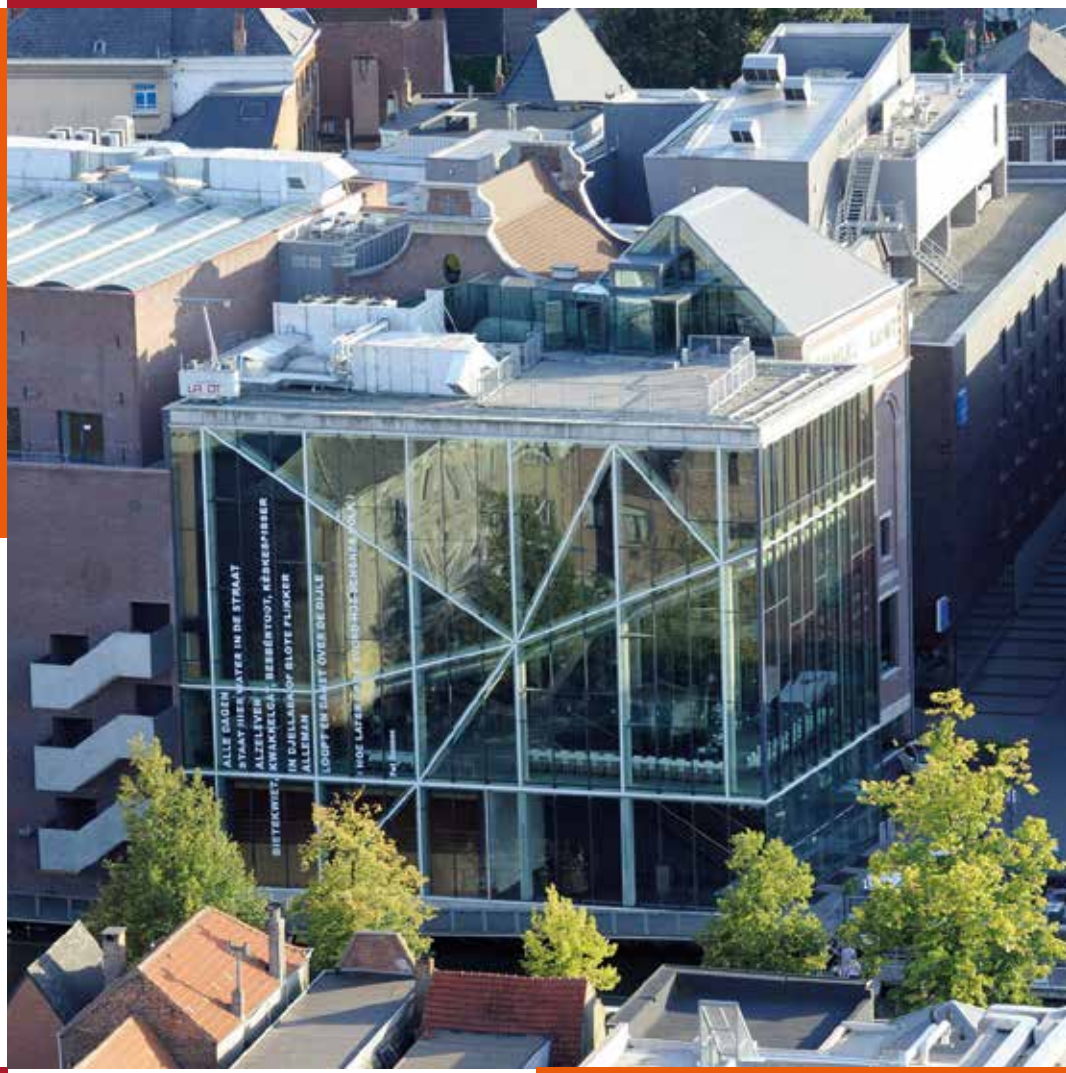
BSTH

Belgian Society on Thrombosis and Haemostasis

32nd ANNUAL MEETING

27-28 NOVEMBER 2025

LAMOT MECHELEN BELGIUM



PROGRAM & **ABSTRACTS**

WWW.BSTH2025.ORG



02

WELCOME TO THE 32ND ANNUAL MEETING

Dear BSTH Members and Participants,

It is my great pleasure to welcome you to the 32nd Annual Meeting of the Belgian Society on Thrombosis and Haemostasis (BSTH). Once again, we gather at the Lamot Congress Center in Mechelen—our trusted host venue for many years.

Each edition of this meeting reflects the enthusiasm and engagement within our community. We are delighted to welcome participants from university hospitals, research institutes, clinical laboratories, and organizations active in the domains of cardiovascular diseases, thrombosis, haemophilia, and other bleeding disorders.

This year's scientific program has been thoughtfully organized by Kristel Vandenbosch, Cécile Oury, and Pierre Peeters, all affiliated with the Université/CHU de Liège. Their outstanding efforts have resulted in a rich and diverse agenda. The state-of-the-art lectures will explore antithrombotics in special situations and key drivers in thrombosis. The educational sessions focus on new therapies in von Willebrand Disease and platelet function.

In keeping with BSTH's mission to foster excellence in basic, laboratory, and clinical research, ten promising young scientists have been invited to present their work. Among them, two will receive the Paul Capel Prize for the best oral presentations. Additionally, one researcher will be honored with the CSL Behring Encouragement Grant to support their research in thrombosis and haemostasis. We also invite you to participate in the poster walks and attend the satellite symposia organized by Novo Nordisk, Pfizer, and Octapharma, which will highlight recent advances in their respective fields.

We are especially honored to welcome Emeritus Professor Anne Demulder, who will deliver the Gaston Baele Lecture in tribute to a remarkable mentor and great man.



Our heartfelt thanks go to all participants, speakers, and sponsors for their continued support in making BSTH a vibrant society at the forefront of scientific and clinical innovation.

Beyond the scientific sessions, I encourage you to take time to connect with colleagues, engage with industry partners, and enjoy the social program prepared for this occasion.

I wish you an inspiring and enjoyable 32nd Annual Meeting of the BSTH.

Warm regards,
Katrien Devreese
President of BSTH

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Sponsored Satellite Symposia

- Novo Nordisk

- Pfizer

- Octopharma

Abstracts of Oral presentations

- Basic Science

- Clinical / Laboratory

Abstracts of Poster presentations

List of sponsors



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GENERAL INFO

WWW.BSTH2025.ORG

CONGRESS MANAGEMENT

Congress care
PO Box 440
5201 AK ‘s-Hertogenbosch
The Netherlands
+31 (0)73 690 14 15
www.congresscare.com



DATES

27-28 NOVEMBER 2025

VENUE

LAMOT congres- & erfgoedcentrum
Van Beethovenstraat 8 /10
2800 Mechelen, Belgium
015 294900

05

BSTH BOARD 2025

THE PRESENT MEMBERS OF THE BSTH BOARD ARE:

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PROGRAM THURSDAY 27 NOVEMBER

08:30 **REGISTRATION, COFFEE, NETWORKING**

09:15 **WELCOME**
Katrien Devreese, BSTH President

09:30 **EDUCATIONAL I**
Chairs: Kristel Vandebosch & Séverine De Bruijn

09:30 **New therapies and monitoring in von Willebrand disease**
Jeroen Eikenboom

10:15 **SPONSORED SATELLITE SYMPOSIUM I – NOVO NORDISK**
Transforming Conversations: Evolving Hemophilia Treatment and Its Influence on Patient–Physician Shared Decision-Making
Prof. Cedric Hermans

11:15 **COFFEE BREAK**

11:45 **ORAL PRESENTATIONS BASIC SCIENCE**
Chairs: Sandrine Horman & Jonathan Douxfils

11:45 O01 **Distinct open ADAMTS13 in acute and subclinical immune-mediated thrombotic thrombocytopenic purpura**
Quintijn Bonnez

11:57 O02 **Targeting antigen-specific B cells in immune mediated thrombotic thrombocytopenic purpura using modular CAR T cells -**
Sara Rovira Puig

12:09 O03 **In vitro validation of the novel anti-CD19 and anti-CD38 UniCAR T cell therapy for refractory iTTP patients**
Lisa Vermeersch

12:21 O04 **Enterococcus faecalis-induced infective endocarditis: first mechanistic insights and role of ticagrelor**
Minoo Jafarzadeh

12:33 O05 **Mechanistic study of the antivirulence activity of ticagrelor at antiplatelet dosage**
Florence Putters

12:45 **LUNCH BREAK AND POSTER WALK**

13:45 **BSTH GENERAL ASSEMBLY**
Exclusively for members

14:15 **STATE OF THE ART I – ANTITHROMBOTICS IN SPECIAL SITUATIONS**
Chairs: Peter Verhamme & Laurence Rozen

14:15 **Thrombosis and antithrombotics needs in bleeding disorders**
Roger Schutgens

14:45 **Antithrombotics management after TAVI**
Patrizio Lancellotti

15:15 **SPONSORED SATELLITE SYMPOSIUM II – PFIZER**
Rebalancing hemostasis with anti-TFPI treatments
Dr Quentin Van Thillo
Dr Susan Halimeh

16:15 **COFFEE BREAK**

16:45 **PROFESSOR GASTON BAELE MEMORIAL LECTURE**
Chair: Katrien Devreese

From Thrombosis to Thrombin: A Journey of Mentorship, Memory, and Meaning
Anne Demulder

17:30 **PAUL CAPEL PRIZE – BASIC SCIENCE**

17:455 **CLOSURE**

19:00 **DINNER**
Hotel Van der Valk Mechelen, Rode Kruisplein 1-4, Mechelen
Cold and warm buffet followed by a small party with a DJ to celebrate together!



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PROGRAM FRIDAY 28 NOVEMBER

08:30 **REGISTRATION, COFFEE & NETWORKING**

09:00 **STATE OF THE ART II – THROMBOSIS AND BEYOND**
Chairs: Simon De Meyer & Quintijn Bonnez

09:00 **Complement-mediated thrombosis**
Christopher Schmidt

09:30 **Antibodies and complement as key drivers of thrombosis**
Konstantin Stark

10:00 **SPONSORED SATELLITE SYMPOSIUM III – OCTAPHARMA BENELUX**
Innovations in VWD and Unexplained Bleeding: Clinical Tools for Better Outcomes
Introduction by Prof. Peter Verhamme (KU Leuven)
Pharmacokinetic-Guided Dosing to Personalize Prophylaxis in von Willebrand Disease
Prof. Ron Mathôt (AUMC Amsterdam)
Introduction by Prof. Peter Verhamme (KU Leuven)
Bleeding Disorder of Unknown Cause: current insights and future directions
Dr. Floor Moenen (MUMC Maastricht)
Q&A

11:00 **COFFEE BREAK**

11:30 **ORAL PRESENTATIONS CLINICAL AND LABORATORY**
Chairs: Jan Emmerechts & Christelle Orlando

11:30 O06 **Venous Thromboembolism in Women on Estrogen Therapy: Presentation, Management, and Outcomes in the RIETE Registry.**
Andreas Verstraete

11:42 O07 **Population-scale proteomics identify new risk markers for venous thromboembolism**
Art Schuermans

11:54 O08 **Longitudinal Changes in Thrombin Generation Before and After Haemodialysis Initiation in Patients with End-Stage Kidney Disease**
Eline Hoes

12:06 O09 **Assay performance in measuring efanesoctocog alfa activity: The impact of calibrator selection on one-stage clotting and chromogenic FVIII assays**
Mohammad Amir

12:18 O10 **Agreement between anti-factor Xa and aPTT in recipients of long term left ventricular assist devices: which is the better predictor of long-term survival?**
Christophe Vandenbriele

12:30 **CSL BEHRING ENCOURAGEMENT GRANT**

12:45 **LUNCH BREAK AND POSTER WALK**

13:45 **EDUCATIONAL II**
Chairs: Claudia Tersteeg & Cécile Oury

13:45 **Platelet Physiology and Dysfunction**
Kerstin Jurk

14:30 **STATE OF THE ART III – DIAGNOSIS AND TREATMENT OUTSIDE THE COMFORT ZONE**
Chairs: Thomas Vanassche & Phu Quoc Le

14:30 **Antithrombotics management after venous stenting**
Arina ten Cate

15:00 **Bleeding Disorders of Unknown Causes**
Ingrid Pabinger

15:30 **PAUL CAPEL PRIZE – CLINICAL & LABORATORY & BEST POSTER AWARD**

15:45 **CLOSING REMARKS**
Katrien Devreese, BSTH President

EVENING PROGRAM

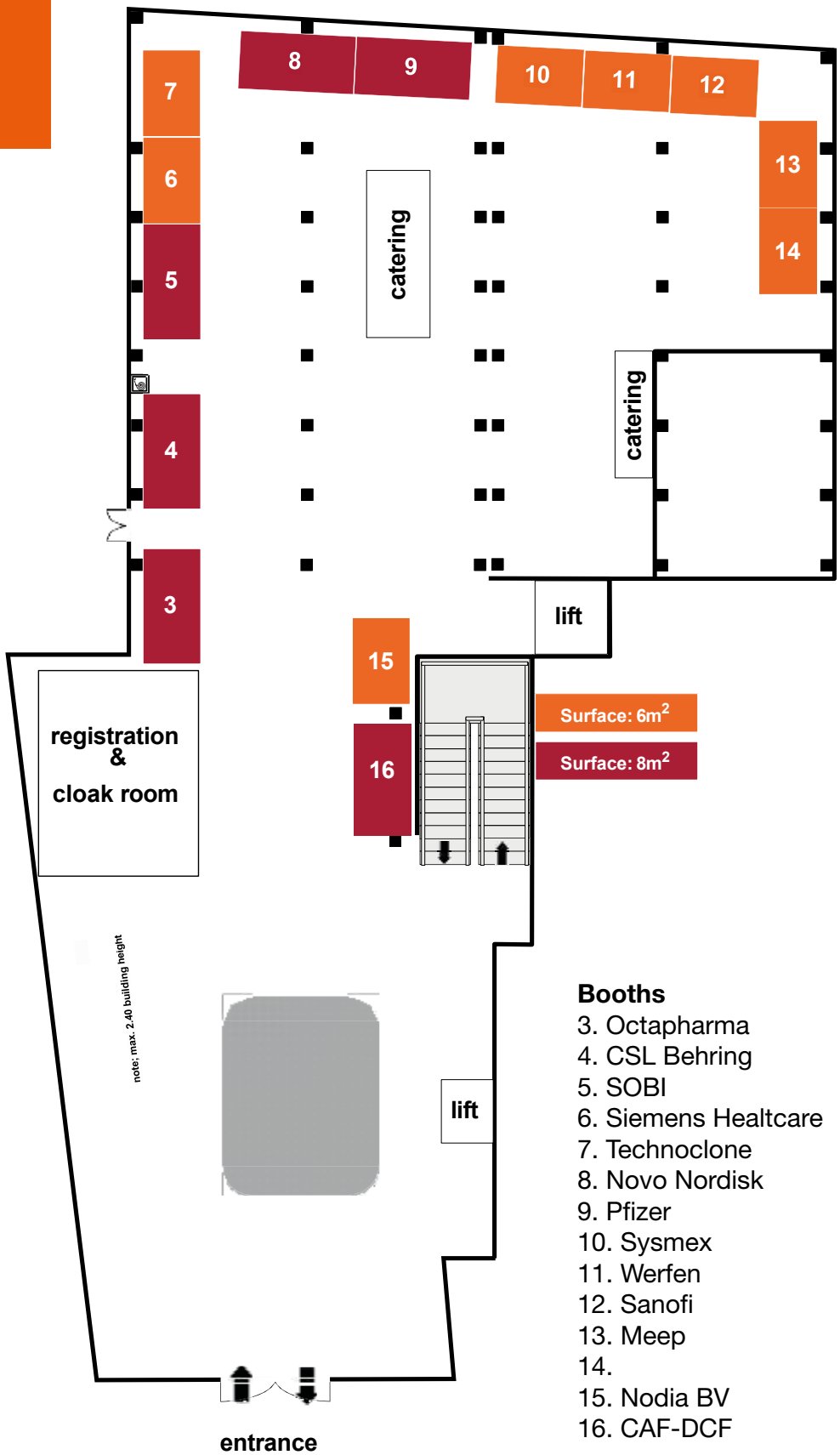
DINNER

From 18:30hrs. you're invited to join our dinner in Van der Valk Mechelen, Rode-Kruisplein 1-4.

Preregistration is required.

08

FLOORPLAN



Booths

3. Octapharma
4. CSL Behring
5. SOBI
6. Siemens Healtcare
7. Technoclone
8. Novo Nordisk
9. Pfizer
10. Sysmex
11. Werfen
12. Sanofi
13. Meep
14.
15. Nodia BV
16. CAF-DCF



09

EXHIBITION RULES & REGISTRATION FEES

EXHIBITION RULES

At our meeting and exhibition at LAMOT certain restrictions are applicable.

FOOD AND BEVERAGE
It is not allowed to distribute prepared food or beverages at the booth or place any food cooking equipment.

MANNING OF STANDS
Exhibitors will be required to ensure that their stands are manned during the opening hours of the exhibition and must not dismantle their stands before the published closing time.

NOISE
Exhibitors may not use audible electronic, mechanical apparatus, or open audio systems that may be heard outside the exhibitor assigned space. Congress Care on behalf of BSTH and its organizers, reserves the right to require any exhibitor to discontinue any activity that may cause annoyance or interference with others.

SECURITY AND INSURANCE
BSTH and its organizers will not be held responsible for any accidents, loss or damage to exhibitors' goods and exhibitors are reminded that they should obtain their own insurance to cover this.

EXHIBITION OPENING HOURS

THU 27 NOV 2025	08:30-18:30
FRI 28 NOV 2025	08:30-15:30

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EDUCATIONAL I



New therapies and monitoring in von Willebrand disease

Jeroen Eikenboom

Head Of Department, Leiden University Medical Center, the Netherlands

Von Willebrand Factor (VWF) plays a major role in the adhesion and aggregation of platelets at the site of vascular damage. As such it is of pathophysiological importance in bleeding as well as thrombosis. When VWF is significantly reduced and associated with bleeding symptoms this is diagnosed as Von Willebrand Disease (VWD). Bleeding in VWD consists of spontaneous mucocutaneous bleeds, traumatic bleeds and bleeding during (surgical) interventions. The clinical burden of bleeding in VWD is often underestimated. Joint and muscle bleeds are very frequent in type 3 VWD (up to 45% and 28% respectively), but also in type 1 and 2 patients report these bleeds up to 20%. Also gastrointestinal bleeds and heavy menstrual bleeding are burdensome.

Current treatment for VWD is based on raising the circulating VWF levels, either by inducing secretion of endogenous VWF by administration of DDAVP, or by infusion of exogenous VWF concentrate. Most patients are treated on demand at the time of a bleed or phylactic during medical interventions, however long-term prophylactic treatment is applied only rarely, even though the latest guidelines suggest long-term prophylaxis in VWD with a history of severe and frequent bleeds. DDAVP and VWF concentrates have their limitations. DDAVP is not effective in all patients, contra-indicated in some, the effect is short-lived and the response is less after repeated administrations. VWF concentrates are usually very effective, but need to be administered frequently and always intravenously. For some bleeds, like gastrointestinal bleeds, the effect of treatment is disappointing.

Several potential, new therapeutic modalities for VWD are being investigated. Some focus on increasing circulating VWF levels. Rondoraptivon pegol is a pegylated aptamer binding the VWF A1 domain and in type 2B VWD this leads to increase of platelet counts, normalization of VWF multimers, and increase in VWF and FVIII levels. Another development is a novel bispecific nanobody, named KB-V13A12, containing two single-domain antibodies, one targeting VWF and one targeting albumin, and thereby increasing endogenous VWF levels through an enhanced half-life of VWF. Bleeding phenotype in VWD may also be improved by enhancing FVIII activity. Studies are ongoing with the very long acting FVIII concentrate efanesoctocog alfa in types 2N and 3 VWD. FVIII mimetics are also being investigated in the setting of severe VWD. Furthermore, some non-factor therapies are being considered for VWD, like synthetic platelet nanoparticles in types 2B and 3, and a protein S-targeting monoclonal antibody blocking the protein S cofactor activity for TFPIα- and APC-mediated inhibition of thrombin generation. There are also pre-clinical developments focusing on silencing the expression of the mutant VWF allele in dominant-negative forms of VWD, either by personalized siRNA based inhibition of mutant VWF alleles or by CRISPR/Cas9 based disruption of the pathogenic VWF allele.

Improving the management of VWD and especially long-term prophylactic treatment is urgently required. In contrast to the development of new treatments in hemophilia, limited progress has been seen in the field of VWD. However, currently several promising new treatment modalities are being investigated in pre-clinical and clinical studies.

Biography

Jeroen Eikenboom received his MD degree in 1988 at the Erasmus University Rotterdam, the Netherlands. He obtained his PhD at the Leiden University in 1994; the subject of his thesis was "The inheritance of von Willebrand disease". He was trained in internal medicine at the Leiden University Medical Centre and registered as internist in 2001. Since then he sub-specialized in haematology and vascular medicine. He was appointed full professor of Internal Medicine/ Haemostasis and Thrombosis in 2011. His clinical work is focused on bleeding disorders, thrombophilia and vascular medicine. His research is focused on the molecular genetics of von Willebrand disease, genotype-phenotype associations in von Willebrand disease, and the biochemical and cell biological aspects of synthesis, storage, secretion and clearance of von Willebrand factor. He is also developing new innovative treatment modalities for von Willebrand disease. He has been (co)chairman of the Scientific Subcommittee on von Willebrand factor of the Scientific and Standardization Committee (SSC) of the International Society on Thrombosis and Haemostasis (ISTH) from 1999-2013. He is chair of the scientific advisory board of the Landsteiner Foundation for Blood Transfusion Research. He is associate editor of the haematology journal HemaSphere. He chairs the Dutch Society representing the Haemophilia Treatment Centres.

f

Platelet Physiology and Dysfunction

Kerstin Jurk
Group leader, University Medical Center Mainz, Germany

As first responders to haemostatic and inflammatory challenges, platelets crucially contribute to the recovery of vascular integrity. Chronic inflammation enhances the activity of platelets in cardiovascular disease (CVD), thereby guiding thromboinflammation and thrombotic events in the arterial and venous system. On the other hand, inherited or acquired platelet defects with impaired platelet responsiveness increase the risk of bleeding. Platelet reactivity is tightly regulated by multiple networks of activating and inhibitory signalling routes. Although phospho-proteomic approaches advance this field, we are only at the beginning of understanding the complexity of interacting pathways and their impact on platelet activation responses and dysfunction. First, this lecture presents an overview about current platelet signaling mechanisms, thereby focusing on the interaction of tyrosine (i.e., SFKs, Syk, Btk) and serine/threonine (i.e., PKC, Raf, MAPK) protein kinases in relation to platelet function. Further, mechanisms of platelet dysfunction due to increased reactivity to ADP and epinephrine and its diagnostic potential by platelet function tests in CVD is highlighted. Finally, current approaches and guidelines for the diagnosis of (inherited) platelet function disorders associated with mild-to-moderate bleeding manifestations (e.g., δ-storage pool deficiency) are considered.

Biography
Prof. Dr. Kerstin Jurk is research group leader at the Center for Thrombosis and Hemostasis (CTH), University Medical Center Mainz, Germany. She obtained her PhD in Biology on the interaction between platelets and leukocytes in the platelet group of Beate Kehrel in Münster, Germany. After completing her habilitation in “Experimental Vascular Medicine”, she established her platelet group and the experimental platform “Platelet Function” at the CTH in Mainz and developed specialized diagnostics of inherited and acquired platelet disorders. Her experimental and clinical research focuses on the crosstalk of platelet activating and inhibitory signaling pathways in relation to platelet function and interaction with leukocytes and vascular cells. Since 2023, she is board member of the German, Austrian and Swiss Society of Thrombosis and Haemostasis Research (GTH).

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EDUCATIONAL II



Thrombosis and antithrombotics needs in bleeding disorders

Roger Schutgens
Hematologist, UMC Utrecht, the Netherlands

Cardiovascular disease is an increasing medical issue in patients with hemophilia (PWH). Primary and secondary prevention of thromboembolic events ask for a balanced approach to fine-tune the delicate balance between thrombosis and haemostasis in PWH. The lack of randomized clinical trials in this population hampers clinical decision making in daily practice. A clinical practice guidance from EHA-ISTH-EAHAD-ESO has been produced to guide us through this process. In general, antithrombotic treatment in PWH is feasible, but not always necessary. Certain clotting factor trough levels are considered to be needed for transient use of anticoagulants. In addition, new innovative procoagulant therapies for patients with bleeding disorders have highlighted that thrombotic complications occur in the early phases of development.

In this presentation, an overview will be given of the EHA-ISTH-EAHAD-ESO guidance document and a focus will be given on the latest issues on thrombosis in patients with bleeding disorders.

Biography
Roger Schutgens is a Consultant Haematologist at the University Medical Centre Utrecht. His main responsibilities include care, research and education in the area of benign haematology and clotting diseases. Prof. Schutgens is the Head of the Van Creveldkliniek, an international expertise center for rare and inherited benign haematologic disorders, thrombosis and haemostasis. He holds a position at the steering board of Child Health at the UMC Utrecht. He is chair of the EAHAD European Glanzmann Thrombasthenia Working Group. Prof. Schutgens areas of focus include patients predisposed to bleeding, congenital abnormalities of platelets and hypercoagulable conditions. He has published over 250 peer reviewed articles.

STATE OF THE ART I



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STATE OF THE ART I



Antithrombotics management after TAVI

Patrizio Lancellotti
Head Of Cardiology Department, University Hospital Of Liege, Belgium

Transcatheter aortic valve implantation (TAVI) has revolutionized the treatment of severe aortic stenosis, extending from inoperable patients to those at low surgical risk. Yet thromboembolic and bleeding events remain major determinants of outcomes. Antithrombotic management after TAVI is complex because of competing ischemic and hemorrhagic risks in elderly, comorbid patients. Over the past decade, randomized evidence and large registries have progressively shifted the paradigm toward treatment simplification. Current recommendations now favor aspirin monotherapy for patients without an indication for long-term oral anticoagulation (OAC), and OAC monotherapy for those requiring anticoagulation, reserving dual antiplatelet therapy (DAPT) only for selected cases such as recent percutaneous coronary intervention. Subclinical leaflet thrombosis, a frequent but often transient phenomenon, remains of uncertain clinical significance. This review integrates current evidence with real-world insights, mechanistic data, and evolving concepts that underpin the contemporary, individualized approach to post-TAVI antithrombotic therapy.

Biography
Prof. Patrizio Lancellotti, MD, PhD, FESC, FACC, FAHA
Professor of Cardiology, University of Liège – Head of the Cardiology Department, University Hospital of Liège (CHU Liège)

Prof. Patrizio Lancellotti is a full Professor of Cardiology at the University of Liège and Head of the Cardiology Department at the University Hospital of Liège, Belgium. He is an interventional cardiologist and internationally recognized expert in valvular heart disease, thrombosis, and infective endocarditis. His clinical and research work focuses on the mechanisms, imaging, and treatment of valvular disorders, with particular emphasis on early detection of myocardial damage, structural interventions (TAVI, MitraClip, Triclip), and the interplay between inflammation, thrombosis, and valve dysfunction.

Prof. Lancellotti has published more than 900 peer-reviewed articles and several book chapters on cardiovascular imaging and valve disease. His translational research has contributed to a better understanding of valve-related thrombosis and the prognostic role of systemic inflammation and infection in cardiac remodeling and outcomes after valve interventions.

He is the Editor-in-Chief of Acta Cardiologica and former President of the European Association of Cardiovascular Imaging (EACVI) and the ESC Council on Valvular Heart Disease. He has also served as Chair or member of several European Society of Cardiology (ESC) guideline task forces. Through his leadership at CHU Liège, Prof. Lancellotti has developed one of Europe's most comprehensive programs in structural and valvular interventions, integrating advanced imaging, clinical research, and multidisciplinary care for patients with complex valve disease and infection-related cardiac complications.

STATE OF THE ART II



Complement-mediated thrombosis

Christopher Schmidt
Professor For Experimental Pharmacology, University of Ulm Medical Center, Germany

Complement activation is a key driver of thrombosis in several rare but severe diseases, most notably paroxysmal nocturnal hemoglobinuria (PNH) and atypical haemolytic uremic syndrome (aHUS). Both disorders are characterized by dysregulated complement activity at host surfaces, leading to cytolysis, endothelial damage, and life-threatening thrombotic events. These thromboses are largely resistant to conventional anticoagulant or antiplatelet therapy but can be efficiently prevented by complement inhibition. The approval of eculizumab, the first-in-class C5 inhibitor, has dramatically improved outcomes by reducing morbidity and mortality in affected patients.
Intriguingly, not all diseases with widespread complement activation are associated with thrombosis. In C3 glomerulopathy (C3G), for example, complement activity is markedly upregulated, yet thrombotic complications are uncommon. This apparent paradox suggests that complement activation alone is not inherently prothrombotic. Instead, the nature and context of activation determine whether a prothrombotic state emerges. Understanding these distinctions is essential to identify which forms of complement dysregulation trigger thrombosis and which do not, thereby guiding the choice of the most appropriate therapeutic strategy.
Mechanistic studies have shed light on this interplay. Complement-mediated haemolysis induces platelet activation primarily through membrane attack complex (MAC)-driven cytolysis. The release of intracellular adenosine diphosphate (ADP) during cell lysis amplifies platelet activation and creates a strong prothrombotic signal. In contrast, isolated complement fragments such as C3a and C5a do not trigger substantial platelet activation. Blocking complement at the C3 or C5 level abolishes this process. Alternatively, ADP receptor antagonists alone can mitigate platelet activation in vitro even in the presence of ongoing complement activity. In vivo models confirm that complement consumption alone is insufficient to cause thrombosis unless terminal pathway activation leads to MAC-mediated cell destruction.

Beyond PNH, aHUS, and C3G, other disorders with complement involvement—such as CD59 or CD55 deficiency, autoimmune haemolytic anemia, and catastrophic antiphospholipid syndrome—further illustrate the diverse ways complement can shape thrombotic risk. Clinical and experimental evidence together highlight a complex but critical principle: only certain modes of complement activation culminate in prothrombotic cell activation.

Biography
Dr. Christoph Schmidt is a Professor of Experimental Pharmacology at the Institute of Experimental and Clinical Pharmacology, Toxicology and Pharmacology of Natural Products, University of Ulm Medical Center. He studied pharmaceutical sciences at the LMU Munich (Germany) and received his Ph.D. at the University of Edinburgh (United Kingdom; under the guidance of Prof. Barlow), working on the structure and function of the complement regulator factor H. After his studies, Dr. Schmidt moved to the US for his postdoc, where he worked at the Innate Immunity/protein Chemistry laboratory (under the guidance of Prof. Lambris), focusing on developing a complement inhibitor.

Since 2017 he has been a group leader at the Institute of Pharmacology of Natural Products and Clinical Pharmacology at Ulm University in Germany. After a short stay as a Professor of Biochemical Pharmacy at the Martin-Luther University of Halle-Wittenberg, he was appointed Professor of Experimental Pharmacology at the University of Ulm Medical Center. He and his team use numerous techniques to investigate the complement system to design new therapeutic molecules. His work has made fundamental contributions to the complement field, which includes extensive work on how the cascade is organized and regulated.

Antibodies and complement as key drivers of thrombosis

Konstantin Stark
Professor For Thrombosis And Vascular Inflammation, Ludwig-maximilians-university, Munich, Germany

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STATE OF THE ART III



Antithrombotics management after venous stenting

Arina ten Cate
Thrombosis Expertise Center (TEC), Heart and Vascular Center, Maastricht University Medical Center (MUMC), the Netherlands

Post-thrombotic syndrome (PTS) is a common complication of deep venous thrombosis (DVT), affecting up to 50% of patients — especially those with iliofemoral DVT. Venous outflow is often restricted, and interventions are performed to restore flow. In the acute thrombotic phase, stenting is used alongside thrombus removal (e.g. following catheter-directed thrombolysis [CDT] or thrombectomy in iliofemoral DVT [IFDVT]) to alleviate symptoms, restore patency and prevent PTS. Stenting is also used to restore venous outflow and reduce venous hypertension and symptoms in patients with existing chronic venous pathology, such as chronic PTS or May–Thurner syndrome. Unfortunately, in-stent thrombosis (IST) is a frequent and clinically significant complication. Many factors (e.g. venous flow, stent characteristics and stent localisation) may affect sustained venous patency following stent placement. The role of periprocedural antithrombotic management in preserving stent patency and preventing PTS is yet unclear. Current international guidelines provide no specific recommendations regarding post-interventional antithrombotic management (although most suggest three to six months of antithrombotic treatment after stent placement). The rationale is that stent implantation in the venous system creates a foreign surface that increases the risk of thrombus formation, particularly in patients with underlying prothrombotic conditions or after acute or chronic deep vein thrombosis (DVT). The increased use of, and expanding possibilities for, venous stent placement, combined with the introduction of novel anticoagulant treatment options, has resulted in a wide variety of post-interventional antithrombotic treatment regimens, none of which are evidence-based. In 2021, we reviewed the literature and identified 64 studies (56 original) that reported on periprocedural antithrombotic management in the context of stenting. At that time, the majority of studies (43/56; 77%) used vitamin K antagonists (VKAs), either with (18%) or without (59%) antiplatelet drugs. However, only two out of 56 (4%) studies directly assessed antithrombotic treatment in relation to in-stent thrombosis. Consequently, the impact of antithrombotic management on stent patency remains unclear. The ARIVA trial recently studied the added value of adding aspirin to rivaroxaban treatment on six-month patency after stenting in patients in the chronic phase with established PTS. The trial found no significant difference in patency, but bleeding risk was significantly increased.
In summary, antithrombotic treatment is standard after stent placement, with therapy tailored to patient risk factors and procedural context, but based on limited evidence.

Biography

Dr. Arina ten Cate-Hoek has long-term experience (>25 years) as a clinician in the practice of thrombosis and haemostasis (Thrombosis clinic, Thrombosis expertise Centre, Maastricht University Medical Centre (MUMC+). She holds an MD, and PhD in medicine, and a Master in Epidemiology. She is the medical director of the Maastricht Anticoagulation Clinic and the medical coordinator for the Thrombosis Expertise Center Maastricht.
She is an associate Professor of Medicine at the Cardiovascular Research Institute (CARIM) at Maastricht University. Her research is characterized by a combination of clinical and translational research, mainly directed at prevention and treatment of venous thrombosis.
Her research is mainly directed at innovation and optimization of (post) thrombotic treatment and its associated impact on patient wellbeing as well as its societal impact. Biomarker research plays an important role in the accomplishment of this aim and is directed at a better understanding of the underlying pathophysiology of different aspects of disease entities and the translation of these findings into clinical practice.
As a board-certified clinical epidemiologist, she is particularly interested in the various methodological aspects of research, and the application of this knowledge.
She is the chair of the committee for standardization of medical conduct for the Federation of Dutch anticoagulation clinics, she is the chair of the network of anticoagulation clinics (STOL) in Limburg, the Netherlands. She is a member of the society of Epidemiology, the Dutch society for Thrombosis and Haemostasis (NVTH), the International Society of Thrombosis and Haemostasis (ISTH), and the European Society of Cardiology(ESC). She has participated in several guideline committees and is a member of the editorial board of Acta Haematologica and section editor thrombosis and coagulation for European Cardiology Review.

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STATE OF THE ART III



Bleeding Disorders of Unknown Causes

Ingrid Pabinger
Professor at the Clinical Division of Haematology and Haemostaseology, Department of Medicine I, Medical University of Vienna, Austria

Patients with an unexplained mild to moderate bleeding tendency are diagnosed with bleeding disorder of unknown cause (BDUC), a classification reached after ruling out other mild to moderate bleeding disorders (MBD) including von Willebrand disease (VWD), platelet function defects (PFD), coagulation factor deficiencies (CFD), and non-hemostatic causes for bleeding. The presentation will outline our diagnostic approach to BDUC, a diagnosis of exclusion, drawing on current guidelines and insights from the Vienna bleeding biobank (VIBB). Data from the Vienna bleeding biobank (VIBB) and other studies have identified a high proportion of up to 70 % of BDUC among MBD patients, who have a similar bleeding phenotype as other MBD, but female predominance and an overrepresentation of blood group O. Specifically, blood group O has been identified as a risk factor for increased bleeding severity and bleeding risk after hemostatic challenges such as surgery. In the VIBB cohort follow-up interviews were conducted with 392 patients with mild to moderate bleeding disorders, 246 of whom (62.8%) were classified as having BDUC. During the follow-up period (median 4.3 years) a higher baseline bleeding severity was significantly associated with the occurrence of any bleeding symptom during the follow-up period (adjusted odds ratio 1.14 per increase of the bleeding score by one point, 95% confidence interval 1.04-1.25). In case of bleeding patients with BDUC are presently treated with tranexamic acid, Desmopressin, platelet concentrates or plasma.

Biography
Ingrid Pabinger's scientific fields of expertise encompass hereditary and acquired bleeding disorders, including hemophilia, and thrombotic disorders. She has published more than 550 papers in peer-reviewed journals. She worked or is working as Section or Associated Editor for several scientific journals, e.g. Haematologica, the Journal of Thrombosis and Haemostasis, Thrombosis and Haemostasis and Thrombosis Research.

Professor Pabinger was the Director of the Haemophilia Center Vienna (1998 to 2018) and was between 1998 and 2025 chair of the World Federation of Hemophilia International Hemophilia training center . She has acted as principal investigator of numerous clinical studies in bleeding and thrombotic disorders as well as immune thrombocytopenia. She has been involved in several international scientific societies, including the Board of the German, Austrian and Swiss Society of Thrombosis and Haemostasis (GTH, chair) and the European Hematology Association (EHA), and committees of the American Society of Hematology (ASH). For the period 2016-2018 she was President of the International Society of Thrombosis and Hemostasis (ISTH) and from 2020 until 2023 she was Chair of the European Thrombosis and Haemostasis Alliance (ETHA). In 2021 she was appointed honorary member of the Austrian Hemophila Society. In 2022 she received the Esteemed Career award from ISTH and in 2024 she received the McFarlane-Biggs Award of the British Society of Haematology.

PROFESSOR GASTON BAELE MEMORIAL LECTURE



Reflections on a Career in Thrombosis and Hemostasis - From Mentorship to Sickle Cell Disease Research

Anne Demulder, CHU Brugmann, Belgium

In this Gaston Baele Lecture, Anne Demulder reflects on a career shaped by mentorship, collaboration, and curiosity in the field of thrombosis and hemostasis. Beginning with early guidance from Professor Pierre Fondu and involvement in the founding years of BSTH, she traces her journey through decades of clinical and laboratory research, culminating in recent work with a dedicated team of technicians, fellows, and students.
The centerpiece of her talk is the lab's application of the thrombin generation (TG) test—a versatile tool for assessing coagulation dynamics. She highlights its evolution from early methods to modern platforms like CAT and ST Genesia, and its utility in evaluating bleeding risk, anticoagulant therapy, and protein C system function.
Focusing on sickle cell disease (SCD), Anne Demulder presents findings from studies led by Denis Nouboussié and collaborators, demonstrating hypercoagulability in SCD patients and altered TG parameters, particularly in response to thrombomodulin. She further explores the impact of hydroxyurea treatment and hematopoietic stem cell transplantation (HSCT), showing partial normalization of TG profiles post-HSCT.
In addition, she highlights recent work on thrombin generation in pediatric oncology, specifically in children with acute lymphoblastic leukemia (ALL) treated with native versus pegylated asparaginase. This study, co-authored with Laurence Rozen, Denis Nouboussié, and others, revealed distinct coagulation profiles depending on the formulation used—an important insight for managing thrombotic risk in ALL patients undergoing chemotherapy.
This lecture is both a scientific overview and a personal tribute to the people and experiences that shaped her career. It underscores the importance of mentorship, teamwork, and the ongoing pursuit of knowledge in advancing patient care and research.

Biography
Pr. Anne DEMULDER earned her degree in Laboratory Medicine in 1987 and completed her PhD in Biomedical Sciences in 1996. With over three decades of clinical and academic experience, she has held senior roles in hematology and hemostasis laboratory at University Hospital Brugmann and LHUB-ULB in Brussels. Since 2006, she served as Chef de Clinique, leading diagnostic services in hematology, bone marrow pathology, and coagulation testing, with a particular focus on pediatric hematology and multidisciplinary oncology care.
In parallel with her clinical work, Pr. DEMULDER played a pivotal role in academic leadership at the Université Libre de Bruxelles (ULB), where she was President of the Master's specialization in Clinical Biology and Master of Conferences at the Faculty of Medicine. She taught courses on the physiopathology of hemostasis and hematology for biomedical students, and continued mentoring future clinical biologists and medical students until 2025, following her retirement in 2022.
Her research has centered on global coagulation assays—including thrombin generation and thromboelastography—and their application in bleeding and thrombotic disorders such as hemophilia, thrombophilia, and sickle cell disease. She remained an active contributor to Hemophilia Reference Center - HemoWaB – HUDERF under the current direction of Pr. Le Phu Quoc

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SPONSORED SATELLITE SYMPOSIUM I - NOVO NORDISK



Transforming Conversations: Evolving Hemophilia Treatment and Its Influence on Patient–Physician Shared Decision-Making

Cedric Hermans, Cliniques universitaires Saint-Luc, Catholic University of Louvain, Belgium

Advances in hemophilia management have profoundly reshaped clinical expectations, treatment goals, and the lived experience of patients. The introduction of extended half-life factor concentrates, non-factor replacement therapies, and gene therapy has expanded therapeutic possibilities and introduced new dimensions of benefit, safety, convenience, and uncertainty.
In this rapidly evolving landscape, shared decision-making (SDM) has become increasingly central to delivering high-quality, patient-centred care. This lecture will examine how new treatments are transforming the dialogue between patients and clinicians and analyses the implications for structured and equitable SDM.
Emerging therapies have redefined what constitutes an optimal outcome, shifting the focus from simple bleed reduction to sustained joint health, improved quality of life, treatment autonomy, and long-term safety. At the same time, these innovations introduce uncertainties related to surveillance, risks of thrombosis, and reversibility, which require transparent, bidirectional communication. Effective SDM depends on the alignment of clinical evidence with patient priorities, psychosocial context, and system-level constraints, supported by appropriate educational tools and multidisciplinary collaboration.
As therapeutic innovation accelerates, the evolution of hemophilia A treatment is transforming clinical conversations and reinforcing the need for robust SDM frameworks to ensure that care decisions reflect both scientific evidence and patient values.
Biography
Cedric Hermans currently serves as Head of the Division of Haematology, the Hemostasis and Thrombosis Unit, and the Hemophilia Center at the Saint-Luc University Hospital in Brussels, Belgium. He was appointed Full Professor at the Faculty of Medicine of the Catholic University of Louvain in 2012 and has held the position of Vice-Dean since 2015.
Professor Hermans has authored or co-authored more than 410 original articles in international peer-reviewed journals. He is an active member of several scientific societies, international advisory boards, and collaborative research initiatives.
A former President of the European Association for Haemophilia and Allied Disorders (EAHAD), he currently sits on the Board of Directors of the World Federation of Hemophilia. He is also an Associate Member of the Belgian Royal Academy of Medicine and serves as Editor-in-Chief of the Haemophilia journal.
His primary research interests focus on haemostasis and thrombosis, with particular emphasis on clinical studies evaluating treatment strategies and the broad spectrum of haemophilia-related complications in both high- and low-resource settings. He is also engaged in research on novel anticoagulants and the management of thrombotic disorders.

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SPONSORED SATELLITE SYMPOSIUM II – PFIZER

Rebalancing hemostasis with anti-TFPI treatments Enabling integration of anti-TFPI treatments in clinical practice

Quentin Van Thillo, Leuven Haemophilia Centre, Belgium
Susan Halimeh, Gerinnungszentrum Rhein-Ruhr, Germany

Biography
Quentin Van Thillo is a haematologist at the Leuven Haemophilia Centre. He trained at UZ Leuven and UZ Gent, and is currently a visiting physician at the Department of Haematology, Cliniques universitaires Saint-Luc.

Biography
Susan Halimeh, Gerinnungszentrum Rhein-Ruhr, Germany
Dr Susan Halimeh is a Medical Director of the Gerinnungszentrum Rhein-Ruhr (CCC) in Duisburg, Germany and she also works in the department for children's haematology in the university hospital in Essen, Germany.

After she completed her medical education at the medical school of medicine in Hannover Germany, she worked as a Resident in the department of pediatrics of Hematology and Oncology at the Münster University Germany, where she obtained her qualification as a specialist in Paediatrics. Afterwards she worked as a resident in the Private Institute for transfusions medicine and blood bank Duisburg where she obtained her qualification as a specialist in Haemostaseology and Transfusion medicine. Afterwards and till 2010 she worked as a Medical Director of the MVZ Laboratory Duisburg GmbH (Germany), a Comprehensive care Centre of Haemophilia and Institute of Thrombosis and Coagulation.

The research interest of Dr Halimeh is focused and concentrated on the diagnosis and treatment of haemophilia with special interest in cases of von Willebrand diseases and rare bleeding disorders.





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SPONSORED SATELLITE SYMPOSIUM III - OCTOPHARMA



Innovations in VWD and Unexplained Bleeding: Clinical Tools for Better Outcomes

Bleeding Disorder of Unknown Cause: current insights and future directions
Floor Heubel-Moenen, Maastricht University Medical Centre, the Netherlands

Bleeding Disorder of Unknown Cause (BDUC) represents a heterogeneous and increasingly recognized clinical entity, characterized by objectively abnormal bleeding symptoms in patients for whom standard hemostatic testing fails to identify an underlying defect. Despite its high prevalence among individuals referred for bleeding evaluation, BDUC remains underdiagnosed, underreported, and insufficiently understood.

In this presentation, you will learn about the current state of knowledge on BDUC, including findings from recent clinical and laboratory studies that have advanced understanding of this condition. You will gain insight into the remaining knowledge gaps spanning diagnostic limitations, pathophysiological mechanisms, and management challenges. The session will also highlight ongoing research efforts and practical strategies to bridge these gaps through translational science, advanced diagnostics, and international collaboration, with the ultimate goal of improving care for patients living with BDUC.

Biography
Dr. Floor Heubel-Moenen is an internist-haematologist and haemophilia practitioner at Maastricht University Medical Center+ (MUMC+), an expert centre for Hemophilia, von Willebrand's disease and Platelet Function Disorders. After completing her PhD on 'Diagnostics and mechanisms of haemostasis in patients with mild bleeding disorders and thrombocytopenia' in 2022, she initiated a national research line on bleeding disorders of unknown cause (BDUC), integrating clinical and laboratory research with patients perspectives and health care improvement.

Recognizing the unmet needs in patients with **(BDUC)**, her research focuses on improving bleeding diagnostics and care using innovative haemostasis testing, such as the Maastricht Flowchamber, which she pioneered for BDUC diagnostics. For her leadership in translating innovative diagnostics into clinical practice, she was awarded the **Translate2Clinic Fellowship (2023)**, securing dedicated research time and a PhD position to advance this field.

She is actively involved in **education**, teaching in the **annual transfusion and haemostasis course**, clinical chemistry training days, and the **NVTH PhD course**. She co-supervises several PhD students and **bachelor's and master's students** in their research internships in medicine. Nationally, she contributes to guideline development as chair of the Dutch bleeding evaluation guideline committee, and serves on the editorial board of the Dutch Journal of Hematology.

Internationally, she is an active co-opted member of the ISTH scientific subcommittee on VWF, working on defining BDUC and co-chaired the ISTH SSC meeting on mild bleeding disorders (2024, Bangkok). Additionally, she was an invited speaker at the European Hematology Congress (2024, Madrid), the Åland Island Meeting on von Willebrand Disease (2024), the AHAD-AP Annual Scientific Meeting (Taipei, 2025) and the ISTH SSC joined session on VWF and Women's Health (2025, Washington). Beyond her research and clinical work, she is engaged in fundraising action for Health Foundation Limburg for the project: 'bloedtesten door dik en dun'. Her vision centers on **collaboration between clinicians, laboratory specialists, fundamental researchers and patients**, believing it to be the key to **innovation and excellence in care for patients with bleeding disorders**.



Pharmacokinetic-Guided Dosing to Personalize Prophylaxis in von Willebrand Disease

Ron Mathôt, hospital pharmacist, clinical pharmacologist, Amsterdam University Medical Center, the Netherlands

Long-term prophylaxis with a von Willebrand factor (VWF) concentrate is recommended for patients with von Willebrand disease (VWD) who experience severe and frequent bleeding episodes. Prophylactic therapy may be individualised by pharmacokinetic (PK)-guided dosing. Effective clinical implementation of PK-guided dosing requires understanding of both interpatient PK variability and the relationship between drug exposure and bleeding risk.

In this lecture a population PK model will be presented for patients with severe VWD receiving prophylactic therapy with the VWF/factor VIII (FVIII) concentrate (Wilate®). The model was derived from pediatric and adult data collected in a prospective single-dose study (WIL-12) and two 1-year prospective, prophylactic phase 3 trials (WIL-31: NCT04052698, and WIL-33: NCT04953884). With derived population model PK profiles were constructed for each individual patient, and VWF/FVIII activity levels were assessed at the time of bleeding events.

The presentation will demonstrate how PK-guided dosing can be applied in clinical practice—showing how individual PK parameters can be estimated from only 3–4 blood samples and how dosing regimens can be tailored to achieve specific target trough levels. The results illustrate the practical value of PK-guided prophylaxis to improve bleed prevention and support personalized management in patients with VWD.

Biography

Prof. Dr. Ron Mathôt is a hospital pharmacist and clinical pharmacologist at the Amsterdam University Medical Center, where he serves as Professor of Clinical Pharmacology in the Department of Hospital Pharmacy & Clinical Pharmacology.

He obtained his MSc in Pharmacy (cum laude) from the University of Leiden (1988), PharmD from Utrecht University (1990), and PhD in Pharmacology from the Leiden/Amsterdam Center for Drug Research (1995). He later specialized in Hospital Pharmacy (1998) and Clinical Pharmacology (2007).

Throughout his career, Prof. Mathôt has held leading positions in several Dutch academic hospitals, including the Netherlands Cancer Institute, and Erasmus MC. Since 2010, he has been Professor and Principal Investigator at Amsterdam University Medical Center, where he also supervises fellows in Clinical Pharmacology.

Prof. Mathôt is principal investigator in two major national research consortia — OPTI-CLOT and SYMPHONY, both funded by Dutch governmental grants and dedicated to optimizing treatment for patients with hemophilia and related bleeding disorders. His research bridges pharmacometric modeling and simulation with clinical implementation, enabling pharmacokinetic-guided therapy and data-driven treatment optimization in hemophilia A, B, and von Willebrand disease. His team, currently consisting of eight PhD students and two postdoctoral researchers, is actively involved in multiple national and international multicenter research collaborations

Prof. Mathôt has authored over 330 peer-reviewed publications, including more than 60 in the field of clotting disorders, reflecting his longstanding contributions to clinical pharmacology, translational hematology research, and precision medicine.

O1

BASIC SCIENCE

Distinct open ADAMTS13 in acute and subclinical immune-mediated thrombotic thrombocytopenic purpura

Bonnez Q[1], Boudry F[1], De Waele L[1], Vermeersch L[1], Kangro K[1], Pareyn I[1], Tellier E[2], Kaplanski G[2], Tersteeg C[1], Joly B[3], Coppo P[4], De Meyer S[1], Veyradier A[3], Vanhoorelbeke K[1]
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Background: Only in open ADAMTS13, an initially cryptic Spacer domain epitope becomes accessible for antibody recognition. As a biomarker for diagnosing immune-mediated thrombotic thrombocytopenic purpura (iTTP) and monitoring increase relapse risks, open ADAMTS13 continues to gain clinical interest. Yet, the exact conformation of open ADAMTS13 remains unknown and it remains unclear whether iTTP patients display one distinct or multiple different open ADAMTS13 conformations associated with acute or subclinical disease.

Aims: To characterize the uniformity of open ADAMTS13 in acute and subclinical iTTP patients.

Methods: In an ELISA screening, 60 monoclonal antibodies were analyzed to identify novel cryptic epitope-recognizing antibodies. Epitopes were considered cryptic when antibodies only bound conformationally opened but not closed ADAMTS13. For healthy donors (n=25) and patients with acute (n=53) or remission (n=30) iTTP, ADAMTS13 activity, antigen and conformation was evaluated. Also, changes in ADAMTS13 conformation were screened in response to IgGs purified from healthy donor or iTTP patient plasma.

Results: Beyond the described cryptic Spacer domain epitope, we identified five mAbs to recognize novel cryptic epitopes distributed across the MP, Dis, T7, T8 and CUB1 domains. As all novel cryptic epitopes remained inaccessible in plasma of healthy donors, ADAMTS13 was found in a closed conformation likely mediated by multiple intramolecular interactions. On the contrary, all acute iTTP patients presented one distinct open ADAMTS13 with each novel cryptic epitope being accessible. This same distinct open ADAMTS13 conformation was also found in remission patients with subclinical iTTP, whereas closed ADAMTS13 is presented by remission patients with sustained treatment response. Unlike IgGs from healthy donors, the IgG fraction purified from iTTP patients induced the same distinct open ADAMTS13 conformation as seen during acute and subclinical disease episodes.

Conclusions: Our study provides new insights into ADAMTS13 conformation in two ways. First, we identified antibodies that recognize novel cryptic epitopes within different ADAMTS13 domains. As closed ADAMTS13 in plasma of healthy individuals did not expose cryptic epitopes, our findings support the requirement of a compactly closed ADAMTS13 to maintain healthy circulation. Secondly, we demonstrated that open ADAMTS13 exposes multiple cryptic epitopes extending beyond the one within the Spacer domain. We revealed that once opened, ADAMTS13 adopts one distinct open conformation that is consistently presented by all patients with acute or subclinical iTTP, but not by well-responding patients in remission. As pathological IgGs are typically present during acute and subclinical disease, we indeed verified that iTTP-purified IgGs trigger open ADAMTS13 with exposure of all cryptic epitopes. Thereby, we provide novel insight into the extent to which ADAMTS13 opens its conformation during acute and subclinical iTTP.

O2

BASIC SCIENCE

Targeting antigen-specific B cells in immune mediated thrombotic thrombocytopenic purpura using modular CAR T cells

Rovira Puig S[1], Delecluyse Y[1], Vermeersch L[1], Gupte R[2], Tersteeg C[1], De Meyer S[1], Voorberg J[3], Bachmann M[2,4,5,6], Arndt C[2,7], Feldmann A[2,4,5,6], Vanhoorelbeke K[1]
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Introduction: Refractory immune-mediated thrombotic thrombocytopenic purpura (iTTP) remains an unmet clinical challenge. Chimeric Antigen Receptor (CAR) T cell therapy directed towards CD19 has shown efficacy in refractory autoimmune diseases such as systemic lupus erythematosus. However, conventional CAR T cells eliminate the entire B cell compartment indiscriminately and lack intrinsic regulatory mechanisms, leading to severe adverse events. A potentially safer approach is the Universal CAR (UniCAR) platform, in which T cells recognize a short peptide epitope contained within a Target module (TM), rather than directly binding a cell surface antigen. The TM, in turn, recognizes the target antigen. Thus, UniCAR T cells are guided by the TM and their reactivity can be controlled in vivo by the presence or absence of the infused TM, providing a built-in safety switch.
By incorporating ADAMTS13 into the TM, UniCAR T cells can be selectively directed against pathogenic B cells expressing anti-ADAMTS13 BCRs in iTTP patients, which will recognize the epitopes within the TM, while sparing non-pathogenic B cells.

Aim: To evaluate the efficacy of the UniCAR T system in eliminating cells expressing anti-ADAMTS13 scFv using ADAMTS13-based TMs.

Methods: Human T cells were transduced with lentiviral vectors encoding the UniCAR construct. Different TMs were generated to contain either ADAMTS13 domains (MDTCS or CUB1–2) or full-length ADAMTS13 (FL), each linked to the UniCAR epitope. Nalm6 cells engineered to express patient-derived anti-ADAMTS13 single-chain variable fragments (scFv) on their surface served as target cells. UniCAR T cells were co-cultured with target cells for 24 hours. Cytotoxicity was assessed by flow cytometric quantification of residual target cells, and cytokines release were measured.

Results: All three TMs induced robust, TM-dependent cytotoxicity. Specific lysis of Nalm6-anti-ADAMTS13 cells reached 84.6% (CUB-TM), 92.3% (MDTCS-TM), and 76.3% (FL-TM), compared to TM-independent killing of 26.8%, 29.6%, and 19.6%, respectively (n=3). In all cases, TM-dependent killing was significantly higher. Additionally, UniCAR T cells released activating cytokines upon target cell recognition in the presence of TMs (n=2).

Conclusion: The UniCAR T cell platform enables selective elimination of cells expressing anti-ADAMTS13 BCRs, supporting its potential as a targeted therapeutic strategy for refractory iTTP. Further studies will include assessing the impact of patient-derived competing antibodies and to evaluate therapeutic efficacy in an iTTP mouse model.

O3

BASIC SCIENCE

In vitro validation of the novel anti-CD19 and anti-CD38 UniCAR T cell therapy for refractory iTTP patients

Vermeersch L[1], Van Loke R[1], Van Dorpe C[1], Rovira Puig S[1], Gupte R[2], Tersteeg C[1], De Meyer S[1], Voorberg J[3], Bachmann M[2,4,5,6], Arndt C[2,7], Feldmann A[2,4,5,6], Vanhoorelbeke K[1]

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Background/Introduction: Chimeric antigen receptor (CAR) T cell therapy targeting CD19 on B cells has demonstrated promising results in treating refractory autoimmune diseases (AIDs), including systemic lupus erythematosus (SLE). However, CAR T cell strategies targeting CD38 expressing plasma cells, which play a crucial role in sustaining pathogenic autoantibody responses, remain unexplored in AID. The efficacy of either approach in managing refractory immune-mediated thrombotic thrombocytopenic purpura (iTTP), a life-threatening condition driven by anti-ADAMTS13 autoantibodies, has not yet been investigated.

Aims: In this study, we explored the therapeutic potential of the Universal (Uni)CAR T cell adaptor platform for the treatment of refractory iTTP. We evaluated in vitro cytotoxicity against engineered Nalm-6 cells expressing anti-ADAMTS13 antibodies (anti-S and anti-CUB2). These cells endogenously express both CD19 and CD38 surface markers. Together, the engineered Nalm-6 cells represent the therapeutic targets relevant to the autoantibody-driven pathology of iTTP.

Methods/Materials: The UniCAR T cell platform consists of either the previously described anti-CD19 target module (TM) or an anti-CD38 TM, which acts as a bridge between the UniCAR T cell and the target cell (engineered Nalm-6 cells). Both TMs are composed of a single-chain variable fragment (scFv) specific for CD19 or CD38, fused to a human La-derived peptide epitope (E5B9). This epitope is recognized by the anti-La5B9 scFv expressed on UniCAR T cells, enabling TM-mediated cross-linking and subsequent target cell elimination.

TMs were produced via lentiviral transduction of 3T3 cells and purified from culture supernatants using Ni^{2} -NTA affinity chromatography. Target cells were generated by lentiviral transduction of Nalm-6 cells with constructs encoding anti-ADAMTS13 antibodies (anti-S and anti-CUB2). UniCAR T cells were derived from healthy donor T cells and transduced with UniCAR constructs. Cytotoxicity assays were performed by co-incubating UniCAR T cells with engineered Nalm-6 cells in the presence or absence of the respective TM. Additionally, an in-house cell-based ELISA was used to assess the binding affinity of each TM to its corresponding antigen.

Results: After successfully generating UniCAR T cells and both anti-CD19 and anti-CD38 TMs, the cytotoxic potential of the UniCAR T cells was evaluated. Both anti-CD19 and anti-CD38 TM bound with high affinity to the Nalm-6 target cells (Kd of 1.42 nM and 3.78 nM, respectively). Co-incubation of UniCAR T cells with engineered Nalm-6 cells (anti-S or anti-CUB2) at a 1:1 ratio in the presence of 25 nM TM resulted in TM-dependent cytotoxicity. Anti-CD19 UniCAR T cells eliminated 78.6% of anti-S and 76.2% of anti-CUB2 Nalm-6 cells, while anti-CD38 UniCAR T cells achieved 83.1% and 82.3% killing, respectively. In contrast, minimal TM-independent killing was observed in the absence of TMs (17.3% for anti-S and 20.1% for anti-CUB2 Nalm-6 cells), underscoring the specificity of the TM-mediated cytotoxic response.

Summary/Conclusion: Our findings demonstrate that the UniCAR T cell adaptor platform effectively eliminates CD19- and CD38-expressing cells in vitro, including engineered cells producing anti-ADAMTS13 antibodies. These results support the potential of UniCAR T cell therapy as a targeted approach for treating refractory iTTP. Ongoing studies are evaluating its efficacy against patient-derived B cells producing pathogenic anti-ADAMTS13 antibodies.

Enterococcus faecalis-induced infective endocarditis: first mechanistic insights and role of ticagrelor

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O4

BASIC SCIENCE

Introduction: Infective endocarditis (IE) is a life-threatening infection, which can affect native or prosthetic heart valves. Enterococcus faecalis (E. faecalis) is a leading cause of IE, particularly in elderly patients. Its ability to adhere to host tissues and prosthetic materials, to form biofilms, and to express multiple virulence factors likely contributes to disease development. However, the pathological mechanisms underlying enterococcal IE are largely unknown. For instance, no studies ever investigated whether E. faecalis interacts with von Willebrand factor (VWF) under conditions of flowing blood. Treatment of E. faecalis IE remains difficult due to antibiotic resistance and limited efficacy of current regimens. Our research team demonstrated that ticagrelor, a platelet P2Y12 receptor inhibitor, also exerts bactericidal effects against gram-positive bacteria, including vancomycin-resistant E. faecalis(VRE).

Aims: Our study aims to understand the mechanisms of E. faecalis IE focusing on known virulence factors, hemolytic activity and bacteria interaction with VWF. We also evaluated potential of ticagrelor as adjunctive therapy to clinically relevant antibiotics.

Methods: A flow chamber model was employed to investigate bacterial adhesion to VWF. Fluorescently labelled E. faecalis strains (E. faecalis ATCC-29212, VRE ATCC-BAA-2365 and a clinical IE isolate) were perfused over VWF-coated slides at shear rate of 1000s-1 for 10 min before quantifying bacterial adhesion.
Hemolytic activity of the three E. faecalis strains was measured using washed human red blood cells, and hemolysis index was determined.
Virulence profiling was carried out in VRE and the clinical IE isolate by quantitative PCR.
Minimum inhibitory concentrations (MICs) were determined according to EUCAST recommendations. To assess potential synergistic interactions, checkerboard assays were performed by combining ticagrelor with each reference antibiotic and fractional inhibitory concentration index (FICI) was calculated.

Results: Our flow chamber assay showed that E. faecalis adhered to VWF under flow conditions. Interestingly, adhesion to VWF was more efficient for IE clinical isolate compared to the two laboratory strains.
Hemolysis assays revealed no hemolytic activity in any strains compared to Staphylococcus aureus (BAA-1556) used as positive control. This result was consistent with PCR-based virulence profiling, which showed no expression of cylA gene encoding for cytolysin in any of the strains, including IE clinical isolate.
MIC testing indicated similar values for ticagrelor against all tested strains (16-32µg/ml). Checkerboard assays showed that although ticagrelor combinations with selected antibiotics (Amoxicillin,Daptomycin) did not exhibit formal synergy (FICI ≤ 0.5), it enhanced the antibacterial activity of nearly all tested agents (0.75 and 0.75 against VRE, 0.75 and 0.6, respectively, against IE isolate).

Summary/conclusions: We demonstrated ability of E. faecalis to adhere on a VWF-coated surface under flow conditions. Our result highlights a potential link between clinical pathogenicity and enhanced interaction with VWF. Ongoing work will further characterize E. faecalis interactions with VWF exposed on activated endothelial cells. Our findings also suggest that ticagrelor could play a role in the prevention of E. faecalis IE. Future studies will include broader collection of IE isolates and will investigate the impact of a pretreatment with ticagrelor on bacterial adhesion on host tissues and prosthetic materials and on virulence factor expression.

O5

BASIC SCIENCE

Mechanistic study of the antivirulence activity of ticagrelor at antiplatelet dosage

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Introduction: Ticagrelor is a widely administered antiplatelet agent reversibly inhibiting the P2Y12 receptor. Additionally, ticagrelor (20mg/L) has antibacterial and antibiofilm properties against Staphylococcus aureus (S. aureus) including methicillin-resistant S. aureus (MRSA). At antiplatelet dose (0.75-1.25mg/L range), ticagrelor reduces MRSA virulence (toxin production, adhesion to fibrinogen, to von Willebrand factor and to activated endothelial cells), it prevents infective endocarditis development in mice and retrospective clinical studies show a reduced risk of S. aureus bacteremia in patients under ticagrelor therapy.

Aims: We aimed to further study the mechanisms of ticagrelor antivirulence activity.

Methods: We first studied the effect of ticagrelor on the Agr quorum sensing system, a major regulator of virulence in S. aureus. For this purpose, we activated Agr signaling in a S. aureus reporter strain expressing the luciferase gene under the control of the P3 promoter with exogenous AIP in the presence or absence of increasing concentrations of ticagrelor (0.3-5mg/L).
We next generated ticagrelor-resistant MRSA using a gradient of ticagrelor concentrations in solid agar medium. These mutants carry a mutation in either ClpX(G226V), ClpP(GP74V) or YjbH(Q105X), which are part of the ClpXP bacterial protease complex. Another mutant carries an insertion mutation in the yjbK(562_563ins) gene of unknown function in S. aureus. We then analyzed the virulence properties of these mutants in terms of staphyloxanthin production (a carotenoid protecting S. aureus from reactive oxygen species), hemolytic activity, and adhesion to fibrinogen as compared to their wild-type (WT) parent strain (ATCC BAA-1556). We also assessed bacteria survival in citrated human blood.

Results: In agreement with an antivirulence activity of ticagrelor, we showed that ticagrelor (from 1.25mg/L) interfered with the AIP induced activation of the Agr quorum sensing system. Ticagrelor (5mg/L) decreased the luminescence signal induced by AIP type II (10nM) by 3.6-fold (p=0,007 vs. vehicle control).
The four in vitro generated ticagrelor-resistant MRSA strains displayed normal growth at 37°C but they produced significantly less staphyloxanthin than WT MRSA (fold-reduction vs. WT: ClpX(G226V): 2.33 ± 0.38, p<0.001; ClpP(GP74V): 1.53 ± 0.34, p=0.02; YjbH(Q105X): 1.78 ± 0.22, p=0.003; yjbK(562_563ins): 3.73 ± 1.52, p<0.001). They induced significantly less hemolysis of washed human red blood cells than WT MRSA (fold-reduction vs. WT: ClpX(G226V): 6.77± 3.36, p<0.001; ClpP(GP74V): 2.31 ± 0.4, p<0.001; YjbH(Q105X): 1.43 ± 0.06, p=0.002; yjbK(562_563ins): 1.8 ± 0.09, p<0.001). Furthermore, two of these mutants adhered significantly less to fibrinogen than WT MRSA (fold-reduction vs. WT: ClpP(GP74V): 2.84 ± 1.1, p=0.03; and yjbK(562_563ins): 2.68 ± 0.44, p=0.02). Some of these mutants showed reduced survival in human blood, indicating less ability to escape the immune system under these in vitro conditions.

Conclusions: The antivirulence activity of ticagrelor at antiplatelet dose involves an effect on the S. aureus Agr quorum sensing system. Ticagrelor-resistant MRSA mutants show decreased virulence compared to their WT parent strain. Our data identify a novel link between the S. aureus ClpXP complex, the yjbK encoded putative protein and bacteria virulence. These mutants represent new tools to further understand the bacteria pathways underlying S. aureus virulence and its interaction with host immunity and hemostasis.

Venous Thromboembolism in Women on Estrogen Therapy: Presentation, Management, and Outcomes in the RIETE Registry

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O6

CLINICAL & LABORATORY

Background: Combined oral contraceptives (COC) increase the risk of venous thromboembolism (VTE) three- to fivefold. Given their widespread use, even a modest relative risk increase translates into a substantial absolute number of VTE events in otherwise healthy young women. However, data in this population remain limited.

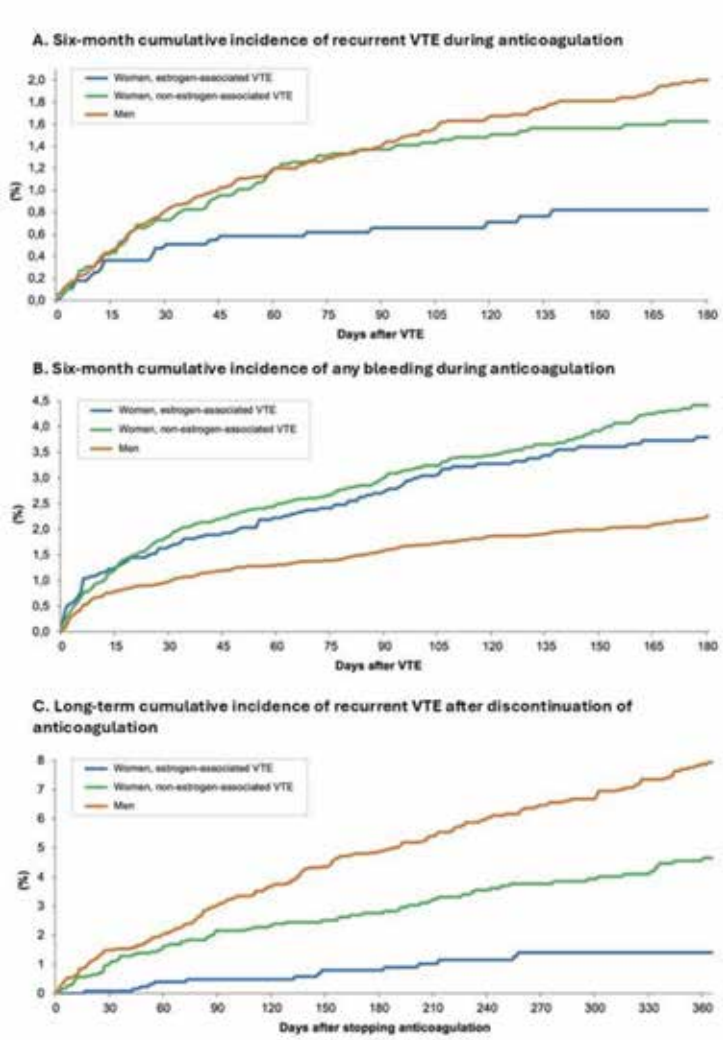
Aim: We aimed to provide real-world insights into the presentation and outcomes of women with estrogen-associated VTE and to evaluate current practices in the management of anticoagulation and contraceptives.

Methods: We used data from the RIETE registry, including non-cancer patients under 50 years old with acute VTE from 2001 to 2024. We analysed presentation, management, and outcomes in women with estrogen-associated VTE compared to men and women with non-estrogen-associated VTE.

Results: Among 18,467 patients, 2,786 women (33% of women) experienced VTE while on estrogen therapy. They were younger (mean [SD] age, 32 [9] years) and presented more frequently with pulmonary embolism (59%) than men (39 [8] years; 52% PE) and women (38 [8] years; 49% PE) with non-estrogen-associated VTE. In 75% of estrogen-associated cases, no additional transient risk factors were present. Estrogen therapy was discontinued in 92% of cases at diagnosis. The median anticoagulation duration was 6 months (IQR 4–9).

Bleeding during anticoagulation was more frequent in women (8.70 and 9.92 per 100 patient-years for estrogen- and non-estrogen-associated VTE, respectively) than in men (5.01 per 100 patient-years), mainly due to uterine bleeding (Figure 1). After discontinuing anticoagulation, recurrence was lowest in women with estrogen-associated VTE (2.07 per 100 patient-years) compared to men (8.46 per 100 patient-years) and other women (4.02 per 100 patient-years). Their median time to recurrence was 23 months (IQR 8-66).

Conclusion: Women with estrogen-associated VTE present with distinct clinical features. Their higher bleeding risk during anticoagulation and low recurrence after discontinuation support short-term anticoagulation.



07

CLINICAL & LABORATORY

Population-scale proteomics identify new risk markers for venous thromboembolism

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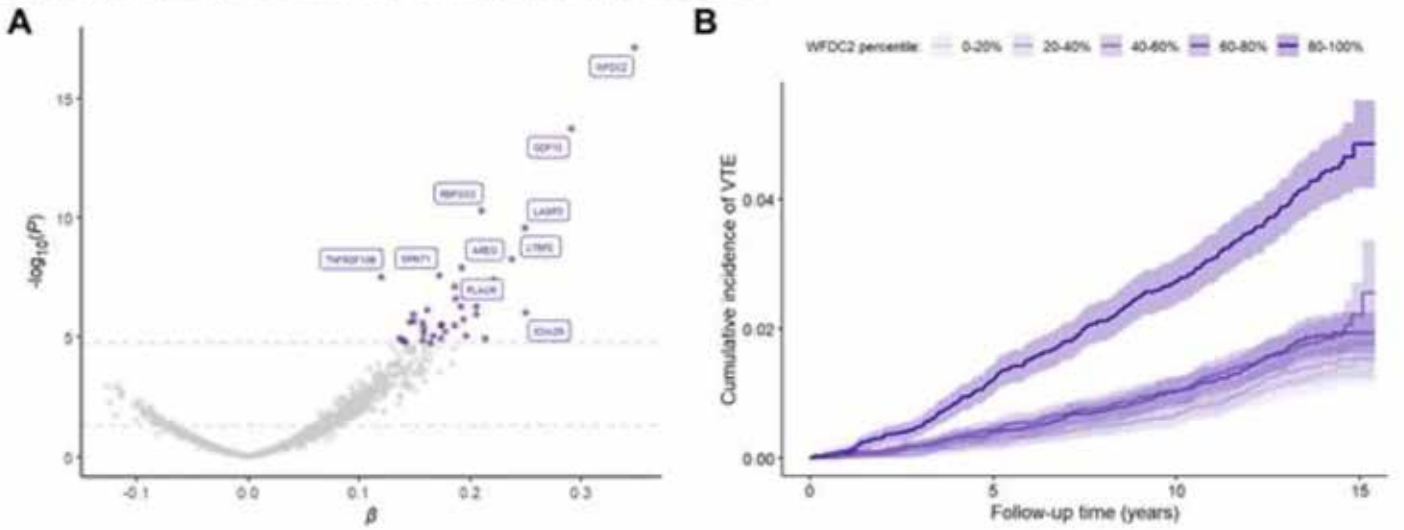
Background: Venous thromboembolism (VTE) is a major global health burden, with limited biomarkers available to accurately identify individuals at high risk of first or recurrent events. In the present study, we aimed to identify circulating proteins associated with incident VTE.

Methods: We analyzed data from the UK Biobank, a large population-based cohort. Participants with proteomic profiling were included, excluding those with >20% missing protein values or a prior history of VTE at baseline. A total of 2,911 circulating proteins were quantified using the antibody-based Olink Explore 3072 proximity extension assay. Incident VTE events were ascertained from linked hospital diagnosis and procedure codes. Associations between proteins and incident VTE were tested using Cox proportional hazards models adjusted for age, age squared, sex, socioeconomic status, smoking status, body mass index, systolic blood pressure, total and high-density lipoprotein cholesterol, antihypertensive and cholesterol-lowering medication use, estimated glomerular filtration rate, high-sensitivity C-reactive protein, prevalent cardiovascular disease, type 2 diabetes, autoimmune disease, and cancer. Secondary analyses assessed cumulative incidence of VTE across protein quintiles using the Kaplan-Meier method. Missing covariates were imputed using stochastic regression for continuous variables and polytomous regression for categorical variables. Statistical significance was defined as P<1.7×10-5 (i.e., Bonferroni correction for 2,911 tests).

Results: A total of 42,931 participants were included (mean age, 56.7 years [SD, 8.2]; 23,155 [53.9%] women). Over a median follow-up of 13.5 years (IQR, 12.8-14.3), 850 incident VTE events occurred. Of 2,911 proteins tested, 36 (1.2%) were significantly associated with incident VTE in multivariable-adjusted models (Figure A). The strongest association was observed for WAP four-disulfide core domain protein 2 (WFDC2; hazard ratio [HR], 1.42 [95% CI, 1.31–1.53]; P=7.5×10-18 per 1-SD increase in protein levels). Other proteins strongly associated with incident VTE included growth differentiation factor 15 (GDF15), RNA binding protein Fox-1 homolog 3 (RBFOX3), and lysosome-associated membrane glycoprotein 3 (LAMP3). Cumulative incidence curves stratified by WFDC2 quintiles demonstrated a markedly higher VTE incidence among participants in the highest quintile compared with all others (Figure B).

Conclusions: We identified 36 circulating proteins, including WFDC2, GDF15, RBFOX3, and LAMP3, that were significantly associated with incident VTE. These findings highlight potential biomarkers for VTE prediction in the general population, warranting further evaluation of protein-based risk scores.

Figure. (A) Volcano plot showing the associations of different circulating proteins with incident venous thromboembolism in the UK Biobank; and (B) cumulative incidence plot visualizing the incidence of venous thromboembolism across WFDC2 fifths.



(A) The x-axis shows the effect size (β) of each association between the indicated protein and incident venous thromboembolism, while the y-axis shows the negative logarithm (base 10) of the corresponding *P*-value. The different proteins are indicated by their corresponding gene names. The dotted lines correspond to *P*-value thresholds of nominal significance (i.e., *P*=0.05) and the Bonferroni significance threshold (i.e., *P*=1.7x10^{-5}). Proteins reaching Bonferroni significance are shown in blue; those not reaching Bonferroni significance are shown in grey. (B) Cumulative incidence plot showing the incidence of venous thromboembolism (VTE) across WFDC2 level quintiles. The shaded regions indicate 95% confidence bands.

Longitudinal Changes in Thrombin Generation Before and After Haemodialysis Initiation in Patients with End-Stage Kidney Disease

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O8

CLINICAL & LABORATORY

Background: Cardiovascular mortality is exceptionally high in haemodialysis patients. Yet, their coagulant state remains elusive, and conventional therapies fail consequently. The thrombin generation assay is a global method to determine haemostatic balance by reflecting both procoagulant and anticoagulant activities in plasma and blood.

Aims: This study aimed to investigate longitudinal changes in thrombin generation following initiation of haemodialysis over a two-year follow-up period.

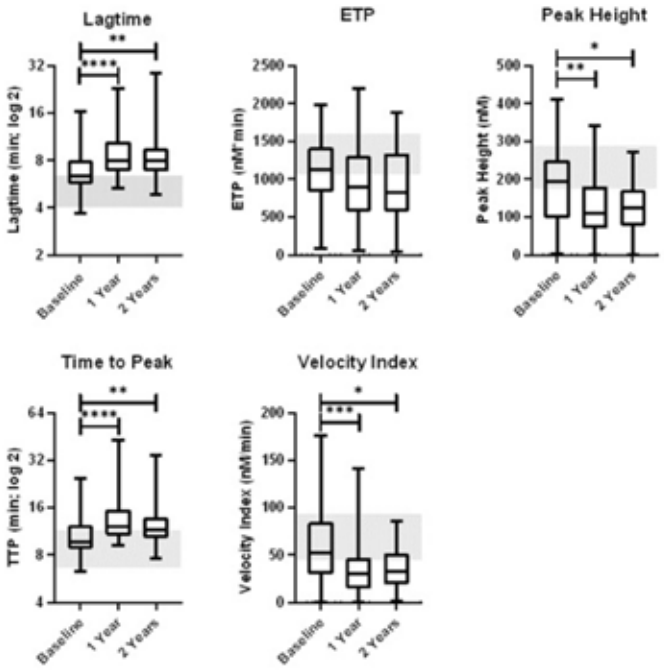
Methods: This study is part of a single-centre prospective cohort currently consisting of 210 patients, investigating haemostasis markers trimonthly in chronic haemodialysis patients. Samples were collected through patients' vascular access prior to haemodialysis treatment. Thrombin generation was assessed on platelet-poor plasma by calibrated automated thrombinography under low and normal tissue factor (TF) conditions. Thrombin generation parameters included lag time, time to peak (TTP), peak thrombin, endogenous thrombin potential (ETP), and velocity index. Data were compared to 120 healthy controls. Kruskal-Wallis test and Friedman test were used for unpaired and paired analysis, respectively.

Results: We collected a total of 214 samples from 115 unique haemodialysis patients (69% male, 71 ± 12 years old). For the cross-sectional analysis, we included 69 samples at baseline, 68 at 1 year, and 53 at 2 years. For the paired analysis, we selected samples from 24 patients with measurements available at baseline, 3 months, and 1 year. Unmeasurable thrombin generation curves occurred mostly in samples obtained through a heparin-locked dialysis catheter and were excluded from analyses (6 at baseline, 5 at 3 months, 8 at 1 year, 10 at 2 years).

Compared with healthy controls, patients who initiate haemodialysis have significantly impaired thrombin generation at baseline, both for low and normal TF: lag time was prolonged ($p < 0.001$), TTP delayed ($p < 0.001$), ETP reduced ($p < 0.001$), and peak thrombin decreased ($p < 0.001$), while velocity index did not differ. After 1 year of chronic haemodialysis, all parameters showed further impairment in the unpaired analyses, except ETP. Velocity index was reduced by >40% ($p < 0.001$). No differences were observed between 1 and 2 years. Excluding patients whose anticoagulant therapy differed between timepoints did not influence results.

Pairwise comparison of baseline and 3-month samples demonstrated that the prolongation of lag time and TTP, together with the decline of peak thrombin and velocity index, already occurred within the first 3 months of haemodialysis. Between 3 months and 1 year, parameters stabilised with no further significant changes.

Summary/Conclusions: Patients with end-stage kidney disease display impaired thrombin generation at the time haemodialysis treatment is initiated. Subsequently, thrombin generation further declines during longitudinal 2-year follow-up. This effect is already evident within the first 3 months of haemodialysis treatment, after which values stabilise and remain stable between 1 and 2 years. Understanding the mechanisms underlying impaired thrombin generation in haemodialysis patients, who are simultaneously at increased risk for thrombotic cardiovascular events, may guide the development of novel targeted cardiovascular therapies.



Boxplots of thrombin generation parameters for low TF environment at baseline (M0), 1 Year (1Y) and after 2 years of haemodialysis (HD) (2Y). Kruskal-Wallis tests were used to compare M0, 1Y and 2Y; significant p-values are shown above the plots. Grey shaded zones represent mean ± SD of the healthy control population.

O9

CLINICAL & LABORATORY

Assay performance in measuring efanesoctocog alfa activity: The impact of calibrator selection on one-stage clotting and chromogenic FVIII assays

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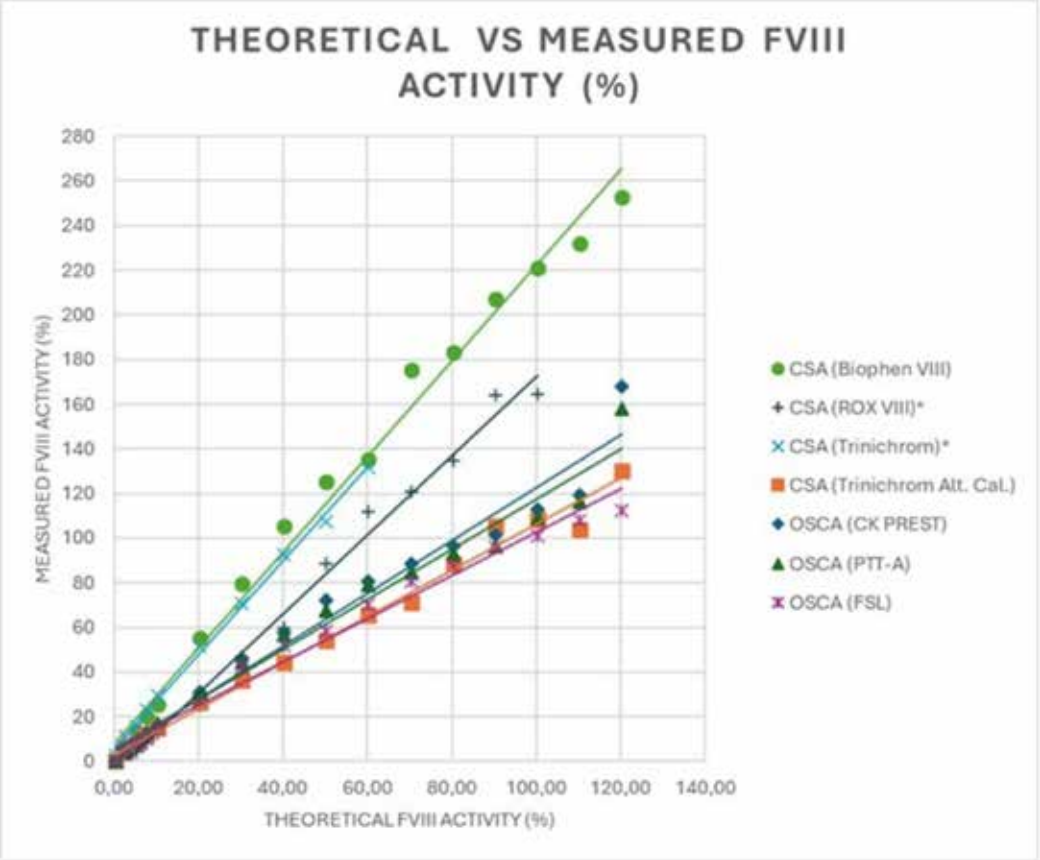
Background/Introduction: Accurate measurement of factor VIII (FVIII) activity (FVIII:C) is vital for effective patient management, particularly when using novel FVIII concentrates such as efanesoctocog alfa. Assay discrepancies, especially between one-stage clotting assays (OSA) and chromogenic substrate assays (CSA), may occur due to structural modifications of such products. A global field study on efanesoctocog alfa demonstrated that while several OSAs (e.g., Actin FSL) provided reliable results, many CSAs consistently overestimated FVIII activity by two- to three-fold[1]. Emicizumab is a humanized bispecific antibody that replicates the cofactor function of FVIII within the tenase complex, thereby enhancing thrombin generation to levels comparable to those observed in individuals with mild hemophilia A. Prophylactic use of emicizumab has demonstrated high efficacy in bleed prevention and is now broadly adopted for patients with hemophilia A across all age groups, regardless of inhibitor status. The standard one-stage coagulation assay (OSA) cannot be used to assess therapeutic FVIII:C in patients receiving emicizumab, as the drug markedly shortens the activated partial thromboplastin time (APTT) and leads to falsely elevated FVIII:C values. In such situations, the bovine chromogenic FVIII assay (CSA) is recommended for accurate measurement of therapeutic FVIII:C[2]. Switching patients from emicizumab to efanesoctocog alfa or combining emicizumab with efanesoctocog alfa results in challenging situations due to absence of reliable laboratory monitoring.

Aims: To assess the performance of FVIII activity assays in patients treated with efanesoctocog alfa specifically evaluating whether calibration using efanesoctocog alfa concentrate improves accuracy of chromogenic assays compared to calibration with a universal standard.

Methods/Materials: FVIII-deficient plasma was spiked with increasing concentrations of efanesoctocog alfa. FVIII activity was measured using chromogenic assays (Trinichrom Stago, Biophen VIII Nodia, ROX VIII Rossix) and one-stage clotting assays (CK Prest Stago, PTT-A Stago, FSL Siemens). All assays were calibrated with the universal calibrator (Unicalibrator, Stago), while CSA Trinichrom was additionally calibrated with efanesoctocog alfa. Accuracy was assessed by comparing measured activity against the expected spiked concentrations.

Results: Chromogenic assay (Trinichrom), calibrated with efanesoctocog alfa, yielded highly accurate FVIII activity values across the tested concentrations. When calibrated with the unicalibrator, CSA (Trinichrom) consistently overestimated FVIII activity. Similar overestimation was also observed with the other chromogenic assays (Biophen VIII Nodia, ROX VIII Rossix) when using the unicalibrator. In contrast, the three one-stage clotting assays (CK Prest, PTT-A, and FSL) provided comparable results across the tested range.

Summary/Conclusions: FVIII measurement of efanesoctocog alfa in spiked FVIII-deficient plasma showed that assay performance depends strongly on the type of assay and the calibrator used. Chromogenic Trinichrom assays calibrated with efanesoctocog alfa yielded accurate results, whereas use of the universal calibrator led to overestimation. One-stage clotting assays, tested with the universal calibrator, produced consistent and reliable results. A key advantage of chromogenic assays is their applicability in patients treated with emicizumab allowing accurate measurement of FVIII activity from efanesoctocog alfa in the same sample. These findings underscore the importance of product-specific calibration and careful assay validation to ensure accurate monitoring of novel FVIII concentrates.



Agreement between anti-factor Xa and aPTT in recipients of long term left ventricular assist devices: which is the better predictor of long-term survival?

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O10

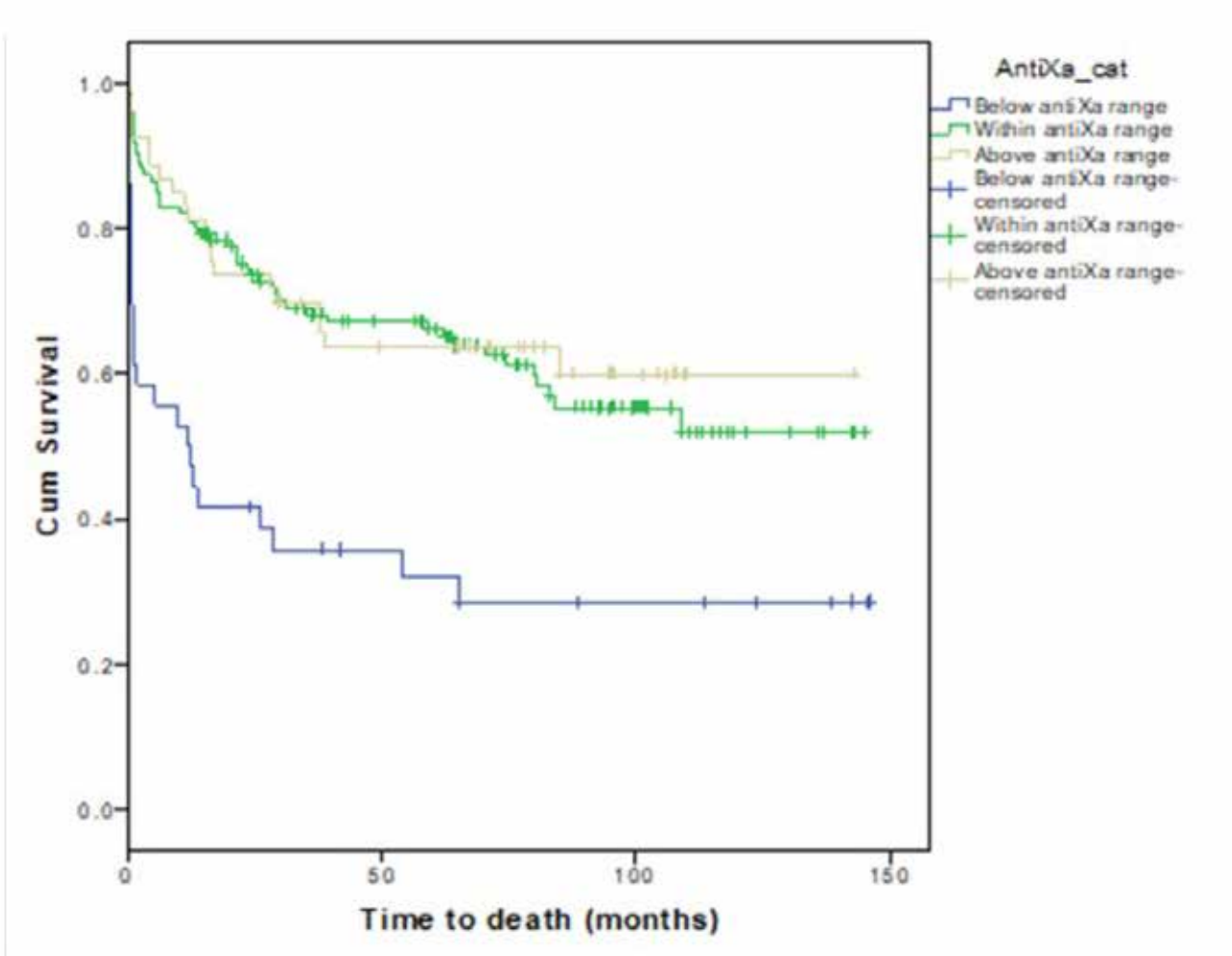
CLINICAL & LABORATORY

Background: Anti-factor Xa (anti-Xa) and activated partial thromboplastin time (aPTT) are utilised in parallel in the monitoring of anticoagulation with intravenous unfractionated heparin (IV-UFH). However, thromboembolic and bleeding events continue to be a challenge in patients undergoing long term (durable) left ventricular assist device (LVAD) implantation and are associated with all-cause mortality. Anticoagulation therapy of LVAD recipients continues to be challenging particularly where there is an anti-Xa:aPTT measurement disparity, the determinants of which are incompletely characterised.

Methods: 235 patients who had an LVAD implanted between 20/09/2010 and 31/01/2023 with a total of 10849 UFH monitoring samples were included in this retrospective, single-arm, single-centre analysis. The target ranges were defined as: aPTT 60-80 seconds and anti-Xa 0.2-0.4 IU/ml. Spearman´s coefficient was utilised to assess the correlation between both tests.
Data were divided into postoperative day 5 to 30 and day 31+ study groups and the relationship between parallel aPTT:anti-Xa concordance and the following influencer variables was assessed: days since device implantation, white blood cell count (WBC), C-reactive protein (CRP), alanine transaminase (ALT), alkaline phosphatase (ALP), bilirubin, total protein concentration and haemoglobin.

Results: Despite a positive correlation between anti-Xa and aPTT according to target ranges, diagnostic correlation was only 42.1% in the post operative day 5-30 group and 51.1% in the post-operative day 31 until systemic warfarinisation group. Therapeutic anti-Xa concentrations were generally associated with subtherapeutic corresponding aPTT values. The risk of all-cause mortality was greater in patients with subtherapeutic mean anti-Xa levels (P logrank<0.001), but not significantly associated with mean aPTT. Post operative day, white blood cell count, C-reactive protein, alanine transaminase and bilirubin exerted a significant effect on the anti-Xa: aPTT relationship over both study periods. Alkaline phosphatase significantly influenced the anti-Xa: aPTT relationship in the early study period whereas total protein level exerted a significant effect in the late period.

Conclusion: Agreement between anti-Xa and aPTT in patients with LVADs on IV-UFH is poor, and is likely influenced by infection, inflammation, coagulation factor consumption and hepatic dysfunction. There is risk of excessive anticoagulation if aPTT is used as gold standard. The association between anti-Xa and mortality suggests that it is a more vital therapeutic tool than aPTT in guiding treatment with IV-UFH in patients with LVADs.



P01

ABSTRACTS
POSTERS

N-glycans: a target for anti-ADAMTS13 antibodies in immune-mediated thrombotic thrombocytopenic purpura

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Background: ADAMTS13 is a heavily glycosylated plasma protein carrying ten N-linked and six O-linked glycans with complex structures capped by terminal sialic acids. Four N-glycans are present on ADAMTS13's Cysteine-rich and Spacer (CS) domains, which are predominantly targeted by autoantibodies in patients with immune-mediated thrombotic thrombocytopenic purpura (iTTP). To date, the exact role of ADAMTS13's glycans for its autoimmune recognition remains largely unexplored.

Aim: To elucidate the impact of ADAMTS13's glycosylation on the autoimmune recognition in acute iTTP patients.

Methods: Recombinant human ADAMTS13 was treated with glycosidases to study the role of glycans in autoantibody recognition. Neuraminidase selectively removed terminal sialic acids, while PNGase F cleaved entire N-linked glycans. Co-incubation of neuraminidase and O-Glycosidase enabled removal of complete O-linked glycans. Glycan removal was confirmed by SDS-PAGE, western blot and lectin binding analysis. From 42 acute iTTP patients, pathological autoantibodies were epitope mapped to characterize IgG binding to various truncated ADAMTS13 fragments. Afterwards, patient autoantibody binding against glycosidase-treated ADAMTS13 was evaluated and all data were expressed relative to binding against untreated control ADAMTS13.

Results: Enzymatic treatment of ADAMTS13 with neuraminidase, PNGase F or neuraminidase and O-glycosidase successfully removed terminal sialic acids, complete N-linked or O-linked glycans, respectively. Profiling of acute iTTP patient IgGs confirmed the presence of pathological autoantibodies targeting multiple ADAMTS13 domains. Compared to untreated ADAMTS13 (100%), neuraminidase-mediated removal of terminal sialic acid significantly reduced patients autoimmune recognition (86.1%). Interestingly, pathological IgG binding was further reduced when removing complete N-linked glycans (81.2%) whereas this additional reduction in autoimmune recognition was not observed upon complete O-linked glycan removal (88.7%). Based on their IgG epitope profiles, patients were stratified to have or not have IgGs targeting ADAMTS13's CS domains. Following complete O-linked glycan removal, a significant reduction in IgG immune recognition was found for patients with or without anti-CS autoantibodies (85.8% and 89.0% respectively). Upon removal of terminal sialic acid or complete N-linked glycans, the IgG immune recognition was significantly lowered in patients with anti-CS autoantibodies (80.2% and 70.2% respectively). On the contrary, no significant reduction in IgG immune recognition was observed in patients lacking anti-CS autoantibodies (94.5% and 98.7%), which suggests the N-linked glycans within the CS domains to particularly modulate the IgG immune recognition.

Conclusions: Our findings highlight the relevance of ADAMTS13's terminal sialylation and N-linked glycosylation for the IgG autoimmune recognition in acute iTTP. Removal of terminal sialic acid or complete N-linked glycans significantly decreased pathological IgG binding which indicates these may form an integral part of the IgG recognized epitopes. This reduction in pathological IgG binding was especially pronounced in acute iTTP patients with autoantibodies targeting the CS domains. With previously identified immunogenic hotspots adjacent to two of the four N-linked glycans (Asn614 and Asn667) present on ADAMTS13's CS domains, our findings suggest both glycans to help shape the predominant immunogenic region of ADAMTS13.

P02

ABSTRACTS
POSTERS

Novel mouse model for immune-mediated thrombotic thrombocytopenic purpura

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Background: Current animal models for immune-mediated thrombotic thrombocytopenic purpura (iTTP) typically rely on passive administration of inhibitory anti-ADAMTS13 antibodies or single-chain variable fragments (scFv), thereby bypassing the complex immunological processes involved in disease onset. To better mimic the human condition, there is a need for models in which the animal's own immune system actively generates clearing or inhibitory antibodies against ADAMTS13, reflecting the autoimmune nature of iTTP.

Aims: This study aims to establish a novel, immune-driven mouse model of iTTP in which ADAMTS13 deficiency arises from an endogenous immune response, thereby providing a more physiologically and immunologically relevant model for studying disease mechanisms and testing novel therapeutic approaches in iTTP.

Methods: Wild-type (WT) mice were immunized with recombinant human (rh)ADAMTS13 (n=12) or injected with saline (n=7) on days 1 and 14. On day 21, anti-rhADAMTS13 antibody levels and endogenous murine (m)ADAMTS13 antigen levels were measured by ELISA. mADAMTS13 activity was assessed using a FRETS-VWF71 assay. To trigger iTTP, both immunized and control mice received an intravenous injection of recombinant von Willebrand factor (rVWF, 1000 U/kg). After 24 hours, blood counts were performed.

Results: As expected, all immunized mice (n=12) developed anti-rhADAMTS13 antibodies by day 21. Interestingly, in 9 of these mice, the endogenously produced antibodies effectively cleared mADAMTS13, resulting in ADAMTS13 deficiency. In contrast, control mice (n=7) showed no anti-rhADAMTS13 antibodies and maintained normal mADAMTS13 antigen and activity levels. Importantly, after triggering with rVWF, immunized mice with mADAMTS13 deficiency (n=9) exhibited iTTP-like signs and symptoms, including severe thrombocytopenia (from 480.3*109/L to 107.9*109/L, $p<0.0001$) and microangiopathic hemolytic anemia (hematocrit: from 22.56% to 6.11%, $p=0.0012$; hemoglobin: from 12.19 g/dL to 9.22 g/dL,

p<0.0001), in contrast to control mice. Ongoing experiments aim to confirm the presence of ADAMTS13-specific B and T cells in immunized mice.

Conclusions: We developed the first animal model for iTTP in which ADAMTS13 deficiency is driven by the animal's own immune system. Interestingly, this unique iTTP mouse model offers a valuable platform for studying disease mechanisms and guiding the development of novel immunomodulatory drugs.

Platelet GARP:TGFβ1 axis regulates endothelial cell activation after myocardial infarction

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P03

ABSTRACTS
POSTERS

Background: Beyond their established role in thrombosis, platelets actively regulate inflammation through cellular interactions and the release of soluble mediators. Notably, platelets are a major source of latent transforming growth factor-β1 (TGFβ1), stored in α-granules and bound to the surface receptor glycoprotein A repetitions predominant (GARP), which enables its activation. While GARP:TGFβ1 is well characterized in regulatory T lymphocytes, its role in platelets remains poorly defined. Using a megakaryocyte/platelet-specific GARP knockout model, we previously demonstrated that platelet GARP is essential for TGFβ1 activation during the early inflammatory phase following myocardial infarction (MI), limiting immune cell infiltration, and promoting cardiac repair. The molecular mechanisms underlying this regulation, however, are still unclear.

Aims: To elucidate how the platelet GARP:TGFβ1 axis shapes the post-MI inflammatory response.

Methods: Megakaryocyte/platelet-specific GARP knockout (pKO) and wild-type (WT) mice underwent permanent coronary artery ligation. TGFβ signaling was assessed 6 hours post-MI by co-immunohistofluorescence of phosphorylated Smad3 with cell-specific markers (monocytes, CCR2 ; neutrophils, Ly6G ; endothelial cells, CD31). Transcriptomic profiling (RNA sequencing, validated by RT-qPCR), was performed on infarcted myocardium at 24 hours post-MI. In vitro, Human Umbilical Vein Endothelial Cell (HUVECs) were stimulated with thrombin in the presence or absence of recombinant TGFβ1, or co-cultured with WT or pKO platelets, and gene expression was quantified by RT-qPCR.

Results: In pKO mice, infarcted myocardium showed enrichment of pathways linked to endothelial activation, cytokine production, and leukocyte recruitment. RT-qPCR confirmed upregulation of endothelial activation molecules (P-selectin, E-selectin). Co-immunohistofluorescence revealed reduced TGFβ signaling in endothelial cells, indicating that platelet GARP:TGFβ1 primarily modulates endothelial responses. In vitro, recombinant TGFβ1 blunted thrombin-induced adhesion molecule expression in HUVECs. Similarly, HUVECs exposed to pKO platelets displayed increased endothelial activation compared to WT platelets.

Conclusions: Platelet GARP:TGFβ1 acts as a regulator of endothelial activation after MI, restraining inflammation and thereby supporting cardiac repair.

Abelacimab and osocimab: What impact on laboratory coagulation assays?

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P04

ABSTRACTS
POSTERS

Background: Over the last few years, several strategies to target FXI(a) have been developed. Abelacimab, a monoclonal antibody that prevents activation of FXI into FXIa, and osocimab, an antibody that directly inhibits FXIa, are among the most advanced agents. Both have already been evaluated in Phase 2 trials, and abelacimab is currently in Phase 3 clinical development. However, their potential effects on coagulation assays remain poorly defined.

Aims: We aimed to assess the impact of increasing plasma concentrations of abelacimab and osocimab on different coagulation assays.

Methods: Normal pooled plasma (Namur Exchange Biobank, Namur, Belgium) was spiked with intermediate solutions of abelacimab and osocimab to yield final concentrations ranging from 0 to 100 µg/mL. The following tests were performed on these samples using an ACL-Top 700 analyzer: fibrinogen quantitation (Clauss method, HemosIL® Fibrinogen C and PT-derived method, HemosIL®RecombiPlasTin 2G), an aPTT-based protein C assay using Protac® as protein C activator (HemosIL®ProClot), a latex particle-based agglutination assay for free protein S determination (HemosIL®Free PS), one-stage aPTT-based FXI, FXII, FVIII, FIX assays and one-stage PT-based FII, FV, FVII, FX assays (HemosIL®Factor Deficient plasmas combined with HemosIL®SynthASil or HemosIL®RecombiPlasTin 2G), dilute Russel's viper venom assays (HemosIL®dRVVT Screen and Confirm). Statistical analyses were performed with the GraphPad Prism software version 10.6.0 (Boston, Massachusetts USA).

Results: At 100 µg/mL, abelacimab and osocimab produced clinically and statistically significant reductions in the measured levels of intrinsic-pathway clotting factors (aPTT-based assays, Table 1.). In the aPTT-based protein C assay, prolongation of the clotting time by either inhibitor led to

a significant apparent increase in measured protein C activity. Neither abelacimab nor osocimab affected fibrinogen assays, the immunoturbidimetric protein S assay, or PT-derived assays of extrinsic and common pathway factors (Table 1.). dRVVT screen and confirm results were unchanged in the presence of abelacimab or osocimab at 100 µg/mL (lupus anticoagulant screen/confirm ratios of 1.11 and 1.09, respectively).

Conclusions: These findings should be confirmed in patients treated with abelacimab or osocimab. Until then, potential assay-dependent effects of these antibodies on routine and specific coagulation assays should be taken into consideration.

Table 1. Results of the different coagulation assays

Coagulation assay	Reagent(s)	Method	Variation from baseline	
			abelacimab 100 µg/mL	osocimab 100 µg/mL
Fibrinogen (Clauss method)	Hemosil® Fibrinogen-C	Chronometric	↑ 2.9% (ns)	↑ 1.8% (ns)
Fibrinogen (PT-derived)	Hemosil® RecombiPlasTin 2G	Chronometric	↑ 1.0% (ns)	↑ 0.1% (ns)
Protein C	Hemosil® ProClot	Chronometric	↑ 118.5% (*)	↑ 272.4% (****)
Protein S	Hemosil® Free Protein S	Immunoturbidimetric	↑ 0.3% (ns)	↑ 0.9% (ns)
FXI (1-stage aPTT-based assay)	Hemosil®FXI Deficient Plasma Hemosil® SynthASil	Chronometric	↓ 96.7% (****)	↓ 79.9% (****)
FXII (1-stage aPTT-based assay)	Hemosil®FXII Deficient Plasma Hemosil® SynthASil	Chronometric	↓ 98.6% (****)	↓ 88.7% (****)
FVIII (1-stage aPTT-based assay)	Hemosil®FVIII Deficient Plasma Hemosil® SynthASil	Chronometric	↓ 98.1% (****)	↓ 88.7% (****)
FIX (1-stage aPTT-based assay)	Hemosil®FIX Deficient Plasma Hemosil® SynthASil	Chronometric	↓ 100.0% (****)	↓ 95.8% (****)
FII (1-stage PT-based assay)	Hemosil®FII Deficient Plasma Hemosil® RecombiPlasTin 2G	Chronometric	↑ 3.5% (ns)	0.0% (ns)
FV (1-stage PT-based assay)	Hemosil®FV Deficient Plasma Hemosil® RecombiPlasTin 2G	Chronometric	↑ 3.8% (ns)	↑ 2.3% (ns)
FVII (1-stage PT-based assay)	Hemosil®FVII Deficient Plasma Hemosil® RecombiPlasTin 2G	Chronometric	↓ 3.5% (ns)	↓ 4.6% (ns)
FX (1-stage PT-based assay)	Hemosil®FX Deficient Plasma Hemosil® RecombiPlasTin 2G	Chronometric	↓ 5.9% (ns)	↓ 7.7% (ns)

Results of the coagulation assays performed in normal pooled plasma spiked with abelacimab or osocimab (0-100 µg/mL), dilution factor=20. Statistical significance was assessed using one-way ANOVA with Tukey's multiple comparison test. The degree of significance refers to the comparison of the 100 µg/mL condition with the assay baseline (normal pooled plasma spiked with phosphate buffer saline, dilution factor=20). ns= not statistically significant. *:P-value <0.05. ****:P-value <0.0001. Values in *italic* correspond to measurements that were outside the calibration range and were therefore extrapolated by the analyzer. The commercial names of the reagents and analyzer were included to ensure scientific transparency and conciseness.

P05

ABSTRACTS
POSTERS

Abelacimab and osocimab: Pharmacodynamic insights from coagulation assays

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Background: Over the past few years, factor XI (FXI) inhibitors have emerged as promising agents for the prevention and treatment of arterial and venous thromboembolic diseases. Several compounds, including the monoclonal antibodies osocimab and abelacimab, have reached Phase 2 and Phase 3 clinical development, respectively. However, little is known about their impact on coagulation assays.

Aims: We aimed to investigate the impact of increasing concentrations of abelacimab and osocimab on different coagulation assays.

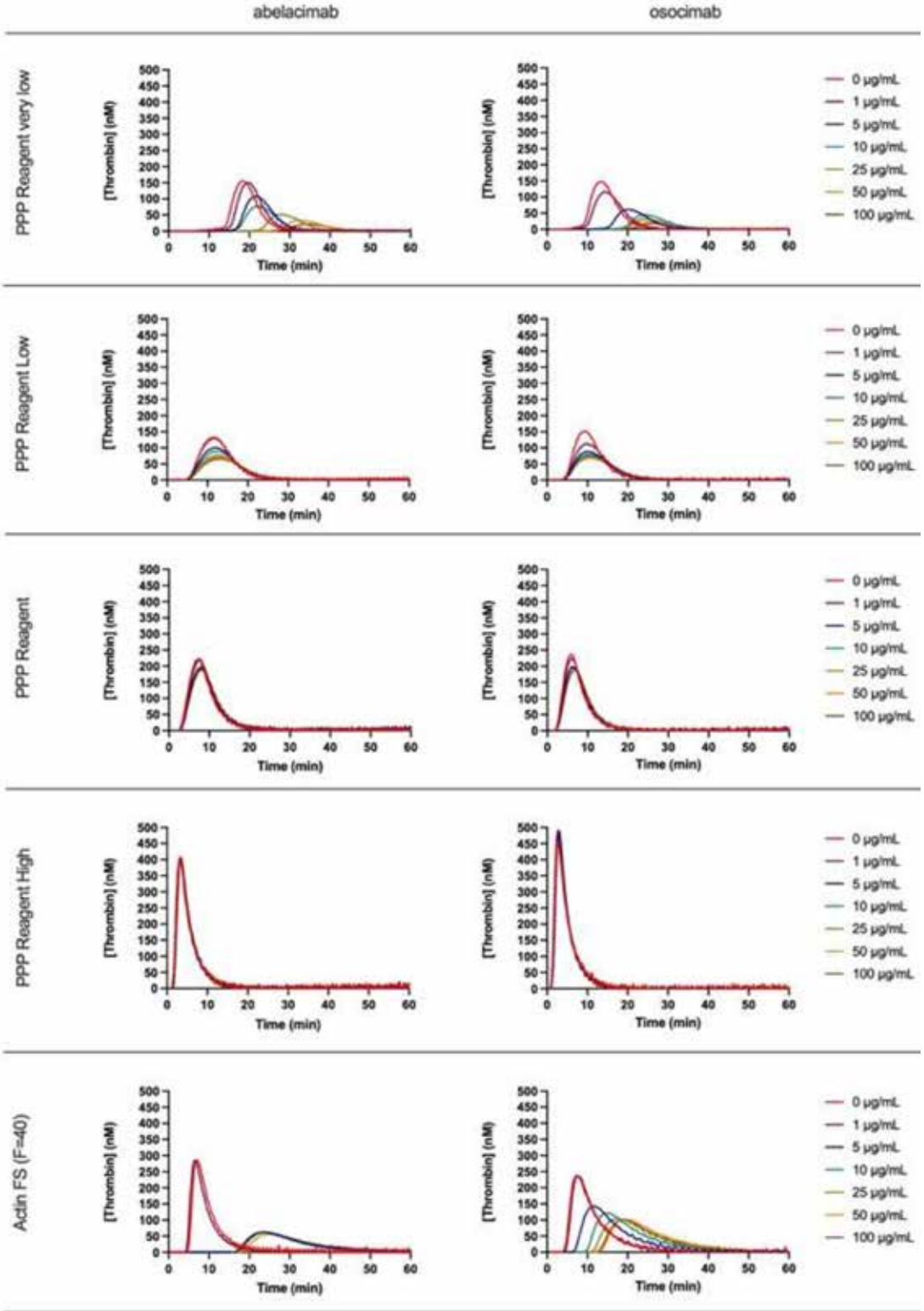
Methods: Normal pooled plasma (Namur Exchange Biobank, Namur, Belgium) was spiked with intermediate solutions of abelacimab and osocimab (dilution factor=20) to yield final concentrations ranging from 0 to 100 µg/mL. Thrombin Generation Assay (TGA) was performed on a Calibrated Automated Thrombogram (CAT). Each plasma solution was tested in the presence of five different reagents: 0.1 pM tissue factor (TF), 4 µM phospholipids (PL) (PPP Reagent very low); 1 pM (TF), 4 µM (PL) (PPP-Reagent Low); 5 pM TF, 4 µM PL (PPP-Reagent); 20 pM TF, 4 µM PL (PPP-Reagent High), and a mixture of ellagic acid 0.42 µM and purified phosphatides (Actin FS®, dilution factor=40). Thrombin generation was triggered by adding FluCa Reagent (fluorogenic substrate, buffer, calcium chloride). aPTT (activated partial thromboplastin time) and prothrombin time (PT) assays were performed on an ACL-TOP 700 (HemosIL® reagents) and a STA R MAX (other reagents). The aPTT was realized with four different reagents: HemosIL®SynthASil (activator= silica), STA®-C.K. Prest (activator=kaolin), STA® PTT Automate 5 (activator=silica) and Actin FS® (activator= ellagic acid). Two prothrombin time (PT) assays were carried out with the following reagents: HemosIL®RecombiPlasTin 2G (human recombinant tissue factor) and STA®-NeoPTimal 5 (rabbit brain tissue factor). Statistical analyses were performed with the GraphPad Prism software version 10.6.0 (Boston, Massachusetts USA).

Results: Abelacimab and osocimab significantly delayed and reduced thrombin generation triggered by TF 0.1 pM or ellagic acid 0.42 µM (Figure 1.). Both antibodies also inhibited thrombin generation induced by TF 1 pM, although to a lesser extent (Figure 1.). In contrast, their effect was minimal with TF 5 pM and absent at TF 20 pM (Figure 1.).
Estimated concentrations for a two-fold prolongation of the aPTT were obtained by non-linear regression (abelacimab: one-phase association model and osocimab: two-phase association model): 4.7 [3.4-6.2] and 55.5 [44.0-70.9] µM (HemosIL® SynthASil); 5.2 [4.2-6.3] and >100 µM (STA®

C.K.Prest); 4.0 [3.1-5.2] and 30.4 [23.2-40.8] (Dade® Actin® FS). With the STA® PTT Automate 5 reagents, no two-fold prolongation of the aPTT was observed with either antibody at concentrations up to 100 µg/mL. The PT ratio and INR obtained in the presence of 100 µM of antibodies with the HemosIL®RecombiPlasTin and STA®NeoPTimal reagents were 1.00; 1.01 (abelacimab) and 0.995; 1.07 (osocimab), respectively.

Conclusions: Both abelacimab and osocimab significantly affected thrombin generation triggered by low TF concentrations (up to 1 pM) and ellagic acid 0.42 µM. Moreover, the concentrations of abelacimab required to observe a two-fold prolongation of the aPTT were significantly lower than those of osocimab for three out of four reagents.

Figure 1. Thrombograms showing the impact of increasing concentrations of abelacimab and osocimab on thrombin generation triggered by five different reagents



PPP reagent very low (0.1 pM TF, 4 µM PL); PPP Reagent Low (1 pM TF, 4 µM PL); PPP Reagent (5 pM TF, 4 µM PL); PPP Reagent High (20 pM TF, 4 µM PL); Actin FS®, dilution factor=40 (ellagic acid 0.42 µM and purified phosphatides).
PL: phospholipids; PPP: platelet-poor plasma; TF: tissue factor.
The commercial names of the reagents and analyzer were included to ensure scientific transparency and conciseness.

P06

ABSTRACTS
POSTERS

Assessment of significant levels of direct oral Xa inhibitors in emergency settings

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Background: Direct oral Xa inhibitors (DOACs) are increasingly used for anticoagulation, and therapeutic monitoring is not routinely performed because of their predictable pharmacokinetics. However, rapid assessment of DOAC levels is crucial in specific situations such as perioperative management, bleeding risk assessment, and initiation of reversal therapy. Clinically relevant DOAC cut-offs are defined as 30, 50 and 100 ng/mL, with, for example, 30 ng/mL being often used for initiation of invasive emergency procedures with high risk of bleeding. While chromogenic anti-Xa assays with DOAC-specific calibrators provide accurate measurements, they are not widely available. Many hospitals, however, provide 24/7 anti-Xa testing calibrated for LMWH/UFH, which could be adapted for urgent DOAC assessment.

Aims: (1) To determine anti-Xa thresholds—both heparin-calibrated (IU/mL) and uncalibrated (optical density, OD)—corresponding to DOAC concentrations of 30/50/100 ng/mL, and (2) to assess the impact of reagent lot variability on these thresholds.

Methods: A total of 104 patient samples (apixaban n=37, edoxaban n=44, rivaroxaban n=23) were analysed to measure DOAC concentrations and corresponding heparin-calibrated anti-Xa values using the INNOVANCE® anti-Xa assay (Siemens) on a CN6000 instrument (Siemens Healthineers). Anti-Xa thresholds corresponding to DOAC levels of 30/50/100 ng/mL were calculated via ROC analysis with interpolation, optimizing sensitivity. Threshold validation used an additional 32 patient samples. The impact of reagent lot variation on threshold stability was evaluated by calculating individual lot-dependent thresholds and assessment of the significance of the difference between these thresholds.

Results: Patient samples showed an excellent linear correlation between their specific DOAC concentration and heparin-calibrated anti-Xa level (R^2 >0.99 in IU/mL and R^2 >0.96 in OD). Usage of different reagent lots had a significant effect on the heparin-calibrated anti-Xa thresholds for DOAC levels of 30 and 50 ng/mL ($p<0.05$), with an average difference of 25% between the thresholds determined with different lots. At the same DOAC levels, the effect of different reagent lots on the OD thresholds was non-significant at 2%.
A universal DOAC cut-off (edo-/api-/rivaroxaban) of >30/50/100 ng/mL corresponded to an optical density ≤0.606/0.562/0.384. Because of the inverse relationship between OD and DOAC concentration, and to improve interpretability, OD values will be qualitatively reported to classify patients in relation to their DOAC levels.
An OD threshold of 0.606 reliably excluded clinically significant DOAC concentrations >30 ng/mL, with a sensitivity of 100% (i.e. no wrongly classified samples with DOAC >30 ng/mL) and specificity of 97–100% (i.e. one sample with DOAC ≤30ng/mL that was incorrectly classified) in both the test and validation sets.

Conclusion: This study demonstrates that existing heparin-calibrated anti-Xa assays can be used to rapidly exclude clinically relevant DOAC concentrations in emergency settings. OD-based thresholds showed superior stability, making them suitable for routine use. Implementing these thresholds for classification of patients under DOAC therapy could help clinicians make urgent decisions, such as safely proceeding with surgical interventions, administering intravenous thrombolysis for stroke, or initiating reversal therapy.

P07

ABSTRACTS
POSTERS

A whole blood flow-based model simulating in vivo haemostasis to evaluate the impact of haemodialysis on thrombus formation

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Introduction: Chronic haemodialysis patients are predisposed to both thrombotic and bleeding complications due to the complex interplay of end-stage kidney disease, cardiovascular comorbidities, and the routine use of anticoagulant and antiplatelet therapies. The extracorporeal circuit of the haemodialysis procedure itself also activates coagulation pathways through blood contact with artificial surfaces, platelet activation, and shear stress.

Aims: Using a microspot-based technique, we evaluate the changes in platelet adhesion and fibrin clot formation in real time using flowing whole blood sampled before and after one dialysis session.

Methods: This study is part of a longitudinal cohort involving 210 patients, investigating coagulation in chronic haemodialysis. For this sub-study, we evaluated the impact of a single dialysis session on flow-dependent thrombus formation in ten prevalent patients (mean age 65 ± 13 years; 9 male). Patients received low molecular weight heparin as routine anticoagulation on dialysis days and acetylsalicylic acid (80 mg) daily. Citrated blood was collected pre-dialysis (PRE) and post-dialysis (POST). Platelet-dependent coagulation was assessed by perfusing whole blood over a thrombogenic surface (microspotted with collagen type I and tissue factor) in a flow chamber under medium arterial shear rate (1000 s-1) and physiological temperature. Blood was stained with Alexa Fluor 546 Fibrinogen and DiOC6 for microscopic analysis of fibrin and platelets. Results were compared to data from 26 healthy volunteers.

Results: We observed an increased coagulability in patient samples compared to healthy controls. In 3 PRE samples and 6 POST samples, clots formed immediately upon flow initiation, unlike the controls. POST runs showed increased clot formation, leading to higher pressure and blood flow loss, occurring in seven cases—compared to one in PRE samples and none in controls. This loss of blood flow caused the final 4 minutes of our experiment to be unrepresentative and unusable for analysis under flow conditions.

Using a linear mixed model, we analysed platelet and fibrin surface area coverage across groups (PRE, POST, healthy controls) and time. Platelet adhesion significantly decreased over time in POST samples compared to PRE ($P = 0.005$), while both patient groups were lower than the healthy controls ($P < 0.0001$). No significant differences in platelet-dependent fibrin formation between PRE and POST dialysis ($P = 0.28$) were found, only POST samples showed a slight decrease of 1.9% in fibrin formation rate compared to controls ($P = 0.004$).

Conclusion: Coagulation is increased in hemodialysis patients, even following the administration of low molecular weight heparin during dialysis. Nevertheless, flow-dependent platelet adhesion was significantly impaired in POST samples compared to PRE, and in both dialysis samples relative to healthy controls. These conflicting observations suggest that platelet thrombus formation already occurs in the plasma of dialysis patients, disrupting adequate platelet adhesion, which might explain their predisposition to both thrombotic and bleeding complications. Platelet activation will be investigated further in our longitudinal cohort study of prevalent haemodialysis patients.

Mapping Laboratory Phenotype-Genotype in Von Willebrand Disease: a Belgian National Survey

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P08

ABSTRACTS
POSTERS

Background: Von Willebrand disease (VWD) is the most common inherited bleeding disorder, resulting from quantitative or qualitative deficiencies in von Willebrand factor (VWF). Its heterogeneous clinical presentation and overlapping laboratory profiles complicate accurate diagnosis and subtype classification.

Aims: The B-Will Study aimed to conduct a national multicenter survey to characterize the phenotypic and genotypic spectrum of VWD in the Belgian population.

Methods: A total of 590 patients with suspected or known VWD were recruited based on predefined inclusion criteria: VWF:Ag<35%, VWF:Ac/VWF:Ag<0.6, VWF:CB/VWF:Ag<0.6, FVIII:c/VWF:A <0.5, or positive low concentration RIPA. Families were enrolled by including the proband and at least one affected first-degree relative. Extensive laboratory phenotyping, including quantification of VWF antigen (VWF:Ag), VWF-glycoprotein Ib binding (VWF:GPIbM), VWF–collagen binding (VWF:CB), factor VIII:C, ristocetin-induced platelet aggregation and VWF multimer analysis, and genetic screening (Sanger sequencing and multiplex ligation-dependent probe amplification (MLPA)) were performed in order to establish definitive VWD classification and subtyping.

Results: VWD was confirmed in 511 patients, with type 1 VWD predominated (270/511; 52.8%), followed by type 2 (229/511; 44.8%), with 2M-GPIb and 2A/IIE as the most frequent type 2 subtypes, and type 3 (12/511; 2.3%). Concordance between laboratory phenotype and multimeric pattern was observed in 84.5% of cases. Sequence analysis identified at least one causal mutation in 92.7% of patients, uncovering 127 distinct VWF variants (101 missense and 26 loss-of-function mutations), of which 57 were novel. 13 recurrent mutations accounted for 50% of the cohort with p.Trp1120Ser being the most frequent (10.4%). MLPA detected 5 additional large gene deletions (exon 25 (n=4), exon 4-5 (n=1), exon 33-34 (n=1), exon 36 (n=1), and exon 47 (n=1)) in patients with previously identified mutations (n=5) and in patients lacking mutations (n=3) by direct sequencing, raising overall mutation detection to 93.4%. Phenotype-genotype concordance reached 80.3%.

Conclusion: The B-Will Study significantly enhances understanding of VWD in Belgium, demonstrating that integrated phenotypic and genotypic assessment significantly improves diagnostic accuracy and subtype classification. The resulting biobank and mutation database offer a valuable resource for longitudinal studies, advanced molecular diagnostics, and international collaboration aimed at optimizing VWD management.

Epidemiology of Venous Thromboembolism in Belgium: A Cohort Study

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P09

ABSTRACTS
POSTERS

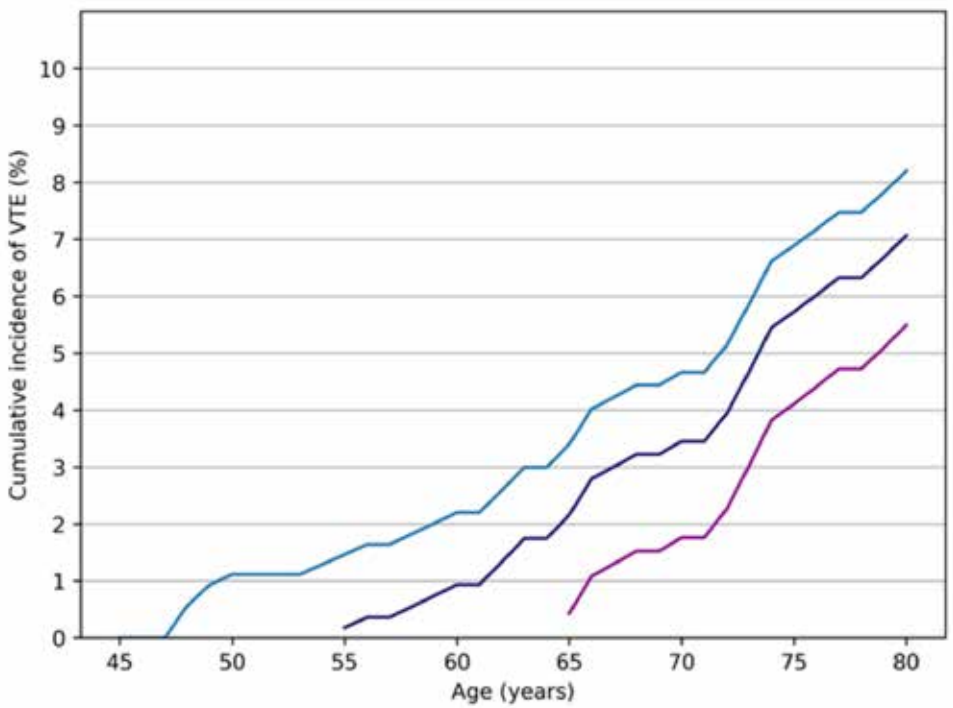
Background: Venous thromboembolism (VTE) is a significant contributor to global morbidity and mortality. Although management strategies and the distribution of risk factors have evolved, contemporary epidemiologic data are limited and have not been previously reported for Belgium. We aimed to characterize the epidemiology of VTE in a contemporary Belgian population.

Aim: To evaluate the epidemiology of VTE in Belgium and identify associated risk factors.

Methods: We conducted secondary analyses of 1448 participants from the Flemish Study on Environment, Genes, and Health Outcomes (FLEMENGHO), an observational, community-based, prospective cohort study. VTE cases occurring between 2000 and 2024 were identified through standardized health questionnaires, medical records, and expert adjudication. The incidence and lifetime risk of VTE were determined, and risk factors for incident VTE were assessed using Cox regression.

Results: Between 2000 and 2024, 63 VTE events occurred during 34906 person-years of follow-up, corresponding to an incidence rate of 1.80 per 1000 person-years. At age 45, the estimated remaining lifetime risk of VTE was 8.2% (95% CI: 5.6-10.8) (Figure). Isolated lower extremity deep vein thrombosis was the most common presentation (42.9%), followed by isolated pulmonary embolism (36.5%). Transient major risk factors were identified in 30.2% of cases. In multivariable analyses, higher BMI (adjusted hazard ratio (HRadj): 1.48, 95% CI: 1.13–1.93) and a history of VTE (HRadj: 10.4, 95% CI: 4.1–26.3) were independent predictors of incident VTE.

Conclusion: Despite advancements in management strategies, the burden of VTE remained substantial in this representative and well-characterized Belgian cohort. The incidence rate is consistent with findings in other Western countries.



P10

ABSTRACTS
POSTERS

Levels, determinants and predictive value of D-Dimer in patients on long-term direct oral anticoagulant for venous thromboembolic disease

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Background/Introduction: D-dimer (DD) testing plays a crucial role in the diagnostic strategy of venous thromboembolic disease (VTED), to determine the duration of anticoagulation and for predicting recurrent VTED after stopping anticoagulant therapy for unprovoked VTED.
Currently, the value of DD assay during long-term (at least 12 months) direct oral anticoagulant (DOAC) therapy to assess antithrombotic efficacy and predict the risk of VTED recurrence is unknown. The hypothesis is that a low (< 250 ng/mL) or normal (< 500 ng/mL) DD concentration on DOAC therapy reflects antithrombotic efficacy and that a high concentration would be associated with an increased risk of recurrence.

Aims: The aim of this study is to evaluate DD concentration in patients undergoing long-term DOAC for VTED, to identify its determinants and its potential predictive value for recurrence during treatment.

Methods/Materials: 190 consecutive annually reviewed patients over 18 years of age with an indication for long-term DOAC therapy for VTED were included. The study took place within the Hemostasis and Thrombosis Unit of the Hematology Division of the Cliniques universitaires Saint-Luc. Several variables that could influence the rate of DD or the risk of recurrence were collected.
This population was categorized based on : DD concentrations (normal or increased for age) and the recurrence of VTED.
We first compared characteristics between groups and then performed multivariate logistic regressions.

Results: The median age of the population was 55 years [43,75 – 66], with 105 males (55,3 %). The median duration of DOAC treatment was 41,5 months [25 – 71,25]. A total of 79 patients (41,6 %) were carriers of at least one thrombophilia. Heterozygous factor V Leiden was the most common trait. More than two thirds (69,5%) were treated with a reduced dose of DOAC.
Twenty-seven patients (14,2 %) were found to have elevated DD levels (> 500 ng/mL), and 18 (9,5 %) when considering age-adjusted DD concentrations. During the study period, 14 patients experienced recurrent VTED (11 with low/normal and three with increased age-adjusted DD levels).
The risk of recurrence was found to be independent of DD concentration. Only active smoking appears to be associated with an increased risk of

recurrence (OR = 9,15). Post-thrombotic syndrome (OR = 6,12) and gonosomal aneuploidy (XXY; XYY) (OR = 115,235) were found to be associated with a higher age-adjusted DD concentration.

Summary/Conclusions: DD concentration during long-term secondary prevention of VTED by a DOAC is low or normal and does not appear to be predictive of recurrence.

From Alert to Diagnosis: Impact of Automated Email Alerts on the Management of Abnormal Coagulation Tests in Preoperative Assessment

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P11

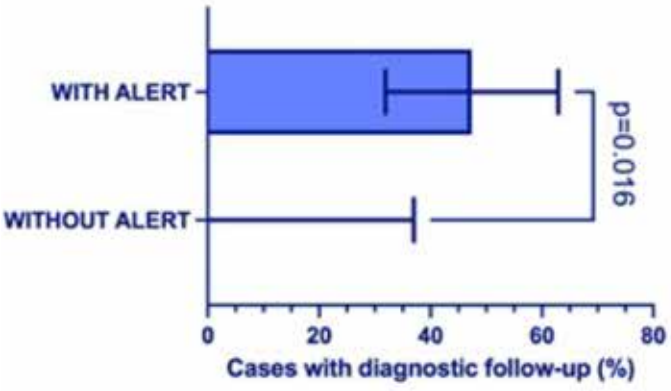
ABSTRACTS
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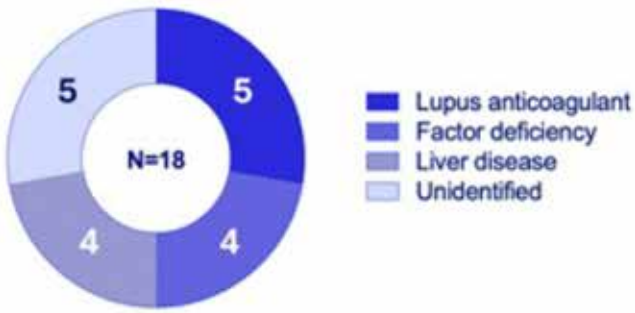
Background: Abnormal coagulation parameters identified during preoperative assessment may indicate underlying bleeding disorders or anticoagulant activity, yet they are often underexplored. Inspired by the automated email alert system implemented for preoperative anemia management (Swennen et al., Transfusion, 2025), we developed and evaluated a protocol sending automated notifications to the treating physician and clinical biologist when abnormal clotting values were detected during preoperative assessment.

Methods: Coagulation tests were requested when an increased risk of perioperative bleeding was suspected based on KCE guidelines (ASA score and type of surgery) or a positive coagulation anamnesis. Subsequently, an automated email alert was triggered when activated partial thromboplastin time (aPTT) exceeded our upper reference level of 37 seconds or when the prothrombin time (PT) fell below 70%. Importantly, an alert was triggered only when the consulting nurse at the preoperative unit had explicitly documented that the patient was not receiving anticoagulant therapy. We retrospectively assessed the number of cases where abnormal coagulation results were further investigated. A case was considered investigated when additional coagulation tests were requested or when an alternative cause was documented in the preoperative notes (e.g. liver disease). Due to a technical incident, no email was generated for a subset of samples with abnormal coagulation results; this group was considered as the control group.

Results: In this single-centre retrospective study conducted from December 2024 until August 2025, 1.8% of all preoperative consultations (n=2928) revealed abnormal coagulation test results in patients without preregistered anticoagulant therapy. In 13% of these cases, the email alert was erroneously triggered because treatment with anticoagulants was not adequately registered in the preoperative documentation. In the remaining cases (n=46), further investigation of abnormal coagulation results was performed in 47% of the patients who received an automated email alert, whereas no further work-up was performed in the control group (n=8). This difference was statistically significant (p=0.016). Of the fully evaluated cases with abnormal results (n=18), the underlying causes were attributed to lupus anticoagulant (n=5), factor deficiency (n=4), and liver disease (n=4). In the remaining cases (n=5), no underlying cause for the abnormal coagulation results could be identified.

Conclusion: Automated email alerts to clinicians and clinical biologists significantly increased the diagnostic work-up of abnormal preoperative coagulation values, although caution is warranted given the small control group. Still, this strategy enabled earlier detection of clinically relevant bleeding disorders and anticoagulant activity, optimizing perioperative safety. Based on these results, the possibility of adding automated reflex tests in the future will be evaluated. It should nevertheless be emphasized that, according to current Belgian reimbursement rules, addition of lupus anticoagulant testing for an isolated prolonged aPTT is not considered an indication for reimbursement. Our findings suggest that automated alerts may represent a scalable approach to standardize and improve preoperative hemostatic assessment.





P12

ABSTRACTS
POSTERS

Evaluation of thrombin generation under Emicizumab as a potential biomarker for Hemophilia A monitoring

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Background/Introduction: The advent of emicizumab—a bispecific monoclonal antibody—has significantly expanded the therapeutic landscape for individuals with hemophilia A. While routine monitoring is generally unnecessary, evaluating a patient's hemostatic function can be valuable in specific situations, such as unexpected bleeding despite treatment adherence, or in preparation for surgery. However, conventional laboratory assays often fail to accurately reflect hemostatic capacity in patients receiving emicizumab.

Aims: To investigate the potential of a modified thrombin generation test (TGT) as an alternative method for monitoring hemostatic activity in patients treated with emicizumab.

Methods/Materials: A modified TGT was conducted on nine samples from both pediatric and adult patients undergoing emicizumab prophylaxis. Emicizumab concentrations were determined using a modified FVIII activity assay, reported as both FVIII-equivalent levels and direct emicizumab quantification. TGT parameters were then analyzed in relation to clinical data and emicizumab levels.

Results: TGT profiles of patients receiving emicizumab displayed intermediate characteristics— positioned between those of healthy individuals and untreated hemophilia A patients—consistent with a mild hemophilia A phenotype. (Figure 1) Significant correlations were observed between emicizumab FVIII-equivalent levels and key TGT metrics, including endogenous thrombin potential (ETP), peak thrombin generation, and velocity index. Additionally, emicizumab quantification showed a notable association with the velocity index.

Summary/Conclusions: These results indicate that the modified TGT may serve as a valuable tool for assessing hemostatic function in emicizumab-treated patients, particularly in clinical situations requiring monitoring.

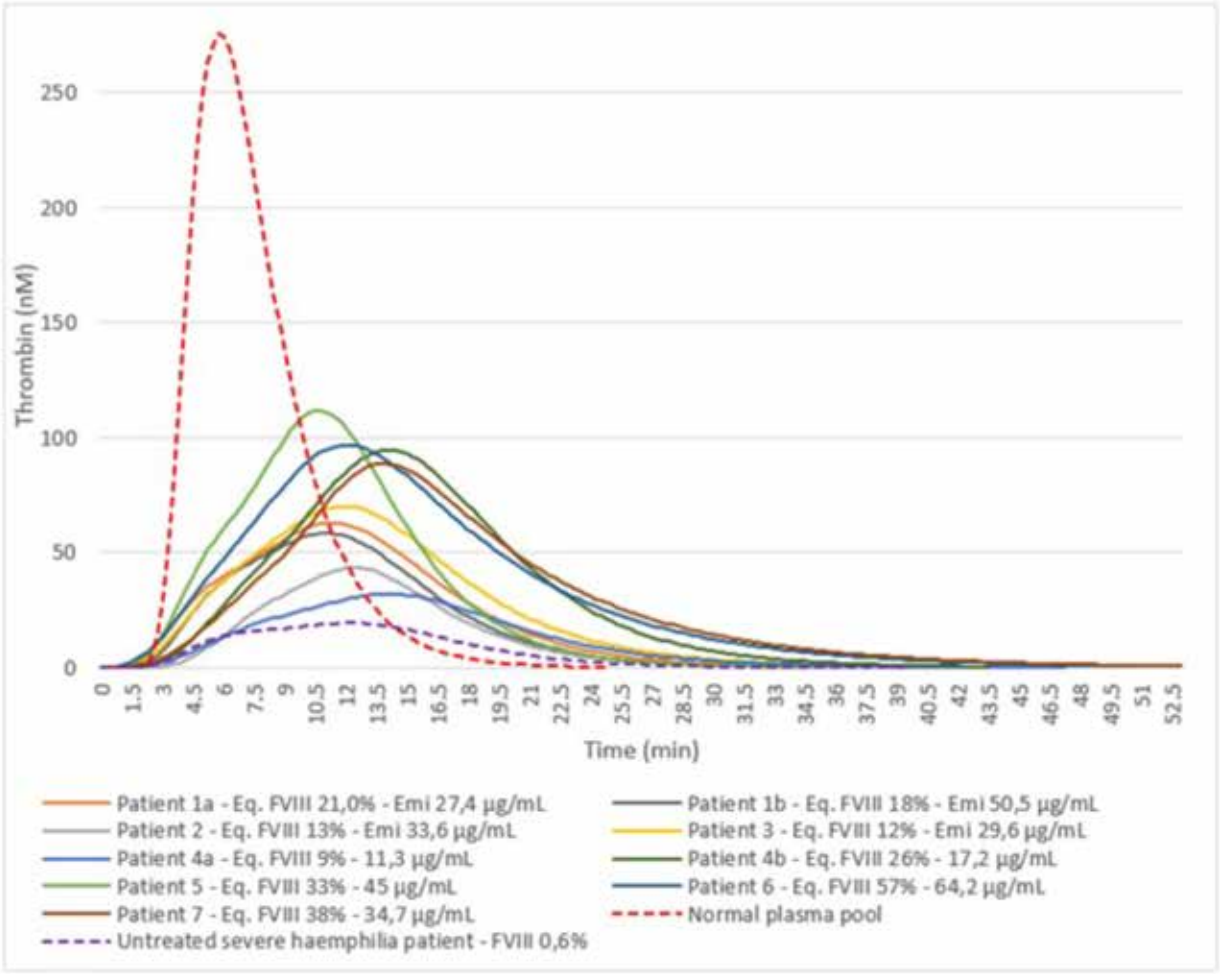


Figure 1 : TGT curves in the presence of FXIa on patient's samples expressed as Emicizumab concentration (µg/mL) and Emicizumab "FVIII equivalent"

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ABSTRACTS
POSTERS

Patient Experiences and Preferences in Hemophilia A and B: Insights from Belgian Patient Advisory Boards

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Background/Introduction: Hemophilia A and B are chronic bleeding disorders that require lifelong management, impacting patients' physical, mental, and social well-being. While advances in therapy have improved clinical outcomes, patient perspectives on treatment satisfaction, administration preferences, obstacles, and daily life impact remain under-explored.

Aims: This study aimed to quantify current treatment satisfaction, preferred administration modes, barriers to optimal care, and suggestions for improvement among adults with Hemophilia A and B. The goal was to inform patient-centered innovation and clinical decision-making.

Methods/Materials: Two semi-structured group discussions to capture qualitative data on treatment experience, satisfaction, obstacles, logistics and preferences were conducted with hemophilia A or B patients in Belgium. To facilitate the discussion, a web-based pre-survey was taken by advisory board members ahead of the meeting. In the survey, respondents were asked a series of best-worst scaling questions about eight treatment characteristics, such as the number of supplies needed, the frequency of administration and the probability of breakthrough bleeds. The survey responses were analysed to derive attribute relative importance. The results were used to guide the advisory board discussion. Verbatim patient quotes were collected to illustrate key themes. Data were analysed using thematic qualitative analysis, focusing on lived experience and primary clinical observations. The questionnaire and treatment characteristic selection was informed by an hemophilia expert and patient representatives.

Results: Treatment satisfaction is generally high, especially among Hemophilia A patients benefiting from modern therapies (notably emicizumab). Core drivers of satisfaction include the effectiveness in preventing spontaneous bleeds, reduction in injection frequency and simplification of administration, with a preference for subcutaneous, prefilled devices. Despite advances, persistent issues include joint damage, cyclical pain before monthly dosing, and ongoing anxiety about unpredictable bleeds. The logistical burden of treatment materials, storage (cold chain), and preparation remains a barrier to spontaneity in daily life, travel, and social activities. Patients describe ongoing mental load, adaptation in work/study, and restricted physical activity. Suggested improvements include longer-acting therapies, oral formulations, room-temperature storage, reduced material complexity, and enhanced bleed coverage. Patients prioritize joint protection and absolute prevention of breakthrough bleeds over convenience.

Conclusions: Patients with Hemophilia A and B express high satisfaction with new therapies but highlight persistent needs for simplified administration, reduced frequency, and improved protection against bleeds and joint damage. During the advisory panel, patient told us preferences vary by age and joint status, with younger patients valuing flexibility and older patients prioritizing joint health. Patient-centered innovations such as prefilled pens, oral options, and room-temperature stability are expected to further improve quality of life and satisfaction. These findings provide actionable insights for tailoring clinical care and guiding future therapeutic development. Validation of these findings is ongoing in a larger quantitative survey.

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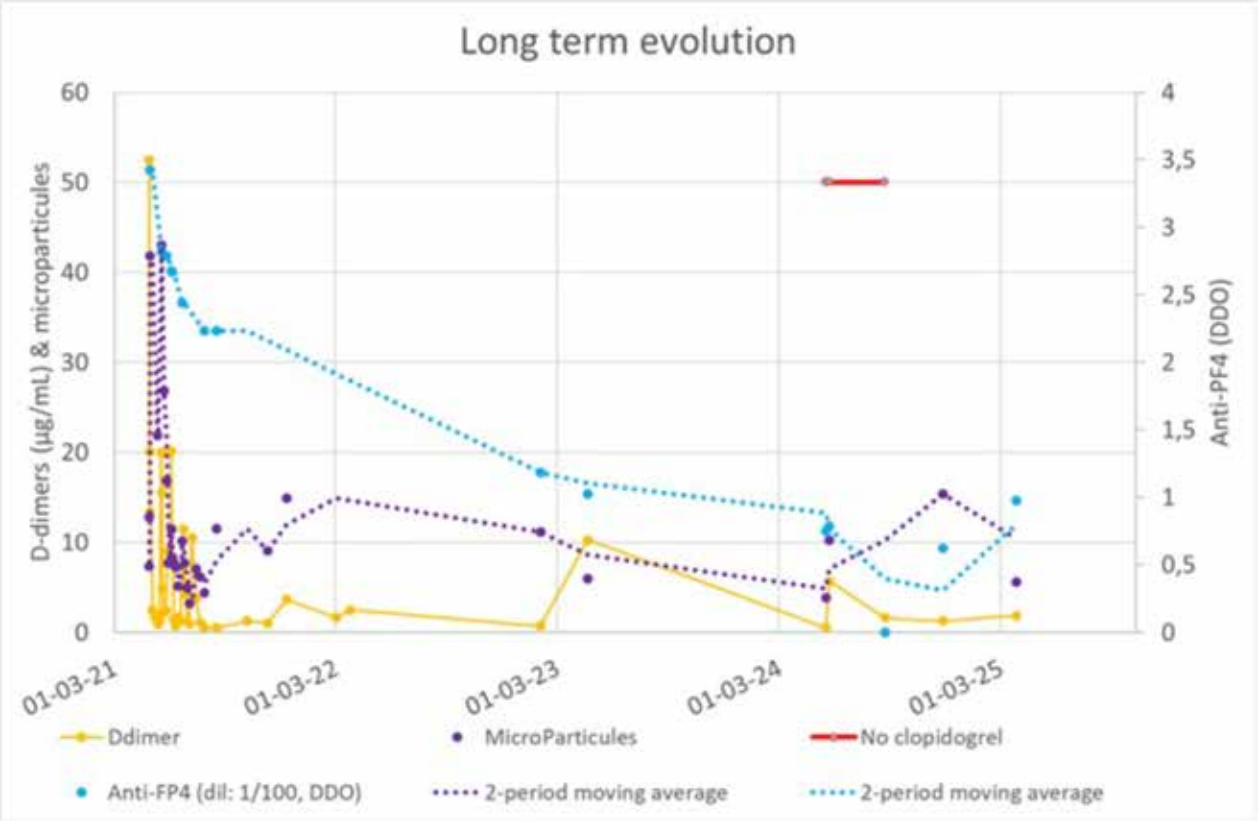
ABSTRACTS
POSTERS

Long time follow-up of a patient with Vaccine Induced Thrombotic Thrombocytopenia following adenovirus vector Covid 19 vaccination

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We report the hemostasis biomarkers follow-up over a 4-year period of a elderly 78-year female patient who developed Vaccine Induced Thrombotic Thrombocytopenia (VITT) following administration of the Astra Zeneca adenovirus vector vaccine for Covid 19. This patient was admitted with hepatic vein thrombosis, thrombocytopenia and high D-dimer. Strong positivity for anti-PF4 polyvinyl sulfate antibodies quickly confirmed the VITT diagnosis. She was successfully treated with a combination of IV IgG and fondaparinux, and then maintained on apixaban and clopidogrel. During the first 6 months, this patient experienced recurrent D-dimer peaks, concomitant with platelet drops, and then tended to stabilize at a slightly elevated level with occasional peaks. Clopidogrel was stopped about 3-years after the VITT disease onset, and this induced increase of D-dimers and microparticles, which normalized when clopidogrel was reintroduced some months after. Platelet count was not impacted.
Platelet counts were performed on a Sysmex XN, D-dimer with STA-Liatest Ddimer (Stago), Platelet procoagulant microparticles (MP) with Zymutest MP-Activity kit, Microparticles exposing TF (MP-TF) with Zymutest MP-TF (all from HYPHEN BioMed) and anti-PF4 IgG isotype using a home-made assay designed with platelet extracted PF4 coated onto an Elisa plate and captured immunoglobulins detected with a goat anti-human IgG peroxidase conjugate. Patient plasma samples were tested at the 1:100, and 1:500 dilutions (positivity for A450 ≥ 0.30).
At patient admission, D-dimers were very high (53 µg/ml) and platelets at 92 G/L. Upon antithrombotic treatment (fondaparinux, followed by apixaban and clopidogrel) platelet count increased and D-dimers concentration decreased. Despite the well-accepted therapy, regular blood activation episodes occurred, concomitant with the D-dimer increase. Anti-PF4 antibodies were at a very high concentration, with an A450 of 2.50 for the dilution of 1:500 (the current assay dilution is 1:100). For the same plasma dilution antibodies to HPF4 had an A450 of about 1.90. Antibody reactivities progressively decreased with time, but stabilized over the past two years. MP and MP-TF followed parallel kinetics to those of D-dimers.
Despite a successful anticoagulant and antiaggregant therapy combination and a rapid normalization of platelet counts the patient had recurrent episodes of hemostasis activation evidenced by D-dimers, MP and MP-TF peaks. Temporary discontinuation of antiplatelet therapy 4 years later resulted in a D-dimers rebound, requiring the reinstallation of the antiplatelet therapy. Today, 4 years after the VITT onset, the patient is correctly stabilized with this dual antithrombotic treatment. This prospective follow-up shows that, at least in this patient, anti-PF4 IgG autoantibodies

generated in VITT, can last for long-time periods of several years, although the concentration is decreased comparatively to that in the acute phase. Following a progressive decrease the first year following the VITT onset, anti-PF4 autoantibodies remain stable at a pathological level, requiring the maintenance of both antiaggregant and antithrombotic therapy (expert opinion open to discussion).



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ABSTRACTS POSTERS

Validation of the Revohem™ FIB LRT Reagent on the CN-3000 Analyzer: Analytical Performance and Method Comparison

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Introduction: Fibrinogen, or coagulation factor I, is a 340-kDa glycoprotein encoded by FGA, FGB, and FGG on chromosome 4. This protein is pivotal for hemostasis, mediating platelet aggregation and acting as the substrate for fibrin formation during hemostasis. Congenital and acquired fibrinogen disorders result in quantitative or qualitative defects and are identifiable by the Clauss method, which measures thrombin-induced clotting in diluted plasma.

Aims: The aim of this study was to evaluate the analytical performance of the Revohem™ FIB LRT reagent on the Sysmex CN-3000 analyzer, addressing repeatability, interday laboratory precision, accuracy, linearity, limit of quantification (LOQ), stability, carryover, and interference. The performance was compared with established thrombin reagents (Dade Thrombin, QFA Thrombin) on both the CN-3000 and ACL TOP CTS 300 analyzers.

Methods and Materials: Analyses were conducted with three reagents on Sysmex CN-3000 and Werfen ACL TOP CTS 300, using calibration with appropriate calibrators and daily quality controls. Repeatability and interday laboratory precision were assessed with plasma pools and control samples. The acceptance limits were set based on Ricos criteria (CV % < 5.4%). Accuracy was quantified with Sciensano external controls. For the method comparison, plasma samples from 40 patients were analyzed using Deming regression and Bland-Altman analyses. Hemolysis interference was evaluated by exposing pooled plasma samples to different levels of hemolysis. This hemolysis was artificially induced in vitro by freezing a small quantity of plasma together with a quantity of red blood cells, recording results at hemoglobin concentrations up to 400 mg/dL. Further evaluations included linearity and LOQ (serial dilutions), stability (0–48h), and carryover were assessed using patients plasma.

Results: Revohem FIB LRT demonstrated excellent repeatability and inter-day laboratory precision, with all CVs below 5.4%. Accuracy was confirmed by Z-scores consistently below clinical thresholds (Z-score < 3). Deming regression analysis indicated that, the Revohem Fib LRT® compared to the Dade Thrombin reagent, the regression slopes showed neither systematic nor proportional bias. In contrast, both a systematic and a proportional bias were observed between the Revohem Fib LRT® and the QFA Thrombin assays.
Notably, the hemolysis interference study revealed reagent-specific differences: Revohem FIB LRT and Dade Thrombin maintained analytical robustness, showing negligible bias, with fibrinogen results stable even at high hemoglobin concentrations. In constrat, increasing hemolysis induced fibrinogen overestimation at low to moderate levels and pronounced variability under severe hemolysis, indicating loss of reliability.

Additional performance for Revohem FIB LRT included linearity from 0.84 to 7.18 g/L, LOQ below 0.7 g/L, <5% sample bias after 48 hours, and a carryover of 1.12%.

Conclusions: The Revohem FIB LRT reagent on the CN-3000 analyzer showed robust analytical performance and high commutability with reference methods. Unlike QFA Thrombin, it maintained analytical accuracy in the presence of hemolysis. These findings support its use for reliable fibrinogen quantification, contributing to improved result standardization and patient care in the clinical hemostasis laboratory.

Reliable monitoring of Efanesoctocog Alfa: Performance of Actin-FS One-Stage assay with EFA-Specific calibration curve

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ABSTRACTS
POSTERS

Background/Introduction: Efanesoctocog alfa (EFA) is an innovative factor VIII (FVIII) replacement therapy for hemophilia A. Its laboratory monitoring remains challenging, as assay performance varies depending on the reagents used. A recent study showed that a one-stage clotting assay (OSA) using Actin-FSL (Siemens Healthineers, Erlangen, Germany) provides sufficiently accurate results, within ±25% of expected FVIII activity.

Aims: To assess the accuracy and precision of OSA using Actin-FS reagent (Siemens Healthineers, Erlangen, Germany) with an EFA-specific calibration curve.

Methods/Materials: Nine lyophilized plasma samples spiked with predetermined EFA concentrations were analyzed by two OSA approaches: one with Actin-FSL and another with Actin-FS incorporating an EFA-specific calibration curve. Measured FVIII activities were compared with target values. For 4 samples, results were also compared with standard OSA and chromogenic substrate assay (CSA) available in our laboratory.

Results: The OSA using Actin-FSL demonstrated an average bias of +17.1% (range –1.5% to 35.6%). In comparison, the OSA using Actin-FS with an EFA-specific calibration curve yielded a lower average bias of 3.0% (range –8.8% to 14.8%). These findings align with previously reported overestimation observed in OSA using Actin-FS with standard calibration, as well as in CSA employing bovine and human reagents. (Table 1)

Summary/Conclusions: The use of Actin-FS reagent in OSA, when paired with an EFA-specific calibration curve, presents a promising and cost-effective method for reliable FVIII activity measurement in patients receiving EFA therapy. While additional validation in clinical samples is necessary, this strategy supports routine laboratory monitoring and has the potential to enhance therapeutic decision-making

Table 1: Results of FVIII activity in plasma samples spiked with different concentrations of Efanesoctocog alfa and ECAT external quality controls with OSA using different reagents.

	Expected FVIII activity (IU/dL)	FVIII activity - OSA Actin-FSL with standard calibration (IU/dL)	FVIII activity – OSA Actin-FS with efanesoctocog alfa calibration (IU/dL)	FVIII activity - OSA Actin-FS with standard calibration (IU/dL)	FVIIIc (bovine) with standard calibration (IU/dL)	FVIIIc (human) with standard calibration (IU/dL)
EFA 100 IU/dL	100	/	97.6	/	/	/
EFA – Dil 1	75	83.9	74.3	/	/	/
EFA – Dil 2	60	69.4	57.8	/	/	/
EFA – Dil 3	33.3	43.6	35.2	/	/	/
EFA – Dil 4	30	37.8	29.7	/	/	/
EFA – Dil 5	15	19.9	14.8	/	/	/
ECAT 24–1	5.0	6.6	5.9	15.0	10.9	12.0
ECAT 24–2	20.0	22.0	21.0	47.6	41.0	57.0
ECAT 24–3	50.0	55.8	52.3	118.1	105.7	123.9
ECAT 24–4	100.0	102.2	102.6	215.4	190.9	211.6

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NOTES

NOTES



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