine therapy recommendations and social events regarding the mental health of the patients as preventive measures for substance abuse in haemophiliacs.

Disclosure of Interest: None declared.

PO297 | Study of the quality of life (QoL) of persons with congenital bleeding disease in the cultural space of estonia

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Introduction: According to WHO, QoL is the indvidual's perception of his position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards, concerns and fears of the living environment. Congenital coagulation defect manifests in frequent bleeding into the joints, function decline, difficulty in movements. Patients wellbeing does not depend only from treatment, but on ability to cope with a disease in his environment. The HaemAQoL questionnaire for people with coagulation disorders consists of 10 parts: physical health, wellbeing, self-image, sport activities, employment, coping, treatment, future views, family planning and partnership. Assessment of the QoL of the Estonian patients with haemophilia.

Methods: Study on QoL in participants of the Kuressaare Hospital rehabilitation project based on the HaemAQoL questionnaire translated and validated for Estonia. Answers are divided to groups:18–34 (younger) and 35–55 years (older) and for severe bleeding disorder (SBD) and mild (MBD).

Results: Twenty-one patients participated: 16 patients with severe and five with mild bleeding disorders, age 25–55 (median 40) years. In SBD, there were eight patients at younger and eight patients at older group. In MBD, two patients were younger and three patients in older group. Results differed according to the age in following categories: physical health, wellbeing, going to work, future views and starting a family. In SBD, older people considered physical health and wellbeing [1st, 2nd set of questions (SoQ)] more worrying than younger people, as well as coping at work (5th SoQ). Family problems did not cause problems for the younger as compared to the older group (9th SoQ). In MBD, there was a greater discrepancy for questions concerning the future and family life (8th and 9th SoQ).There was equal concern about coping with haemophilia (6th SoQ) on a daily basis in all disease severity levels and ages. Sports and leisure activities were also equally disturbed in all age and severity groups (4th SoQ). Coagulation-related treatment was more likely to cause concern in patients with SBD (7th SoQ).

Discussion/Conclusion: QoL enables a more objective understanding of the patients perspective in their living environment. There are generation-related differences in QoL assessment that are necessary to help rehabilitation team to make longer and more individual plans for the future treatment facilities and national social rehabilitation system.

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PO298 | Health-related quality of life (HRQoL) in greek patients with von Willebrand disease (VWD)

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Introduction: Von Willebrand disease (VWD) is the most frequent inherited bleeding disorder caused by the qualitative or quantitative deficiency of von Willebrand factor (VWF). The aim of the study is to determine health-related quality of life (HRQoL) in adult Greek patients with VWD and evaluate the impact of clinical and demographic features.

Methods: The study was conducted in a Reference Centre for Bleeding Disorders in 2022–2023. All participating patients completed two general questionnaires of quality of life, SF-36 and EQ-5D-5L, while BAT score (Bleeding Assessment Tool) was used to assess bleeding events. Statistical analysis was performed using SPSS 22.0.

Results: The study included 127 patients (32 males and 95 females) with a median age of 40 years and an average BAT score of 10.2 (±7.6). By means of SF-36, HRQoL was found statistically significantly impaired in almost all SF-36 domains, compared with the Greek general population. Specifically, lower mean scores were observed in the dimensions of Physical Role (PR) (68.1 ± 39.8 vs. 79.74 ± 37.72 in general population), Bodily Pain (BP) (65.5 ± 27.3 vs. 72.98 ± 31.66), General Health (GH) (57 ± 20.8 vs. 67.46 ± 23.54), Vitality (V) (52.5 ± 19.3 vs. 66.53 ± 22.39), Emotional Role (ER) (61.4 ± 39.9 vs. 81.53 ± 36.31) and Mental Health (MH) (59.3 ± 19 vs. 68.23 ± 21.26). Increased BAT score was strongly and negatively correlated with Physical Functioning (PF) (r-0.27), Physical Role (r-0.25), Bodily Pain (r-0.216), General Health (r-0.30), and the Physical Component Score (PCS) (r-0.31) of SF36 and EQ-5D (r-0.24).

According to multivariate analysis, various clinical and demographic features were identified as significant predictors of decreased HRQoL. Increased BAT score was found to reduce BP and GH, increasing age reduced PF, PCS and EQ-5D, female gender largely decreased vitality by 8.3 points, while urban living hugely impaired PR, BP, MH, ER and PCS by several points. Increased educational level was a predictor of improved HRQoL, largely affecting almost all SF36 subscales.

Discussion/Conclusion: HRQoL of VWD patients was found to be lower compared to general population. Age, gender, place of residence and increased BAT score were independent factors negatively affecting distinct SF36 dimensions, whereas educational level exert positive influence in most SF36 subscales.

Measuring quality of life with SF-36 and EQ-5D-5L will provide important insights into patients' daily life with their perception of well-being and their specific health care.

Disclosure of Interest: None declared.

PO299 | Physical activity awareness among people with haemophilia and their caregivers in central Europe

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Introduction: Regular physical activity (PA) has several benefits for people with haemophilia (PWH), including preventing bleeding and joint problems and increasing quality of life. A survey has been conducted with the aim to understand physical activity patterns among PWH and their awareness of the level of factor and non-factor protection against bleeds.

Methods: An online survey with 23 questions was distributed to people with haemophilia or their caregivers across eight Central European countries between August and September 2023.

Results: Of 374 respondents, 91.9% of PWH had participated in physical activity (≥30 min) within the last 2 weeks. The most frequent physical activities were walking (69.0%), swimming (28.1%) and biking (28.1%). Most respondents (64.4%) indicated they understood the changes in factor levels over time following administration, but only 35.2% understood factor levels required for high-intensity physical activity. Factor equivalence achievable with currently available non-factor therapy were understood by 73.8% of respondents. Respondents indicated joint health (68.7%), disease severity (69.3%) and capability of physical activity (62.3%) as having significant/greatest influence on PWH's ability to live well with haemophilia.

Discussion/Conclusion: Awareness of the importance of physical activity and joint health in PWH is high. However, knowledge of how factor and non-factor levels protect against bleeds is inconsistent among PWH and could form the basis for education programs.

Disclosure of Interest: None declared.

PO300 | Psychosocial intervention for tobacco addicted people with haemophilia

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Introduction: Haemophilia is an incurable bleeding disorder due to deficiency of clotting proteins in the blood. Replacement therapy is main stay in the management and is challenging. Teenage is the most vulnerable period for habitual addiction. Prevalence of tobacco addiction is more in Northern part of Karnataka State. Life style makes young generation curious and addict for tobacco, but in haemophilia it can aggravate complications due to inherent bleeding and cause increased morbidity and mortality. To study the tobacco addiction and its implications among people with haemophilia (PwH) is the main objective.

Methods: We analysed 1-year clinical data from 260 PwH, revealing that 56 (21.5%) were addicted to tobacco. Clinical examination, radiological evaluation and dental screenings were performed, leading to surgical interventions as needed. Following medical treatment, we addressed underlying psychological issues using psychological scales, cognitive-behavioural therapy and stress reduction exercises. Additionally, we conducted webinars and skits on deaddiction programs to raise awareness.

Results: Result shows that tobacco addiction in PwH led to various challenges, including depression 10.7%, fear of life-threatening bleeds 7.1%, school/job disruptions 19.6% and social/financial insecurities 17.8%. Dental issues were also prevalent, with 33.9% suffering from chronic gingivitis and various other dental problems. Upper gastrointestinal bleeding was observed in 19.6% of cases, requiring surgical intervention. Ultimately, 42.8% of individuals successfully quit tobacco, while one unfortunate case resulted in death due to oral cancer.

Discussion/Conclusion: Addressing tobacco addiction among PwH is crucial, as it worsens bleeding complications and dental health. A comprehensive approach involving medical and psychosocial interventions is necessary to prevent further complications. Maintaining oral hygiene and adopting healthy habits can significantly improve the quality of life for people with haemophilia.

Disclosure of Interest: None declared.

PO301 | Sufferings beyond the physical impact of haemophilia—A mixed method study on personal, social, economic domains and its association with quality of life in patients with haemophilia (PWH) and their caregivers (WE CARE)

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Introduction: Haemophilia is a bleeding disorder requiring continued care and is considered a costly disease globally. Haemophilia is associated with significant morbidity including premature joint arthropathy, inhibitor development, infections such as HIV, HCV, along with age related ailments which leads to increased burden amongst PWH and their caregivers. Genetic disorders such as haemophilia, lifelong diseases such as cancers substantially affect the caregivers physically, emotionally as well as financially. There are few studies done globally related to caregiver burden, but there is paucity of studies from India.

Methods: Face to face interviews were conducted for PWH and their caregivers as per the predefined semi structured interview guide. A written informed consent was taken individually from the PWH and their caregivers for conducting as well as audio recording the interview. The recordings of these interviews were transcribed and analysed using thematic analysis.

Results: Thirty PWH and their caregivers (15 each) participated in the semi-structured interviews. The identified themes from the patient

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interviews were—dealing with severe pain, choosing a different career option than desired due to haemophilia, being prone to get angry easily, frustration, being called crippled behind their backs and having suicidal thoughts. As for the caregivers, the themes included difficulties due to lack of awareness, restricted social interaction due to being a caregiver, feeling terrible to see their child/spouse in pain and struggling to arrange factors during the patient's childhood. A common concern for both PWH and the caregivers was the financial burden associated with the disease which adds to their cost of living.

Discussion/Conclusion: The identified themes and areas of concern from this study would be useful in a better understanding of the impact of haemophilia and improving patient care.

Disclosure of Interest: None declared.

PO302 | Mapping the patient experience in a paediatric haemophilia unit: Our patient journey

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Introduction: Haemophilia A and B are rare X-linked bleeding disorders. Severe bleeding phenotype patients suffer from joint haemorrhages that can lead to a chronic arthropathy. Although prophylaxis has improved bleeds, there still are unmet needs that should be addressed such as the evaluation of patient reported outcomes and patient experience. The patient journey is a visual tool that illustrates patients' relationship with the healthcare provider through time that helps to identify patient needs, potential concerns ('pain points') and gaps in care.

Methods: Qualitative study in a paediatric haemophilia unit using a human-centred design methodology to develop a patient journey in children with haemophilia. First stage: discover and empathise with semi-structured in-depth interviews to families, patients and different stakeholders, and observation techniques to patients and professionals ('shadowing'). Second stage: analysing and understanding all the collected information and creation of the patient journey.

Results: A preliminary clinical journey was created using the information obtained from seven interviews to the multidisciplinary haemophilia team (haematologist, rehabilitation, nurses, pharmacist and social worker). Main detected phases: diagnosis, prophylaxis initiation, caregivers training, follow-up, teenager training and transition to an adult haemophilia unit. Patient association meetings, patients/caregivers' interviews at home, and patient 'shadowing' allowed to compare the clinical journey with the patient's reported experience.

Patient/families 'pain points' were detected at different moments through time: before diagnosis, at diagnosis, during disease assimilation, at first treatment dose, during caregivers training and when the patient is old enough (7–8 years) to ask about his condition.

Investigators detected two potential moments during the journey to improve the patients and families experience. Both were related to the learning and empowerment process of caregivers/patients.

Discussion/Conclusion: Knowing the paediatric haemophilia patient journey led us to better understand patient and families experience related to the disease at different scenarios. Caregivers and patient learning process are significant moments where the multidisciplinary team should focus to offer valuable solutions to improve outcomes. Further research is required, particularly empirical research, to amend/confirm our patient journey.

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PO303 | Phenomenological study on social challenges of mothers with severe haemophiliac children in Iranian culture

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Introduction: Haemophilia can be genetically transmitted or arise spontaneously, posing unexpected psychosocial challenges for the affected person's family and reducing their quality of life. Caring for children with severe haemophilia necessitates constant care and lifestyle adaptations. Previous studies have identified varying psychosocial challenges among families of boys with haemophilia. Given the cultural differences, it is crucial to address the social challenges encountered by caregivers of children with haemophilia in Iran. The main goal of this research was to study the lived experience of social challenges of mothers with children with severe haemophilia.

Methods: The study utilised a phenomenological approach and employed an analytical thematic framework for data analysis. In this phase, the MAX.QDA 2020 was used to enhance data categorisation and organisation. All data were collected through semi-structured in-depth interviews with 15 mothers of children with severe haemophilia, while observing cultural considerations (such as conducting all interviews by a female psychologist) and ethical standards at the Mofid Comprehensive Care Centre for Haemophilia. The consolidated criteria for reporting qualitative research (COREQ) were also utilised to ensure the credibility of the data.

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Results: Analysis yielded seven themes and 20 sub-themes. This research's focal points encompass concerns, social pressure, social comparisons, lack of knowledge, social restrictions, social support and confronting environmental crises. The predominant findings pertained to the last two areas.

Discussion/Conclusion: Concerns about medication shortages, unemployment, children's marriages and lack of legal support for women in Iran were their main concerns. They mentioned significant social pressures, such as interference of others (especially in-laws) in their parenting style and constant blaming for having the gene along with social stigmatisation. They also reported using social comparisons in equivalent, ascending and descending forms, which increased their anxiety after diagnosis but over time played a role in emotional regulation. The role of internal support (spouse and family) and external support (friends, colleagues and healthcare professionals) in overcoming these challenges has been significant. By providing more support and increasing awareness, we can improve the well-being of this vulnerable group.

Disclosure of Interest: None declared.

PO304 | Psycho-social support for Haemophilia patients rehabilitation

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Introduction: Issues: Haemophilia patients rehabilitation services are not well-developed concept in resource-poor nations due to poor economics and lack of expertise. With limited resources we wanted to explore these rehabilitation services in rural villages.

Aims: Rural/tribal areas of India haemophilia patients lack rehabilitation support available only in city hospitals. Our 12-year CBO is training youth volunteers and traditional faith healers in marginalised communities to provide rehabilitation.

Methods: Around 417 cases of haemophilia will be in rural/tribal of India by 2025, but hospitals lack dedicated rehabilitation program. Patients returning to villages after therapy in cities urgently need rehabilitation support to suit their economic, social, cultural background. Since August 2018 Our NGO clinic started free advice on rehabilitation. [$n = 32$ haemophilia subjects]. With six trained nurses, two physicians, we screened patients. Average age 38 years, M:F ratio 70:30. Our support psycho-social services devised as-per need of patients in consultation with family and stretched over 2 months included counselling, physiotherapy, occupational therapy and rehabilitation. Responses assessed with Quality of life scale by Flanagan Quality of Life Scale (QOLS) and psychological evaluation by Likert psychometric scale. This presentation demonstrates project in developmental stages and basic operational facts. Initially started as practically oriented guidance centre and later developed in well-organised set-up offering free rehabilitation services in villages. It comprises NGO staff and traditional faith healers.

Results: Our program highlights variability of psychological and socio-medical aspects in rehabilitation. Patents needed medical interventions in 60%, psychological approaches in 80%, 35% needed combination of both.

Discussion/Conclusion: This is pilot project running on community donation. We plan to document, evaluate this in large sample size, but resource restriction did not permit. To overcome this, we plan networking of European NGO's, patients advocacy experts at EAHAD-2024 Venue for better study design, technical support and collaborative efforts. I do not claim 'I transformed whole community of haemophilia patients but we had certainly taken initiative by this cost-effective approach'.

Disclosure of Interest: None declared.

PO305 | Status report on palliative care in haemophilia patients: Dark reality in resource poor nations

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Oncology, SFCCP, Meerut, India

Introduction: Issues: Social stigma, fatigue, sexual dysfunction, sleeplessness, depression commonly seen in haemophilia patients. Palliative inaccessible in rural/tribal areas. Hence Our NGO took initiatives to help alleviate suffering of women with Parkinson patients since October 2018.

Objective: $n = 32$. Of these statistically over 90% express sexual-dysfunction, 60% experience loneliness; 70% suffer social neglect/humiliation, 85% had depression. Importance of spirituality/religion in coping with terminal-illness is increasingly recognised. Hence Our NGO-nurses involved community-leaders to make more women involved in our spiritual healing sessions.

Methods: We surveyed 32 subjects through QOL-questionnaires. After 8 weeks therapy with psychosocial support. Counselling and palliative care with anti-depressants/pain-killers/nutrition, QOL improved to statistically significant level. Requirement of palliative care evaluated by Palliative Care Problem Severity Scale (PCPSS). Traditional faith-healers involved for more psychological impact on patients community. Community leaders involved to reduce social stigma/discrimination among community.

Results: Currently 165 specialist palliative care beds required for our rural/tribal population of 1,600,000. But only 40 available. 90% expressed that religious/community support/faith was most important factor that helped them to cope with Haemophilia. higher scores of QOL (ANOVA $p < .001$) correlated with lack of sexual dysfunction/pain. Our NGO-initiative suggests that over 70% patients will need well trained specialist for home-based-care.

Discussion/Conclusion: Life-span/QOL of Parkinson patients-sufferers depends on social acceptance and appropriate-palliative-care. NGO-personals should be trained in palliative-care-services. Field of spiritual/psycho-social/community support is fertile ground for further investigations. We need focussed platform like

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EAHAD-2024 to discuss our project ideas/concerns/difficulties with senior researchers.

Disclosure of Interest: None declared.

PO306 | Psychological assessment and QOL improvement project for haemophilia subjects

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Introduction: To study effectiveness of two cognitive-behavioral-therapies (CBT), Guided-Mental-Imagery (GMI), Cognitive-Restructuring-Technique (CRT), in changing negative thinking/mind-set of haemophilia-patients-with-epilepsy in developing-nations. Psychosocial-health status crucial in treatment-outcome. Limited scientific literature/data available on this burning issue.

Methods: Fourteen months longitudinal quasi-experimental research-design. Target: haemophilia patients, 30–65 years, $N = 118$. Control $n = 50$. With aid of inventory of negative thought scale, information collected pre/post-training on: occurrence/frequency of negative-thoughts in response to diagnosis, incidence of negative-statements as result of automatic dysfunctional-thoughts, underlying-beliefs, incidence of joint pain. Correlation of epilepsy with depression evaluated. Training/data collection for psycho-analysis done by psychiatrists. 14-Item structured questionnaire contained: items on characteristics/knowledge of respondents on risk-factors, symptom, Rx-outcomes, current stress levels, beliefs, fear, despair, suicidal-tendencies, family-support and depression-level. Epileptics went through counselling-sessions of CRT/CBT.

Results: Applied statistical-methods. 80% Subjects received GMI/CR training able to notice/monitor their unhelpful thinking patterns than controls (multivariate-ANOVA) and able to control them better when compared with control-group (improving-QOL-quotient). 80% Participants better-equipped to cope with stress/despair [60%], reduced Occurrence/frequency of negative-thoughts [90%], decreased negative statements [80%] and reduced incidence of headaches/migraine [40%].

Discussion/Conclusion: CBT/CRT techniques in watering seeds of happiness are efficacious in haemophilia subjects. This underscores need to train health-care-professionals these psychological-techniques. Our-study shows importance of ability to cope, psycho-social support, understanding emotions, relief of acceptance of belief system and positive-thinking. In future, such study with greater sample-size and more QOL-factors needed.

Recommendations: More participation of developing-nations in such research needed. Treatment-modalities limited to few resourceful-patients. Our-project helps patients in better-recovery and is helpful in better happiness-quotient this improving QOL in haemophilia-related-epilepsy-patients.

Disclosure of Interest: None declared.

PO307 | National haemophilia data registry: Need international consensus

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Introduction: National-Haemophilia-Registry provides detailed information on incidence/trend/survival statistics. Neurology-registries are population-based and seek to describe incidence/rates/trends of stroke-patients-data. Also information on staging/treatment and allied-clinical-data required to monitor clinical care/outcomes. Development of such comprehensive-database long-awaited in Asian-nations.

We took initiative to develop a primary-plan in consultation with seven-divisional-hospitals and Health-ministry; aim to establish platform for multi-clinician, multi-centric collation of datasets with haemophilia patients as pilot disease entity; plan to integrate this concept at major institutes with expertise from EAHAD/WHO. Proposal of intent approved at national-level.

Methods: As-policy-plan we relate our-experiences of initiative aimed at establishing methodology, statistical-analysis, supportive-control centre for multicollaborator haemophilia data-collection, to establish national haemophilia data repository.

Results: Initiated from four-sites, modern technology of data-collection, storage/analysis/distribution is optimised towards implementation of sustained comprehensive and multi-collaborator data registry. Need for minimum datasets, customisation of technology to suit needs, data-capture, storage/retrieval. These can be leveraged to inform future direction of initiatives: expanding scope of database, optimising variables for data-analysis and addressing data-privacy, security/ownership concerns need participation of private haematology care-clinics. Total study-participants projected by 2025 are 410.

Discussion/Conclusion: Our experience with this initiative over past 5-years shows: data be collated centrally in secure/private manner. Multicentre, multi-clinician collaboration is possible with collaborative efforts with EAHAD/WHO. Major concern is haphazard data/protocol maintenance by private entities. Most difficult data outsourcing was about survival statistics. National Registry is distant dream in resource-poor-nations. But we have taken step in forward direction on this burning-issue.

Disclosure of Interest: None declared.

PO308 | Biofeedback for reducing anxiety associated with injections in people with haemophilia: A randomised controlled trial

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Introduction: Haemophilia is a hereditary bleeding disorder that requires regular injections of clotting factor to prevent or stop bleeding. However, injections can be painful and anxiety provoking. Biofeedback is a technique that allows people to learn to control their autonomic nervous system. Biofeedback may be used to reduce anxiety associated with injections in people with haemophilia.

Methods: A randomised controlled trial was conducted among patients follow-up and treated in our haemophilia centre to evaluate the effectiveness of biofeedback for reducing anxiety associated with injections in people with haemophilia. Twenty people with haemophilia were randomly assigned to either a biofeedback group or a control group. Participants in the biofeedback group received 10 biofeedback sessions aimed at reducing heart rate and blood pressure. Participants in the control group received no biofeedback. The study has IRB approved $n = 20$, median age 43 years.

Results: Participants in the biofeedback group reported significantly less anxiety during injections than participants in the control group [mean difference = −2.7 points, 95% confidence interval (CI) −4.0 to −1.4, $p = .003$]. In addition, participants in the biofeedback group reported higher levels of satisfaction with injections (mean difference = 1.8 points, 95% CI 0.6–3.0, $p = .02$).

Discussion/Conclusion: These results suggest that biofeedback is an effective method for reducing anxiety associated with injections in people with haemophilia.

Disclosure of Interest: None declared.

PO309 | Factors influencing parents'/carers' choice of treatment for their previously untreated child with severe haemophilia A (SHA)

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Introduction: Patients with SHA require regular replacement therapy with factor concentrates or other haemostasis products to prevent musculoskeletal complications from recurrent joint and muscle bleeds. For decades, factor VIII (FVIII) concentrates have been infused intravenously; however, more treatment options are now available for patients with SHA giving parents'/carers' greater choice when making treatment decisions for their child.

Aim: To examine factors influencing parents'/carers' choice of treatment for their previously untreated child with SHA.

Methods: A mixed method research design using quantitative descriptive surveys and/or qualitative semi-structured interviews was used to establish factors influencing parents'/carers' treatment decisions for their child with SHA. Participants were recruited using convenience sampling, via advertisement on haemophilia charitable websites and social media. Survey participants completed the validated SURE test (Legare et al., 2010) and a Likert scale.

Results: Nine participants completed the survey. Six on non-FVIII replacement therapy, three on standard half-life FVIII products. Descriptive statistics were used to analyse data. 78% felt SURE of their treatment choice. Factors with most influence were frequency of treatment, ease/difficulty of venous access, child's age at start of prophylaxis, family support and lifestyle. Two participants took part in interviews. Main influencing factors on treatment choice were earlier haemostatic cover, less invasive, less frequent, perceived low maintenance, lifestyle and family experience. Similar findings observed between quantitative and qualitative data and on comparison with existing research. Due to small sample size, generalisations challenging.

Discussion/Conclusion: Healthcare practitioners support families in treatment decisions, prescribing treatment and monitoring outcomes. Better understanding of factors influencing parents'/carers' treatment decisions will help practitioners provide pertinent information when discussing optimal management of their child with SHA.

Disclosure of Interest: None declared.

PO310 | A new tool to assist in treatment selection—The World Federation of Haemophilia (WFH) shared decision-making (SDM) tool

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Introduction: The treatment landscape for haemophilia has become more complex in the recent past with several new treatment classes available, making a truly informed decision about treatments more challenging for both people with haemophilia (PwH) and their healthcare team. A framework for informed and shared decision making on treatment options will help facilitate discussion and help navigate the complexities of factor and non-factor replacement as well as gene therapies. The newly launch World Federation of Haemophilia Shared Decision Making (SDM) tool provides a stepwise process to aid a patient's decision-making when multiple treatment options are available.

Methods: The WFH SDM tool was developed with the intent of assisting PwH in their ability to evaluate and compare treatment options based on their current values, preferences and concerns, and help facilitate a discussion between PwH and their healthcare teams.

The SDM tool, a web-based interactive decision-support system, includes evidenced-based educational content on five prophylaxis treatment classes for haemophilia [standard half-life clotting factor concentrate (CFC), extended half-life CFC, bispecific antibodies, haemostatic rebalancing agents and gene therapies], and an accompanying interactive PDF booklet. Users are guided through a series of

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value-based questions to reflect on, educational content on each treatment class with the ability to compare important attributes of each, and a PDF individualised summary output, which forms the basis for discussions.

Results: The SDM tool was launched on 1 August 2023 with a 3-month public comment period. It is currently available in English, French and Spanish with additional language translations underway. A global training program is in development to aid PwH and health care teams in incorporating the tool into clinical practice.

Discussion/Conclusion: SDM is a key component of PwH and healthcare team partnership. In the context of complex information, the WFH SDM tool provides a framework to make an evidence-based personalised treatment decision.

Disclosure of Interest: None declared.

PO311 | Biopsychosocial challenges of an iranian family with a child with co-occurring haemophilia and autism spectrum disorder: A phenomenological case study

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Introduction: The significant increase in the prevalence of autism spectrum disorder (ASD) since the beginning of the century (approximately 317%) has led to an increased risk of co-occurrence of this developmental disorder with haemophilia. Some recent studies have reported a co-occurrence rate of 6.5% between haemophilia and ASD. This co-occurrence can cause confusion for healthcare providers and families, creating serious obstacles to managing haemophilia and treating ASD. The objective of this research is to study the biopsychosocial challenges faced by an Iranian family with a child who has co-occurring haemophilia and ASD.

Methods: This is a phenomenological case study, and its data was collected through four semi-structured in-depth interviews, each lasting 100 min (two sessions with the father and two sessions with the mother), while considering cultural considerations and the ethical codes of the American Psychiatric Association, at the Mofid Comprehensive Care Centre of Haemophilia (MCCCH). The data analysis was conducted using Van Manen's six-step approach and the MAX.QDA 2020 software package. Additionally, to enhance the credibility of the data, natural observations of father–child interactions during prophylaxis at the MCCCH, interactions with the medical staff and review of findings with a health psychologist were conducted.

Results: The findings of this study consist of six themes and 26 sub-themes, which, in a case study, demonstrate the notable challenges experienced by parents. The obtained themes include: disrupted emotional exchanges within the family, dual unrealistic environmental evaluations, parenting disturbances, interference with the child's autonomy development, mismatched expectations with the child's developmental stage and neglecting the psychological needs of a child with both haemophilia and ASD.

Discussion/Conclusion: The severe anxiety caused by this comorbidity, as well as the strained family dynamics (especially in terms of emotional exchange), resulted in parenting difficulties. Impaired parenting hindered the child's autonomy and had noticeable consequences in the absence of integrated and coordinated treatment for haemophilia and ASD. It should be noted that in such a context, in addition to the failure of integrated treatment, the psychological damages inflicted on the siblings are significant.

Disclosure of Interest: None declared.

PO312 | Intergenerational impact of the contaminated blood scandal

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Introduction: The contaminated blood scandal (CBS) has had a significant psychological impact on the families involved, alongside the physical and financial cost [1]. Very little is known about the intergenerational impact. This study explores the impact of the CBS on intergenerational impact on those affected.

Methods: This is a qualitative research study at an early stage, conducted within the haemophilia community.

Ethical approval was received from the University of Gloucestershire.

Results: Findings—two strong themes of silence and trust emerged from initial analysis of data from female participants. These were not present in discussions with male participant.

Silence—silencing or dismissing of participants by healthcare professionals was clearly resented, and narratives suggested this resulted in reduced trust in the advice provided by those individuals.

Trust in healthcare treatments—some participants identified a need to have information about the treatments for their children, which may be more detailed and specific than they may have otherwise needed, including precise details of the treatment being administered, safety studies and so on. This also affected those without children, in other healthcare related choices such as vaccines.

Discussion/Conclusion: The impact on healthcare choices was an element that, given the increasing life span of people with haemophilia, may become increasingly relevant as this generation develop chronic conditions.

The fears of history repeating itself has been seen in the Exigency study [2]. Our study illustrates the reasons for that trust dynamic. Trust in individual clinicians was evidence throughout, if they had demonstrated empathy towards the person or had shown distress at the story of the parent/sibling who was infected. It is not in the past; the ripples continue.

Disclosure of Interest: None declared.

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PO313 | Sexual functioning amongst men with haemophilia in the Netherlands: Data from the haemophilia in the Netherlands-6 study

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Introduction: Sexual functioning is important to health-related quality of life (HRQOL), since it can reinforce relationships, personal identity and sense of self-worth. Men with haemophilia may experience problems in sexual functioning due to symptoms and consequences of prolonged bleeding. Despite these problems in sexual functioning, provision of information and communication about problems in sexual functioning by health care providers is scarce. The aims of the study were: (1) gain insight in sexual functioning in men with haemophilia; (2) gain insight in communication about sexual functioning between men with haemophilia and health care providers during outpatient visits for haemophilia and (3) determine if sexual functioning is associated with HRQOL in men with haemophilia.

Methods: Data for this study was collected through the 'Haemophilia in The Netherlands 6' study, that was conducted during 2018–2019. Participants were adult Dutch men with haemophilia of all severities. Sexual functioning was measured with a set of standard questions and HRQOL with PROMIS-29.

Results: A total of 719 respondents (median age 51; range 18–88 years; response rate 41.2%; 34.5% severe) completed the questions about sexuality. In total, 11% of the men reported restricted sexual functioning. The strongest predictor for being restricted was adjusting positions during sexuality. Most men (81%) reported that sexual functioning is not discussed during outpatient visits. Restricted sexual functioning is associated with poorer scores on the following domains of HRQOL: Physical Functioning ($\beta = -0.11$, $p = .002$), Satisfaction with participation in social roles ($\beta = -0.16$, $p = < .001$), pain ($\beta = 0.14$, $p = .002$) and sleep disturbance ($\beta = 0.12$, $p = .02$).

Discussion/Conclusion: Although 11% of men with haemophilia report restrictions in sexual function, it is generally not addressed by health care providers during outpatient visits. As sexual restriction is associated with reduced HRQOL it is important to develop approaches to make this topic conversational at the outpatient clinic.

Disclosure of Interest: None declared.

PO314 | Treatment Preferences in people with severe haemophilia A: A discrete choice experiment in the United States

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Introduction: The evolving severe haemophilia-A treatment landscape with new modalities such as gene therapy requires understanding the aspects of treatment that drive treatment choices. This study assesses treatment preferences of people with severe haemophilia-A (PwSHA) using a discrete choice experiment (DCE).

Methods: Based on qualitative interviews six attributes and levels were developed: treated bleeds per year, treatment frequency and route of administration, 1st-year treatment requirements, increase in theoretical risk of cancer, 1st-year treatment response and impact on daily life. PwSHA, recruited via patient organisations in the United States, self-reporting severe haemophilia-A were invited to the DCE. Data were analysed using a multinomial-logit model. Relative attribute importance (RAI) and trade-offs were calculated.

Results: A total of 77 respondents, with a median age of 35 years (IQR: 29, 39), who completed the survey were included in the analysis. Most respondents had more than three treated bleeds in the past 12 months (3–5 bleeds: 43%; > 5 bleeds: 25%) and most were receiving subcutaneous injections treatment (SC) [62% vs. 38% on intravenous (IV) treatment].

A reduction in treated bleeds (from 5 to 0 bleeds per year) was seen as the most important attribute (RAI of 32%), followed by a reduction in treatment frequency (IV twice a week to IV one-time with 10-year durability: 21%), and a reduction in theoretical treatment-related risk of cancer (21%). Next, 1st-year treatment response (10%), 1st-year treatment requirements (9%) and impact on daily life (7%) were similarly important.

PwSHA viewed a reduction from IV twice a week to a one-time IV with 10-year durability as equivalent as reducing the number of treated bleeds per year from 5 to 2.6. A one-time IV with 10-year durability was 36% more valuable than a one-time IV with 5-year durability. A one-time IV with 5-year durability was 32% more valuable than SC every 4 weeks.

Discussion/Conclusion: In this US sample, two key drivers of treatment preferences for PwSHA were reductions in treated bleeds and

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less frequent administration. PwSHA were willing to tolerate additional treatment requirements, such as clinic visits and steroid use, for increased efficacy or reductions in treatment frequency. This study provides insights into patients' treatment preferences and may inform clinical decision-making.

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PO315 | The Dutch version of the PROMIS® sexual function and satisfaction measures for individuals with haemophilia

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Introduction: Sexual functioning is an important aspect contributing to quality of life. Individuals with chronic health conditions, such as haemophilia, may experience various sexual problems due to symptoms and consequences of prolonged and excessive bleeding. Additional pain, limitations in joint movement and heavy menstruation can further restrict the ability and desire to engage in sexual activities. Therefore, it is relevant to get insight in and communicate about the difficulties in sexual functioning these individuals may experience. The relevance of measuring this patient reported outcome is also mentioned by the Dutch working group for value based healthcare. However, generic and validated Dutch patient reported outcome measures to measure sexual functioning are limited. The aim of this study is to translate and validate the PROMIS Sexual Function and Satisfaction (PROMIS SEX) into the Dutch language and to evaluate reliability and validity of the PROMIS SEX in individuals with haemophilia.

Methods: The components of PROMIS SEX (a screener, a profile, seven scales, seven custom short forms) were translated using standard back and forth translation and will be administered to 200 individuals with haemophilia to evaluate reliability and validity.

Results: Multiple native Dutch and English speakers were involved in the translation process. The translated items will be tested by conducting cognitive debriefing (data collection in progress) and evaluated regarding their reliability and validity.

Discussion/Conclusion: This Dutch generic measure will help to get more insights into the sexual functioning of Dutch-speaking individuals of the general population and with haemophilia. This could facilitate discussions about sexual health in clinical practices and allow for interventions to be adjusted accordingly. The next steps of the study consist of comparing sexual functioning between people with haemophilia and the general Dutch population, determining what the association between health-related quality of life and sexual functioning is and implementing the PROMIS SEX in clinical practice.

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