EAHAD 2025

Congress Review

Review of the 18th Annual Congress of the European Association for Haemophilia and Allied Disorders

Location:	Milan, Italy
Date:	04.02.25-07.02.25
Citation:	EMJ Hematol. 2025; 13[Suppl 1]:8-24. https://doi.org/10.33590/emjhematol/SXWL9673

The 18th Annual Congress of the European Association for Haemophilia and Allied Disorders (EAHAD) was held this year in Milan, Italy, from 4th–7th February. Each day was packed with an array of insightful sessions, spotlighting the latest advancements in the diagnosis, treatment, and prevention of haematological conditions.

A valuable opportunity for professionals from diverse fields to come together and exchange knowledge on this rapidly evolving technology

DAY 1

AHP Professionals Day

THE ALLIED Healthcare Professionals (AHP) Day, which took place on 4th February 2025, was a multi-disciplinary event designed for nurses, physiotherapists, and psychosocial professionals in the greater field of bleeding disorders. It was an opportunity to celebrate and raise awareness of the pivotal role AHPs play in the management of bleeding disorders for patients.

The theme for this year's AHP Day was 'bleeding disorders through life', and began with a collaborative, joint session between the Nurses', Physiotherapists and Psychosocial Professionals Committees. Fitting in with the theme, three case studies were presented that followed bleeding disorders through different stages of one's life: adolescence, menopause, and mature age. This was then followed by 'SLAM sessions', in which submitted research abstracts were awarded. The abstract 'Nurse-led education for female hemophilia carriers throughout their lives', presented by Nuria Caballero, Hospital Sant Joan de Déu (SJD), Barcelona, Spain, was commended as the best. This abstract presented a programme, developed by a multidisciplinary team, that created five leaflets designed to provide tailor education to female haemophilia carriers at distinct stages of their lives.

Other noteworthy abstracts presented at these SLAM sessions, include 'Psychometric Evaluation of the Timed Up and Go (TUG) Test in Adults with Haemophilia' by Fabian Tomschi, University of Wuppertal, Germany, and 'Thermographic change and muscle strength examination in children with haemophilia who had at least one time history of bleeding at lower extremity' by Hande Güney Deniz, Hacettepe University Faculty of Physical Therapy and Rehabilitation, Ankara, Türkiye, from the physiotherapists SLAM.

> **It was an opportunity to celebrate and raise awareness of the pivotal role AHPs play in the management of bleeding disorders for patients**

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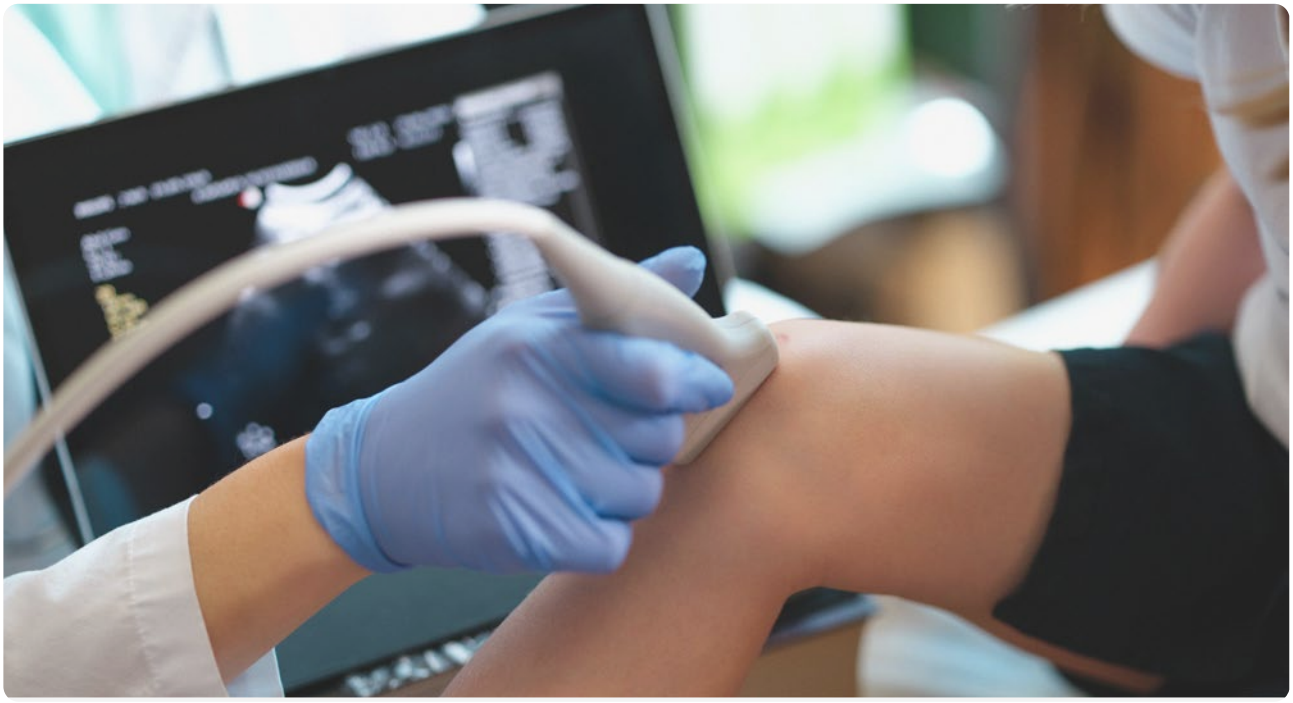
DAY 2

The second day of the EAHAD 2025 Annual Congress offered an insightful multidisciplinary educational session, led by members of the executive committee, followed by a series of engaging satellite symposia.

Multidisciplinary Session

CHAIRED by Jan Blatný, EAHAD Executive Committee President, and Roberta Gualtierotti, University of Milan, Italy, this year's multidisciplinary session focused on the topic of ultrasound.



The session featured an engaging panel discussion, where the audience had the opportunity to pose questions, vote on them, and hear the panellists' insights and responses. A variety of thought-provoking questions were raised, covering key issues such as the importance of regular ultrasound screening for early detection, the growing role of AI in the analysis of ultrasound data, and the numerous benefits ultrasound examinations offer in clinical practice. Between each voting session, presentations were given by the following experts: Carlo Martinoli, Cattedra di Radiologia - DISC, Università di Genova, Italy; Roberta Gualtierotti, Università degli Studi di Milano, Italy; Maj Friberg Birkedal, Chair of the EAHAD Nurses Committee; Roberto Cairoli, ASST Grande Ospedale Metropolitano Niguarda, Milano, Italy; and finally Merel Timmer, University Medical Center Utrecht, the Netherlands. The session was a valuable opportunity for professionals from diverse fields to come together and exchange knowledge on this rapidly evolving technology.

Symposia Summary

THE SATELLITE symposia covered key aspects of bleeding disorder treatments.

- **Sanofi** focused on thrombin generation in haemostasis, exploring its role in haemophilia treatments and the clinical use of thrombin generation assays.
- **F. Hoffman-La Roche** explored the evidence on physical activity in haemophilia A and key considerations for shared decision-making and management strategies.
- **CSL Behring** presented real-world gene therapy experiences in haemophilia B, providing insights into clinic preparations for gene therapy.
- **LFB Biomedicaments** looked at redefining treatment options for haemophilia patients with inhibitors.
- **Takeda** focused on advancements in von Willebrand disease care, emphasising how genetic insights enhance early diagnosis.
- **Novo Nordisk** reviewed innovations in non-factor therapies for haemophilia and the role that these treatments play in modern haemophilia care.
- **Pfizer** explored practical considerations in haemophilia care, especially in the new era of marstacimab therapy.
- **BioMarin** discussed emerging treatment strategies in haemophilia care, namely valoctocogene roxaparvovec.
- **Sobi** explored the impact of normalised haemostasis in people with haemophilia A across their lives, using clinical data and real-world experiences.
- **Octapharma** highlighted the need for equity in treating severe von Willebrand disease and severe haemophilia A.
- **Kedrion** focused on hereditary factor X deficiency, addressing disease management and clinical challenges.

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DAY 3

The third day of EAHAD 2025 was filled with a diverse range of sessions, highlighting milestones such as the 100th anniversary of the discovery of von Willebrand disease and the presentation of the prestigious EAHAD Lifetime Achievement Awards.

Modern Era of Diagnosis and Treatment

THIS WAS an insightful session featuring three talks; firstly, Wolfram Ruf, Johannes Gutenberg University Mainz, Germany, addressed novel concepts to know in haemostasis; followed by Rosanna Asselta, Humanitas University, Milan, Italy, who looked at the innovative use of next generation sequencing in bleeding disorders; and finally, Sergio Mascetti, Department of Computer Science, Università degli Studi di Milano, Italy, highlighted the potential of AI in improving early diagnosis in bleeding disorders.

Coagulation revisited

Within his talk, Wolfram Ruf, drew on several insightful papers, including a 2024 paper by Johannes Taler and colleagues.[1] Bodily fluids, such as saliva, contain extracellular vesicles that can stimulate blood coagulation by exposing extrinsic tenase complexes of tissue factor and activated factor VII (FVIIa). In this study, researchers demonstrated that the saliva of patients with severe haemophilia A, that is people with FVIII deficiency, still contain these extracellular vesicles. Therefore, extracting the vesicles from the blood and adding them to the FVIII-deficient blood of haemophilia A patients, resulted in salivary-induced blood coagulation. In people with haemophilia A, the deficiency in FVIII leads to a deficiency of intrinsic tenase complexes (FVIIIa/FIXa) and thus reduction in FXa activation and clot formation. This study was significant as it demonstrated a way to bypass the limiting FVIII factor and still generate FX. The authors were then able to

reproduce similar results in patients with FVII deficiency; where introduction of saliva EVs from the patients induced FXa generation.[1]

> **This study was significant as it demonstrated a way to bypass the limiting FVIII factor and still generate FX**

Citing a 2013 study by Schuijt TJ et al.,[2] in which a recombinant tick salivary protein (TIX-5) was added to inhibit FXa-mediated activation of FV, it was concluded that FX plays a pivotal role in the generation of the first amount of activated FVa, which then binds with FXa to produce thrombin. In a follow-up study from 2017, Ruf and colleagues found that the extrinsic complex, TF-FVIIa, not only generates FIXa but also the first amounts of FXa.[3] Additionally, they concluded that by inhibiting the naturally occurring TPFI inhibitory pathway you are able to generate more FXa, which in combination with FVa in turn generates more thrombin. Overall, this research deepens our understanding of the coagulation cascade pathway, and provides possible therapeutic uses in haemophilia, where patients are deficient in essential clotting factors such as FVIII. Finally, he explained that glycoprotein V (GPV) cleavage is required for limiting fibrin formation, and that GPV supresses GPIbα -thrombin dependent platelet activation, as demonstrated in a 2023 publication.[4] GPV is a surface membrane protein found on the surface of platelets, that helps adhere to exposed collagen in the initial stages of haemostasis.

Next generation sequencing in bleeding disorders

Asselta took the stage to discuss the role of next-generation sequencing in bleeding disorders. Bleeding disorders are a group of conditions resulting from an impairment of the clotting process, associated either with defects in coagulation factors or platelets, both of which can be inherited or acquired. She highlighted the incidence versatility of bleeding disorders. The most common bleeding disorders include Von Willebrand disease, haemophilia A (which is a deficiency of FVIII), and haemophilia B (a deficiency of FIX). Less common bleeding disorders encompass fibrinogen deficiency, prothrombin deficiency, and deficiencies of various clotting factors, including FV, FVII, FX, FXI, and FXIII. Platelet disorders also fall under this category. Extremely rare conditions include α2-antiplasmin deficiency, α1-antitrypsin deficiency, and combined factor deficiencies.

As explained by Asselta, genetic diagnosis is traditionally achieved through PCR amplification of the exons and splice sites followed by Sanger sequencing. Additionally, multiplex ligation-dependent probe amplification (MLPA) analysis is a genetic technique that can be used to identify mutations or structural variations in the genes associated with bleeding disorders. Asselta highlighted the advantages and disadvantages of traditional diagnostic approaches. While these methods are easy to use and standardised, they are also time-consuming, costly, and, by design, fail to provide insights into intronic or regulatory regions.

Next-generation sequencing (NGS) is a cutting-edge technology that rapidly and accurately determines the sequence of DNA or RNA, providing valuable insights into genetic variation and its role in diseases and other biological processes. This technique has revolutionised genomics by enabling the sequencing of hundreds of human genomes in a single run. In stark contrast to the original Human Genome Project, which took from 1990–2003 and cost approximately 2.7 billion USD, NGS today can sequence genomes in just a few days at a fraction of the cost, typically between $500–700 USD.

Asselta summarised the evolution of genetic techniques used to study disorders, specifically bleeding disorders. She began by discussing the linkage analysis approach, popular in the late 20th century, which involved genotyping large families and calculating LOD scores to identify genomic regions linked to diseases. She highlighted the success of this method in identifying genes responsible for haemophilia. Moving

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> **The most common bleeding disorders include Von Willebrand disease, haemophilia A (which is a deficiency of FVIII), and haemophilia B (a deficiency of FIX)**

to more modern techniques, she described genome-wide association studies (GWAS), which use SNPs to identify genetic markers associated with bleeding phenotypes. Asselta also introduced polygenic risk scores (PRS), which estimate an individual's likelihood of developing a disorder based on numerous genetic variants.

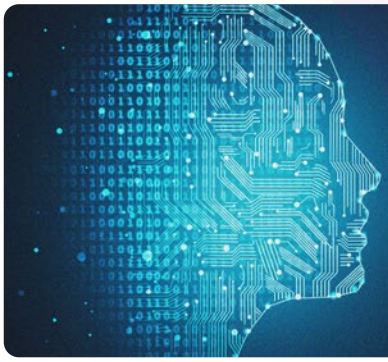
The presentation then focused on the use of whole-exome sequencing, which allows for the sequencing of all protein-coding genes. Asselta also discussed unexplained bleeding disorders (UBD), suggesting that they may have a polygenic or non-coding genetic basis. Finally, she shared her lab's research on UBDs, using multi-omics approaches, like whole genome sequencing and methylation analysis, to investigate potential genetic causes. She concluded by emphasising the importance of integrating data and AI in advancing genetic research.

How can AI improve early diagnosis in bleeding disorders?

Mascetti introduced a groundbreaking telemedicine solution aimed at enhancing the self-management of patients with haemophilia. The solution, called GAJA, is a tablet application paired with a portable ultrasound probe that allows patients to self-acquire ultrasound images for remote evaluation. It provides step-by-step guidance throughout the imaging process, helping patients properly position the probe and apply ultrasound gel. The system incorporates AI to ensure that images are taken correctly by comparing the real-time positioning of key anatomical landmarks to a set of reference images acquired by the medical practitioner during a brief in-person training session. This approach is designed to address the challenges of patient training, which is often long and prone to patient forgetfulness.

Mascetti also discussed the CADET system; a web application designed to assist medical practitioners in evaluating these remotely acquired images. The CADET system leverages AI-based tools to automatically order images by suitability, suggest diagnoses, and generate semi-automatic medical reports to streamline the evaluation process. The system's deep learning algorithms offer suggestions based on image analysis, including detecting joint effusion levels, which aids in quicker and more accurate diagnoses.

The GAJA and CADET systems have already demonstrated their effectiveness for knee joint assessments, with plans to expand to other joints, such as the elbow and ankle. Future work will focus on further refining the AI models, improving image acquisition and annotation standards, and evaluating the impact of these systems in longitudinal studies.



> **The GAJA and CADET systems have already demonstrated their effectiveness for knee joint assessments, with plans to expand to other joints, such as the elbow and ankle**

A Century of Von Willebrand Disease

VON WILLEBRAND disease (VWD) is a type of clotting disorder characterised by the deficiency or defect in von Willebrand factor (VWF), a protein involved in the aggregation of platelets and thus blood clot formation.

First discovered by Erik von Willebrand in 1924, the disease has now reached its centenary anniversary and was spotlighted at the EAHAD 2025 meeting.

Diagnosis and optimal treatment

Giancarlo Castaman, Careggi University Hospital, Florence, Italy, opened this session providing an informative summary of the disease diagnosis and optimal treatment. VWF plays a significant role in haemostasis; it mediates platelet adhesion to the exposed sub-endothelium via collagen and GLP1 interactions, and as a carrier protein of FVIII, VWF also protects FVIII from rapid proteolysis. There are three main types of the disease: Type 1, the most common and mildest form, in which the patient produces little VWF; Type 2, which is divided in different subtypes (2A,2B,2M,2N) and is characterised by a defect in the protein; and Type 3, which the rarest and most severe. People with Type 3 produce no VWF.

Looking to the diagnosis, Castaman highlighted the ASH ISTH NFH WFH 2021 guidelines, created to provide a standardised approach in the diagnosis of the disease. In summary, the guidelines recommend for an initial screening test using the Bleeding Assessment tool (BAT), followed by laboratory tests with distinct cut-offs for Type 1 and 2 VD, as well as the use of genetic testing versus phenotypic assays for types for distinguishing between the subtypes of Type 2. He highlighted the diverse array of phenotypic tests available for VD diagnosis, such as VWF:Ag, (antigen test), VWF:Act (testing functional activity of the factor), and VWF:CB (collagen binding assay) to assess the adhesion capabilities of VWF, or PFA-100 to assess platelet function. Moving from diagnosis to treatment, the key determinants of treatment efficacy for VWD is FVIII levels, which are in turn effected by the deficiency of VWF, and the function of VWF itself. The current main treatment strategies include desmopressin, VMF concentrates or tranexamic acid.

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Demographics and epidemiology of VWD using big data

Omid Seidizadeh, University of Milan, Italy, subsequently took the stage to provide a comprehensive overview of the epidemiology of VWD. Understanding the prevalence of a disease is incredibly important, as it can impact research focus, resource allocation, healthcare planning, and public health initiatives. There are several traditional methods of determining disease prevalence, such as national/international registries, population surveys or screening programs. However, as highlighted by Seidizadeh, VWD is a complex disease, and these traditional methods carry risks of underreporting, sampling bias and data inaccuracy. Alternatively, genetic prevalence, defined as 'the estimated proportion of a population that has a causal genotype for a genetic disorder', allows for a larger population scale analysed across diverse ethnicities and more precise estimation.

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It was estimated that the final global prevalence of VWD in 1,000 individuals was 74 for Type 1, three for Type 2A, three for Type 2B, six for Type 2M, 0.31 for Type 2N, and 0.7 for Type 3.

So how is VMD inherited? For Types 1, 2A, 2B, and 2M, it follows autosomal dominant inheritance, meaning a person needs only one copy of the mutated gene to express the disease phenotype, whilst Type 2N and Type 3 follow autosomal recessive inheritance, meaning both copies of the mutated gene must be inherited for expression. In 2023, Seidizadeh co-authored a paper where exome and genome data, gathered by the genome Aggregation Database (gnomAD) were analysed and global prevalence of both dominant and recessive forms of VMW were estimated.[5] Based on Seidizadeh's research, it was estimated that the final global prevalence of VWD in 1,000 individuals was 74 for Type 1, three for Type 2A, three for Type 2B, six for Type 2M, 0.31 for Type 2N, and 0.7 for Type 3.[5]

Novel therapies for VWD

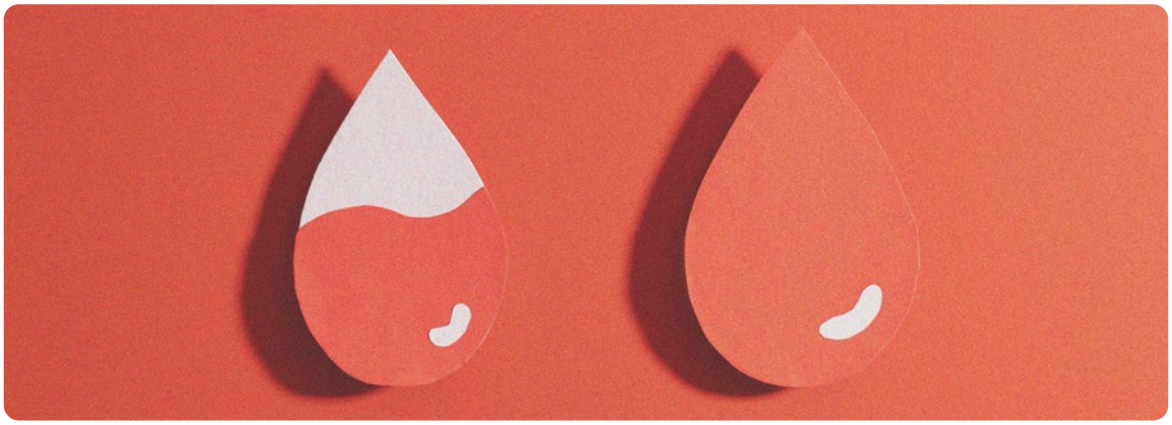
To conclude the session, Jeroen Eikenboom, Leiden University, the Netherlands, discussed future therapies for VWD, emphasising the limitations of current treatments. Desmopressin, commonly used to treat bleeding, is an analogue of vasopressin that stimulates the release of endogenous FVIII and VWF. In people with Type 2 VWD, where VWF is abnormal, desmopressin only increases the production of faulty protein, limiting its effectiveness. Alternatively, exogenous VWF concentrate can be used for all VWD patients, but it requires frequent injections, has a short half-life, and carries the risk of alloantibody formation.

So, what new treatment approaches are on the horizon for VWD? Firstly, new treatments are looking to tackle the root cause of the disease by increasing the VWF levels directly. BT200, also known as rondoraptivon pegol, for example, is a pegylated aptamer that binds to the A1 domain of VWF. Eikenboom also drew on the nanobody KB-V13A12, a bi-functional molecule that binds both VWF and human albumin, effectively prolonging the half-life of endogenous VWF in circulation. An alternative to targeting VWF directly, is to target FVIII levels, as these are affected in the disease. For instance, emicizumab is a bispecific antibody that binds both activated FIX and FX, helping to facilitate coagulation. Elfanescotocog alfa is also currently under investigation in a Phase I open label study to assess the pharmacokinetics and safety and tolerability in adults with Type 2N and Type 3 VWD.[6]

RNA interference and gene editing is also an incredibly exciting area of research for treating VWD, by targeting the mutant gene itself and silencing the mutant VMF alleles. One promising method involved silencing the mutant allele responsible for producing faulty VWF. The research explored the use of small interfering RNAs (siRNA) to degrade mutant VWF messenger RNA and reduce abnormal protein production. This targeted approach improved VWF's multimer formation, particularly in Type 2A and 2B patients, where mutations caused the protein to be retained in the endoplasmic reticulum.

Current and Rapid Developments Around Novel Therapies

IN A collaboration between the EAHAD and the International Society on Thrombosis and Haemostasis (ISTH), this session featured two renowned experts: Peter Lenting, Director of Research Inserm, Le Kremlin-Bicentre, France, who discussed the opportunities and challenges of novel therapies; and Armando Tripodi, Hemophilia and Thrombosis Center, IRCCS Ca' Granda Maggiore Hospital Foundation in Milan, Italy, who explored advancements in monitoring haemophilia treatments.



Expanding haemophilia therapies to other bleeding disorders

Lenting started by introducing the different therapeutic options for patients with haemophilia A and B, like the traditional replacement therapies, bypassing agents, bispecific antibodies, monoclonal antibodies, siRNA, and gene therapy.

Lenting described the need to shift the focus in haemophilia treatment to consider the different patient groups affected by other bleeding disorders, such as VWD, women with haemophilia, and deficiencies in FV, FII, FVII, and FX. He explained how treatments for these conditions could be applied beyond haemophilia. Providing two examples, Lenting first discussed VWD Type 3, where it remains unclear to what extent VWF and FVIII each contribute to the bleeding tendency in patients with a combined deficiency of both proteins. This raised the question of whether improving FVIII-like activity could increase the haemostatic potential of a patient with VWD. Lenting referenced the current literature, noting a few studies on patients with VWD Type 3 who also had anti-VWF antibodies. In these cases, VWF concentrate, and surgical interventions were ineffective, but continuous FVIII infusions showed good haemostatic efficiency. Lenting concluded that correcting FVIII levels in VWD Type 3 improved the haemostatic potential, though the short half-life of rFVIII made it unsuitable for prophylactic treatment.

> **This raised the question of whether improving FVIII-like activity could increase the haemostatic potential of a patient with VWD**

Lenting then highlighted the potential of non-factor therapies in addressing these challenges. However, he stressed that while these therapies are effective for FVIII deficiency, they are not suitable for VWF deficiency. Nonetheless, they could be used regardless of whether the patient has VWF and/or FVIII deficiencies. Two examples of such treatments were emicizumab and ETX-148. Lenting explained that emicizumab could significantly reduce bleeding episodes by correcting FVIII deficiencies, even without addressing the underlying VWF deficiency. Meanwhile, ETX-148, an siRNA targeting protein Z-dependent protease inhibitor (ZPI), demonstrated enhanced

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> **Tripodi advocated for using chromogenic assays with bovine reagents, which are insensitive to emicizumab's effects, allowing accurate measurement of endogenous or infused FVIII levels**

thrombin generation and reduced blood loss in mouse models, making it a promising adjunct therapy for VWD.

Despite the promising data, Lenting acknowledged several challenges. One major concern was therapeutic balance, as there was a risk that repurposed therapies could excessively increase thrombin generation, leading to thrombosis. Additionally, he pointed out that most supporting data for these novel therapies came from animal studies, which may not fully replicate human coagulation processes. Lastly, Lenting highlighted the significant financial and regulatory hurdles in bringing new treatments for rare disorders to market.

Innovations in monitoring haemophilia treatments

In the following session, Tripodi explored advancements in monitoring haemophilia treatments. Tripodi began by highlighting the disparities between different assays used to measure FVIII and FIX activities, particularly for long-acting concentrates. He explained that these inconsistencies arise from differences in how modified and native coagulation factors are recognised by these assays. Long-acting factors being modified to extend half-life do not always behave identically to native factors, leading to variance in assay results.
Tripodi also discussed the challenges in monitoring non-replacement therapies like emicizumab, a bispecific antibody that mimics FVIII, and fitusiran, an siRNA targeting antithrombin. Traditional APTT and one-stage clotting assays proved ineffective, often producing misleading results. Even low concentrations of emicizumab can normalise APTT, masking underlying deficiencies. Similarly, one-stage assays produced paradoxically highFVIII activity results, and Tripodi advised against using these for emicizumab monitoring.

To address these issues, Tripodi advocated for using chromogenic assays with bovine reagents, which are insensitive to emicizumab's effects, allowing accurate measurement of endogenous or infused FVIII levels. Additionally, he emphasised the importance of measuring emicizumab concentration directly using certified standards for reliable monitoring.

For fitusiran, which enhances thrombin generation by reducing antithrombin, the primary challenge lies in the lack of sensitive assays to measure low levels of antithrombin effectively. Current commercial kits, designed for congenital antithrombin deficiencies, are inadequate for monitoring fitusiran-treated patients. Tripodi highlighted the need for the development of new, more sensitive assays to accurately assess residual antithrombin levels and ensure safe and effective dosing.

Awards Session

EAHAD Lifetime Achievement Award
Monica Gobbi
Wedding & Event Planner, Monica Gobbi D'Alò , Italy

EAHAD Lifetime Achievement Award
David Lillicrap
Queen's University, Canada

EAHAD Honorary Membership
Mike Makris
University of Sheffield, UK

Poster awards

Top AHP Poster Award
Nuria Caballero
Hematology Department, Hospital Sant Joan de Déu, Barcelona, Spain
Poster title: *'Nurse-led education for female hemophilia carriers throughout their lives'*

3rd Poster Prize
Alessandra Loureiro Prezotti
HEMOES, Vitoria, Brazil
Poster title: *'Reclassification of hemophilia carriers and analysis of their hemorrhagic phenotype: experience from a center in Brazil'*

2nd Poster Prize
Roberta Gualtierotti
Angelo Bianchi Bonomi Haemophilia and Thrombosis Center, Milan, Italy
Poster title: *'Circulating miRNA Landscape in Hemophilic Arthropathy: Distinguishing Disease Conditions and Identifying Potential Biomarkers'*

1st Poster Prize
Claire Kelly
National Coagulation Center, St. James Hospital, Dublin, Ireland
Poster title: *'Spinal Stenosis: An Emerging Complication of Aging in People with Haemophilia'*

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DAY 4

The final day of the EAHAD 2025 Annual Congress was truly exceptional, featuring a dynamic SLAM session showcasing cutting-edge research in the field, followed by a discussion on EAHAD's ongoing activities. The day also included an insightful session on the ageing population with rare bleeding disorders, as well as a presentation of the latest clinical trial results.

Ageing Population with Rare Bleeding Disorders

AGAINST a backdrop of an ageing population, EAHAD 2025 put the spotlight on managing rare bleeding disorders in older persons in a session chaired by EAHAD Honorary Member, Pier Mannucio Mannucci, and EAHAD Committee Member, Fariba Baghaei Sahlgrenska University Hospital, Gothenburg, Sweden. In the era of modern medicine, where people are living longer with disease, these insights are crucial for empowering healthcare professionals to optimise care for this patient cohort.

Defining frailty

The session started with a presentation by William McKeown, Antrim Area Hospital, Northern Ireland, who discussed frailty in people with haemophilia. After explaining that frailty is an age-associated condition, he emphasised that secondary to effective therapeutic interventions for haemophilia, physicians will see an increasing number of older patients with this condition.

Frailty is a state of increased vulnerability due to accumulation of deficits which lead to a poor resolution of homeostasis after a stress event. The impact of a stressor is much more significant in those with frailty and recovery may take longer and/or the individual may not recover back to their original baseline. Spotlighting research by Sangha et al.[7] that looked at frailty in the haemophilia population, McKeown noted the study found that frailty levels were higher, and also more likely to be of greater severity in these individuals, with a frailty incidence of 28.6% in the study population compared to just 10% in the general population.[7]

Frailty syndromes

Frailty syndromes, defined as the presence of ≥1 of falls, immobility, delirium, incontinence, or susceptibility to medication side effects, should raise suspicion for frailty, according to McKeown. He noted

The prevalence of falls, cognitive impairment, and polypharmacy in older people with haemophilia are approximately **32.4%**, **73.0%**, and **40.8%**, respectively.

that whilst data on these syndromes are limited, best estimates show that the prevalence of falls, cognitive impairment, and polypharmacy in older people with haemophilia are approximately 32.4%, 73.0%, and 40.8%, respectively. All of these have an impact on loss of dependence and mental health.

In terms of a solution, the gold standard intervention for frailty is the comprehensive geriatric assessment (CGA), which includes a multidisciplinary team (MDT) assessment to identify problems and propose solutions.

World Federation of Hemophilia (WFH) guidelines recommend coordinated delivery of comprehensive care by an MDT with expertise and experience in haemophilia. McKeown made recommendations that pharmacists, dieticians, speech and language therapists, occupational therapists, audiologists, and opticians should also be included in this MDT. He stated that the haemophilia MDT for older people should be expanded urgently to help meet their needs.

Venous thrombosis in haemophilia

Whilst the concept may seem paradoxical, Cihan Ay, Medical University of Vienna, Austria, spoke on management of venous thrombosis in older people with haemophilia.

Similarly to those without haemophilia, major orthopaedic surgery is a risk factor for venous thromboembolism in those with haemophilia. Ay also noted that venous thromboembolism can potentially occur during factor replacement therapy, and with non-factor therapies and after gene therapy. Furthermore, thrombosis risk increases significantly with age, and Ay drew attention to evidence from a small study which showed those with haemophilia exhibit an accelerated biological ageing.

Whilst there is limited evidence, Ay spotlighted a recent joint EHA-ISTH-EAHAD-ESO initiative, which suggests treating venous thromboembolism in haemophilia with a limited duration of anticoagulation, maintaining trough factor levels >20 IU/dL, and eliminating the potential trigger.

He stressed that approaches should be individualised, and clinicians should look to balance the risk of VTE progression/recurrence without anticoagulation against the risk of bleeding whilst receiving anticoagulation and the severity of haemophilia. He noted that for those with haemophilia and venous thromboembolism, direct oral anticoagulants are recommended over vitamin K antagonists. However, Ay recommended considering an alternative approach of full dose heparin whilst maintaining a FVIII/FIX trough level >20 IU/dL for 5–7 days, and if no bleeding, then switching to a direct oral anticoagulant at a standard dose.

> **“The important role haemophilia centres and national member organisations have in supporting the ageing community to improve their quality of life”**

Psychosocial aspects of ageing with haemophilia

Christina Burgess, Haemophilia and Bleeding Disorders Counselling Association, UK, closed the session by discussing the psychosocial aspects ageing with haemophilia. Emphasising how haemophilia impacts quality of life as we age, Burgess highlighted severe joint damage, long-term chronic pain, HIV and/Hepatitis C infection, unresolved psychological trauma, missed educational or employment opportunities due to long hospital stays, and comorbidities as key factors influencing psychosocial wellbeing. She concluded the important role haemophilia centres and national member organisations have in supporting the ageing community to improve their quality of life.

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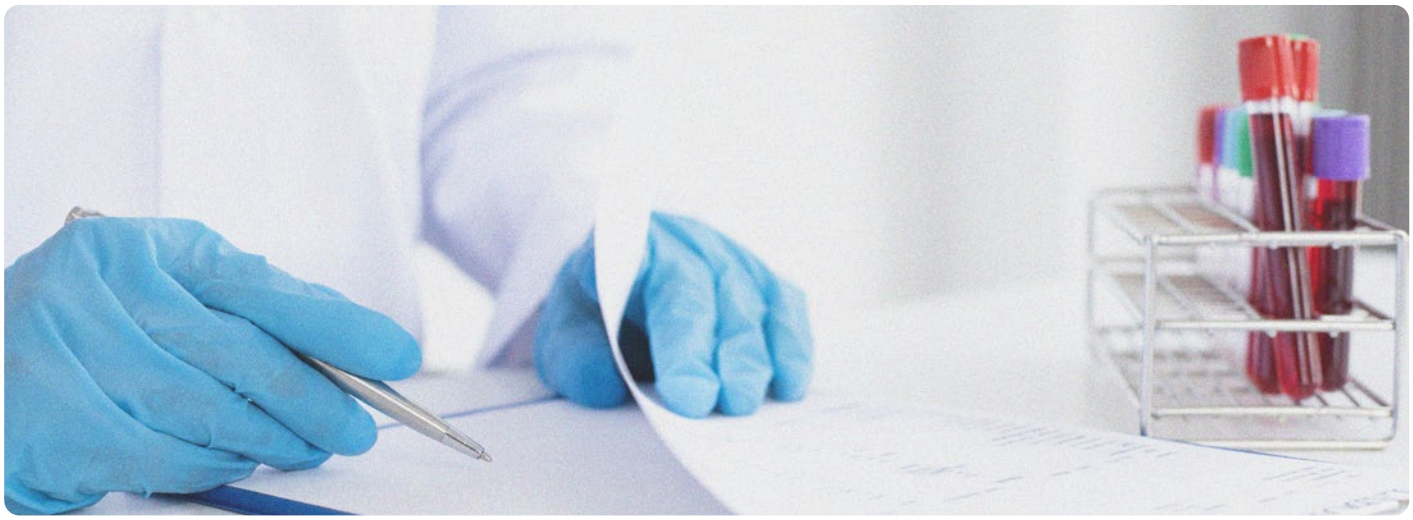
The Latest Clinical Trial Updates



A HIGHLYANTICIPATED session covering recent data from six clinical trials took place at EAHAD 2025, and was chaired by the Congress President, Flora Peyvandi, and Executive Committee President, Jan Blatny. These presentations provided experts with key updates into long-term safety and efficacy data for therapeutic agents used in bleeding disorders, as well as insights into new interventions currently in early-phase trials.

Trial updates for haemophilia

Mike Makris, University of Sheffield, UK presented the 15-year European Haemophilia Surveillance System (EUHASS) data on thrombotic rates in individuals with bleeding disorders treated with bispecific antibody or concentrate.

Diving into the data, Makris compared the thrombosis rates per 1,000 treatment years for individual product classes and different bleeding disorders. The thrombosis rate per 1,000 treatment years for those with haemophilia A treated with plasma FVIIII/VWF was 1.19 (95% CI: 0.90–1.54), compared with a rate of 0.70 (95% CI: 0.54–0.90) for those who received standard half-life recombinant FVIII, and a rate of 0.50 (95% CI: 0.20–1.02) for those who received extended half-life recombinant FVIII.

For those with haemophilia B, the thrombosis rates per 1,000 treatment years were 0.98 (95% CI: 0.39–2.01), 0.73 (95% CI: 0.35–1.35), and 0.52 (95% CI: 0.11–1.52) for those treated with plasma derived FIX, standard half-life recombinant FIX, and extended half-life recombinant FIX, respectively. Makris also drew attention to the fact that risk of thrombosis may be higher when treating patients with FXIII deficiency, FXI deficiency, or afibrogenemia.

Following this, Lynn Malec, Versiti Blood Research Institute, Wisconsin; and Medical College of Wisconsin, USA, presented 2-year data on the outcomes of once-weekly efanesoctocog alfa prophylaxis in children with severe haemophilia A, as part of a second interim analysis of the XTEND-ed Phase III study. The primary endpoint of this study is the occurrence of inhibitor development.

After covering the trial design and safety data, Malec concluded that FVIII inhibitors did not develop over the course of the extension study, mean annualised bleed rates remained low at <1 with median annualised bleed rates of 0, the percentage of patients with zero bleeding episodes remained high, and that the

2-year results have shown that once-weekly efanesoctocog alfa in previously treated children with severe haemophilia A continues to be well tolerated and effective at bleed protection.

Davide Matino, McMaster University, Ontario, Canada, presented the long-term efficacy data for marstacimab in adults and adolescents with severe haemophilia A or B without inhibitors who completed the BASIS trial. He summarised the study design, marstacimab exposure in both BASIS and the open-label extension, and safety data.

> **HMB-001 showed dose-proportionate pharmacodynamics and pharmacokinetics with peak FVIIa accumulation 4–8 days post-dose in part A and B of the study**

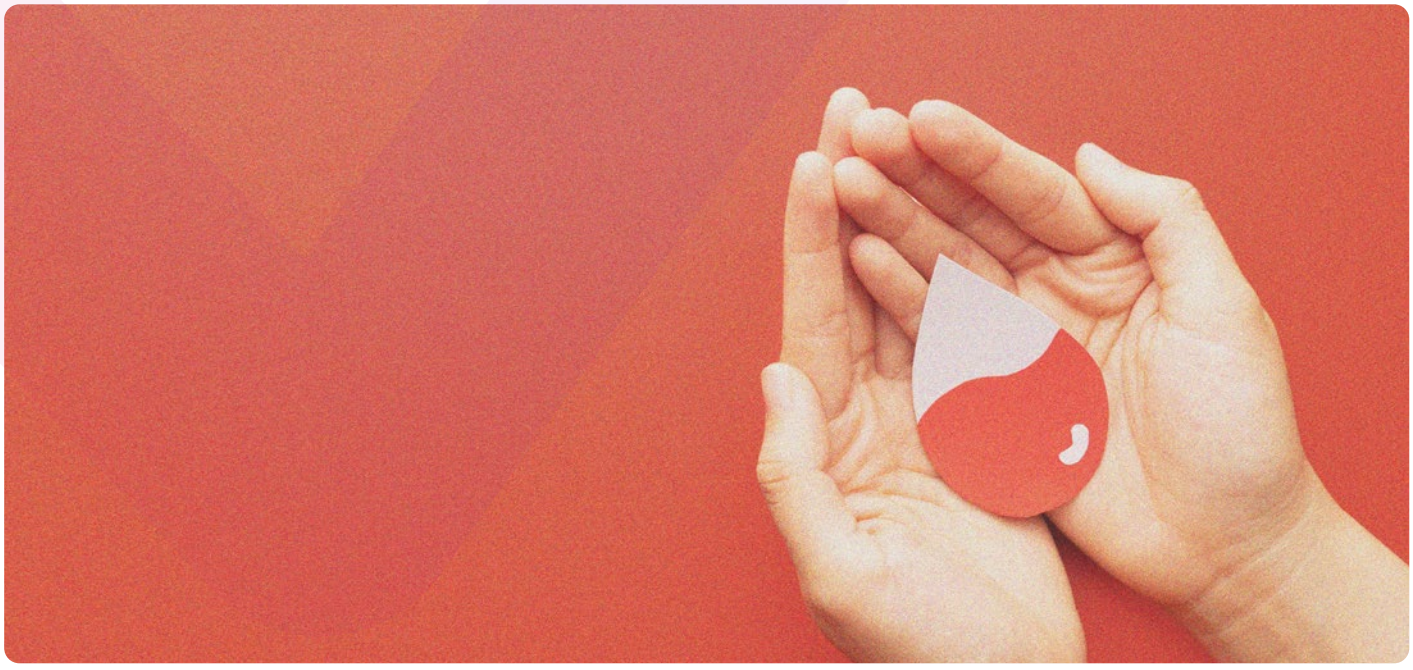
From the trial findings, Matino reported that once-weekly, subcutaneous marstacimab demonstrated sustained/improved efficacy for treated and total annualised bleeding rates in the patient cohort, without inhibitors. This was found to be consistent in those who received on-demand or routine prophylaxis factor replacement therapy at baseline. Matino concluded that overall, marstacimab was safe and well tolerated.

Steven Pipe, University of Michigan, Ann Arbor, USA, discussed long-term safety and efficacy data of etranacogene dezaparvovec from the Phase III HOPE-B trial in adult males with severe/moderately severe haemophilia B. The trial looked at durability of FIX expression, bleed data, exogenous FIX consumption, and safety over 4 years after treatment.

After summarising key components of the trial design, participant demographics, annualised bleeding rates, endogenous FIX levels over time, exogenous FIX use during the study period, and safety data, Pipe concluded that treatment-related adverse events were almost absent after the first 6 months following gene therapy, FIX replacement use decreased from baseline by 95%, that mean FIX activity levels were stable and in the near-normal range over the duration of follow-up, and that etranacogene dezaparvovec resulted in significant annualised bleeding rate reduction across the 4-year follow-up compared with the lead-in FIX prophylaxis period.

Trial updates for glanzmann thromboasthenia

Suthesh Sivapalaratnam, Queen Mary University of London; and Barts Health NHS Trust, UK, presented the interim analysis of



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a Phase I/II study on safety and efficacy of HMB-001 as a prophylactic treatment for Glanzmann Thromboasthenia. He explained that there are currently no approved prophylactic therapies for this rare genetic bleeding disorder.

> **HMB-001 showed dose-proportionate pharmacodynamics and pharmacokinetics with peak FVIIa accumulation 4–8 days post-dose in part A and B of the study**

Sivapalaratnam explored the mechanism of HMB-001 bispecific antibody and explained the three study parts. He went on to discuss patient demographics and safety data, before concluding that HMB-001 showed dose-proportionate pharmacodynamics and pharmacokinetics with peak FVIIa accumulation 4–8 days post-dose in part A and B of the study, and that at lower doses there were no thromboses or serious adverse events. However, he did highlight one serious adverse event and D-dimer increase at a higher dose.

To conclude his presentation, Sivapalaratnam explained that there were clinically meaningful reductions in treated bleeds across all dose levels and that the phase II study is ongoing to further investigate the lower doses to confirm their safety and efficacy as a prophylactic for individuals with this condition.

Trial updates for von willebrand disease

Carolyn M. Millar from Imperial College London and Imperial College Healthcare NHS Trust, UK, presented the findings from a Phase I study of VGA039 in individuals with von Willebrand disease (VWD). VWD is a genetic bleeding disorder caused by a deficiency or dysfunction of VWF, essential for blood clotting. The Phase I study aimed to evaluate the safety, tolerability, and pharmacokinetics of VGA039, a novel therapeutic candidate designed to address this condition.

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