ECTH2016

ECTH2016

European Congress on
Thrombosis and Haemostasis

The Hague, The Netherlands

28 - 30 September

ECTH 2016

28 - 30 September

WELCOME

It was a great pleasure to welcome you to The Netherlands, a country marked by rich cultural heritage and a long and prestigious history of seminal scientific discoveries.

The Hague was the perfect location to bring together researchers and health professionals from across Europe in the spirit of collaboration, discussion and the translation of science. The first European Congress of Thrombosis and Haemostasis was an important event for the advancement of the field in Europe.

In addition to selected abstract presentations, state of the art lectures and plenaries, we had guided 'TEDx-style' science showcases in the "Science, Fast and Furious" sessions. We had poster sessions, integrated academia-industry symposia, and thematic host areas where you have met your colleagues for discussions about new ideas and future challenges.

In this magazine you will find the highlights of the first ECTH.

THE ECTH BOARD

Tilman Hackeng

John-Bjarne Hansen

Danijela Mikovic

Pierre Morange

Flora Peyvandi

Bernhard Nieswandt

Frits Rosendaal

Trevor Baglin

Bleeding | Clotting | Platelets | Vessel wall

ECTH 2016 | European Congress on Thrombosis and Haemostasis

ECTH 2016

Wednesday 28 September

PHD CAREER LUNCH

It is lunchtime and the brightly lit foyer of the World Forum has filled with young ECTH attendees.
While enjoying lunch, these young academics of more than 40 different nationalities, seize the opportunity to meet and greet with their possible future employers.

ATTENDEES IMPRESSIONS

FREDRIK DENORME

From Belgium | PhD at Katholieke Universiteit Leuven

Fredrik is researching ischaemic stroke.

"I would like to connect to new people, and to get an update on recent findings in the field. I am at the end of my PhD and hope to make new connections for my post doc."

ERNA VAN BALEN

From The Netherlands | PhD student at LUMC, Clinical Epidemiology

Erna's is doing research about improving care in haemophilia.

"This field is fairly new to me and I basically want to learn as much as I can about blood. To expand my horizon but also deepen my knowledge about my own field."

YACINE BOULAFTALI

From France | Research scientist at Inserm, specialized in Vascular Biology

"The fast and furious talks were very interesting, since they are quite similar to TED talks, that I love very much. It felt like the speakers were more present in the talk and enjoyed to be on the stage, trying to convince the audience of their research."

"It's a nice first congress and it looks like it is designed for the next generation of scientists. I do have a suggestion for future editions to maybe have smaller rooms, where especially young scientists will feel more comfortable to ask questions. Even if they seem stupid."

Introduction on Malcolm Macleod:

"This lecture touches upon our field, but isn't about thrombosis. It's about so much more, it is meta thrombosis perhaps."

"He has done excellent research in science, and has an interest in quality of science, or perhaps I should say: a lack of quality of science."

MALCOLM MACLEOD

Malcolm Macleod is a clinical neurologist and stroke trialist, with a special interest in the quality of laboratory research and the reduction of what he calls research waste

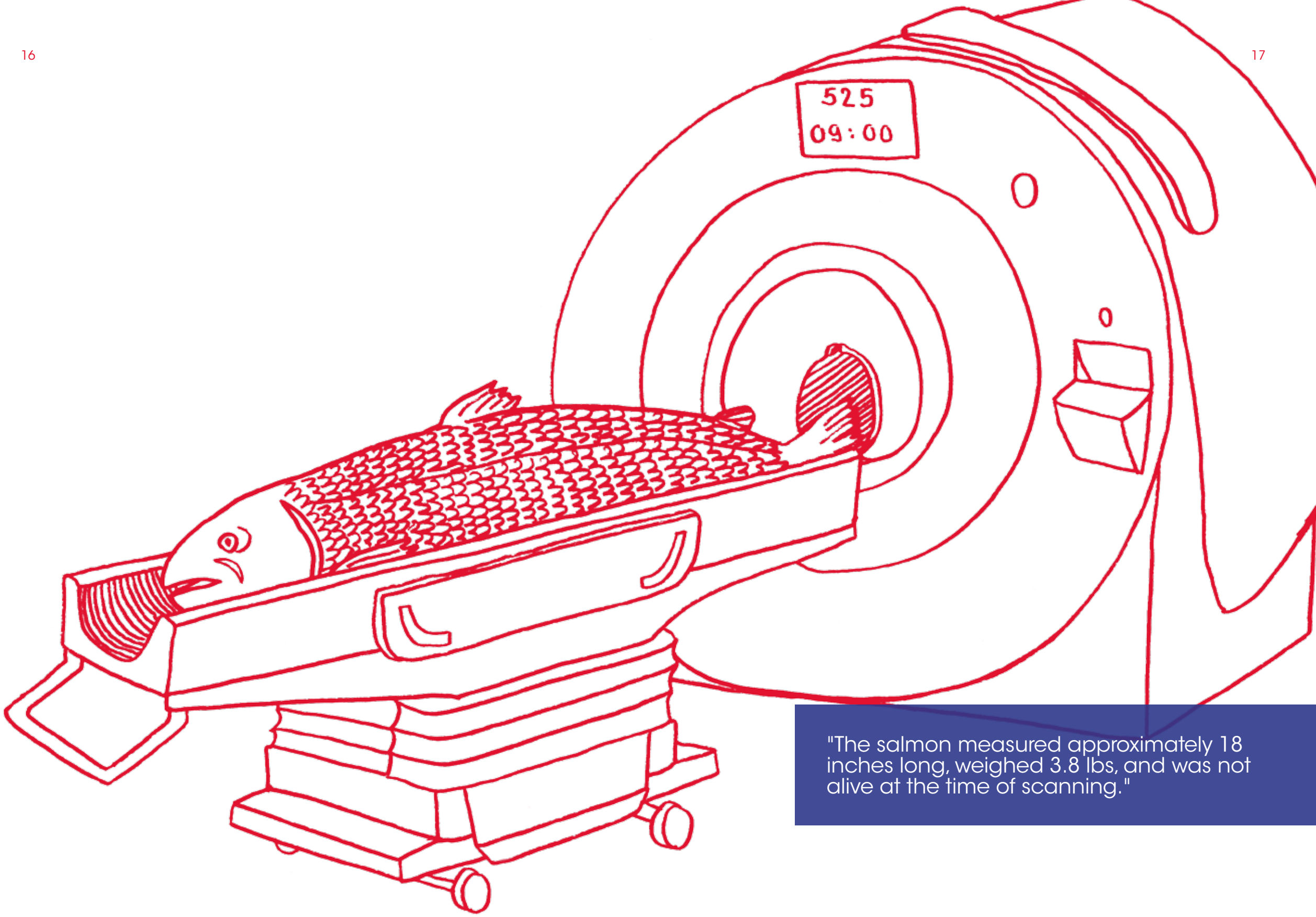
"I do have a slight interest in thrombosis, but I want to talk to you about what I have learned in neurology and the newer science and how we can improve the quality of the research that we do."

"I want to tell you a little bit about how I think research goes wrong and how we can put it right."

"Allow others to check your work. Make all your data available, even if you need a sunrise clause."

"Setting research priorities is about asking questions relevant to users of research. High-level questions are addressed, important outcomes assessed and clinicians and patients are involved in setting research agendas."

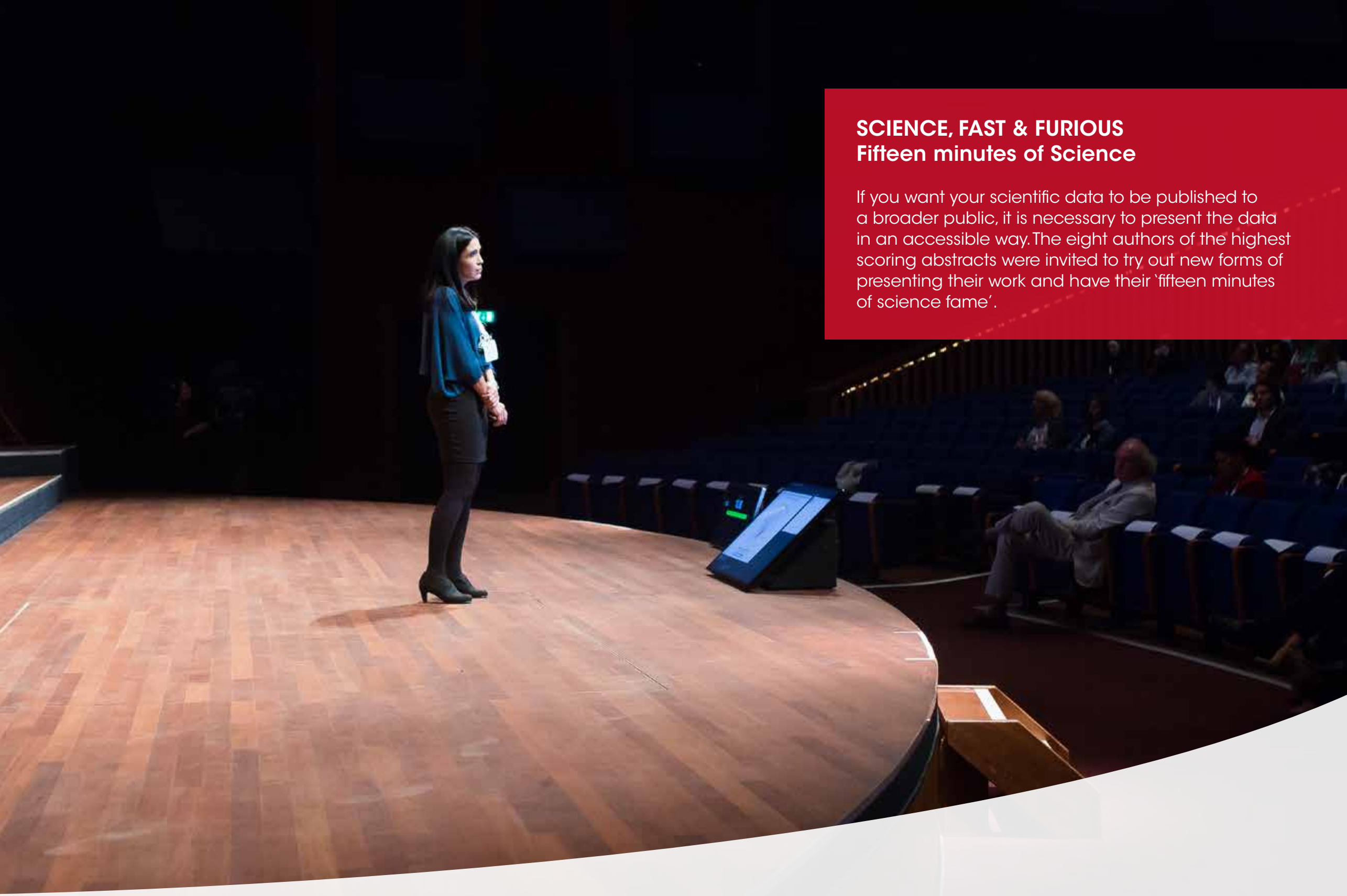
"So what's happening with the publication bias, is that the investigators sometimes decide to set their studies aside if the results don't tell us anything. Therefore, the responsibility for publication bias rests, at least in part, in this room."



"The salmon measured approximately 18 inches long, weighed 3.8 lbs, and was not alive at the time of scanning."

ECTH 2016 | European Congress on Thrombosis and Haemostasis

"Allow others to check your work. Make all your data available, even if you need a sunrise clause."



SCIENCE, FAST & FURIOUS
Fifteen minutes of Science

If you want your scientific data to be published to a broader public, it is necessary to present the data in an accessible way. The eight authors of the highest scoring abstracts were invited to try out new forms of presenting their work and have their 'fifteen minutes of science fame'.

MARIA LUISA LOZANO

Characterization of two novel RASGRP2 variants leading to defective CalDAG-GEFI- mediated RAP1 activation and platelet dysfunction

"During this congress there has been a major contribution in uncovering the molecular and functional basis of the defect in significant number of patients. These patients were previously categorized as having platelets signalling defects."

"We now know that more than 10% of the patients previously lumped into the group of platelet signalling disorders have mutations in RASGPR2, causing platelet and neutrophil dysfunction."

"The dream would be to take a microscope, and a bone and take the bone into the microscope and analyse the whole bone. But real life is more difficult."

"We could prove through the combination of 3D microscopy and computational simulations that megakaryocytes do not directly migrate towards vessels."

MARI GORELASHVILI

Light sheet fluorescence microscopy (LSFM) and subsequent quantitative structural analysis of megakaryocytes in intact murine bone

JASMIJN TIMP

Modeling the risk of recurrent venous thrombosis – Where are we now and what can we add?

"To determine the optimal duration of anticoagulant treatment, after a first venous thrombosis event, we need knowledge of the risk of recurrent VT."

"The predictive performance of the currently available prediction models for recurrent VT seems suboptimal and the discriminative performance of the models decreased somewhat when we used the exact studies' definition of unprovoked VT and the performance decreased with C-statistics below 0.6."

"Considerations for an optimal prediction model are: to build on existing work, include additional predictors, and develop a prediction model for all patients with VT."

"It was known that platelets and T-cells are major contributors to infarct progression in ischaemic stroke."

"When using advanced microscopy we revealed that in the absence of T-cells fewer thrombi are observed in the ischaemic brain."

"However, our data indicate that occlusive thrombus formation is not the major cause for infarct progression in ischaemic stroke."

DAVID STEGNER

Thrombotic activity in the acutely ischaemic brain is dramatically reduced in T-cell deficient mice

OPENING CEREMONY

After the last presenter of the Science, Fast and Furious talks has taken a seat, the King Willem Alexander room quietens and darkens. From above, we can hear the subtle sounds of a horn section, playing the James Bond tune, followed by a dazzling drum performance on stage. The European Congress on Thrombosis and Haemostasis is officially opened.

"In The Netherlands we have a longstanding tradition in research and clinical work in the field of thrombosis and haemostasis. We make up about 5% of the ISTH members."

"What do our 250 Dutch NVTH members share? A true passion for thrombosis and haemostasis, regardless of background or affiliation and institution."

"This congress is counting 760 delegates, from 42 countries of whom 69% are not from The Netherlands."

SASKIA MIDDELDORP
Host ECTH 2016 and president NVTH

FRITS ROSENDAAL
Board ECTH 2016

"Putting the congress together was like doing an existential exercise. We began finding the answers to the following short questions, which were: Why, How, What, Where and Who."

"Instead of flowers, every invited speaker in this congress will receive a Waka Waka. It's the smallest personal power station on earth that works on solar energy."

"When you buy one, you give one. Every year, over 300,000 people in Africa die, due to fires from kerosene that people use to have light after sunset. Every round of applause that you will give to a speaker, means help for people in Africa that have fallen victim to kerosene fires."

MAURITS GROEN
Co-founder WakaWaka

The keynote lecture of this ceremony was supposed to "reflect on ways to increase synergy across Europe to improve the chances of funding and the relevance of research". But as soon as the fictional "Daniel Rüge, the German Minister of Education and Health" entered the stage and started talking, it became clear that this speech was going to be quite different than expected.

When Rüge entered the stage and started speaking in German - leaving everyone in the room flabbergasted.

One of the crew members appeared from the curtain behind him, saying: "Professor, English please."

Rüge then continued: "Ladies and gentleman, I am afraid my English is not great. So please excuse my terrible accent. Several times I've had people joking, telling me: if it weren't for "Allo Allo", we would not understand a word you were saying."

DANIEL RÜGE
Staatssekretär im Bundesministerium für Bildung und Forschung

OPENING CEREMONY

& Welcome reception

ECTH 2016 | European Congress on Thrombosis and Haemostasis

ECTH 2016

Thursday 29 September

PLENARY LECTURE

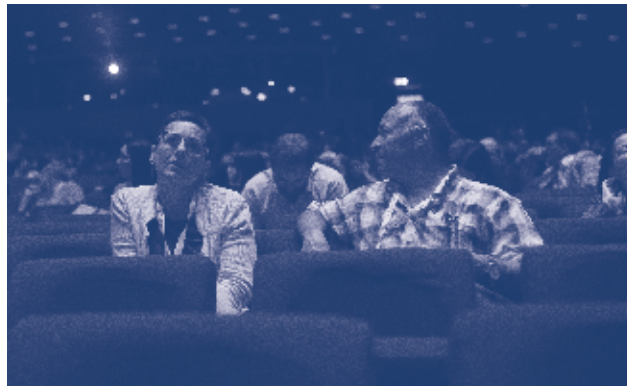
Antithrombotic therapy: now and in the future
by Harry R. Büller

Introduction on
Harry R. Büller:

"He is a professor of internal medicine, specialised in Vascular Medicine at the Academic Medical Center in Amsterdam. I don't think Harry Büller needs any introduction, because he is the most famous trialist."

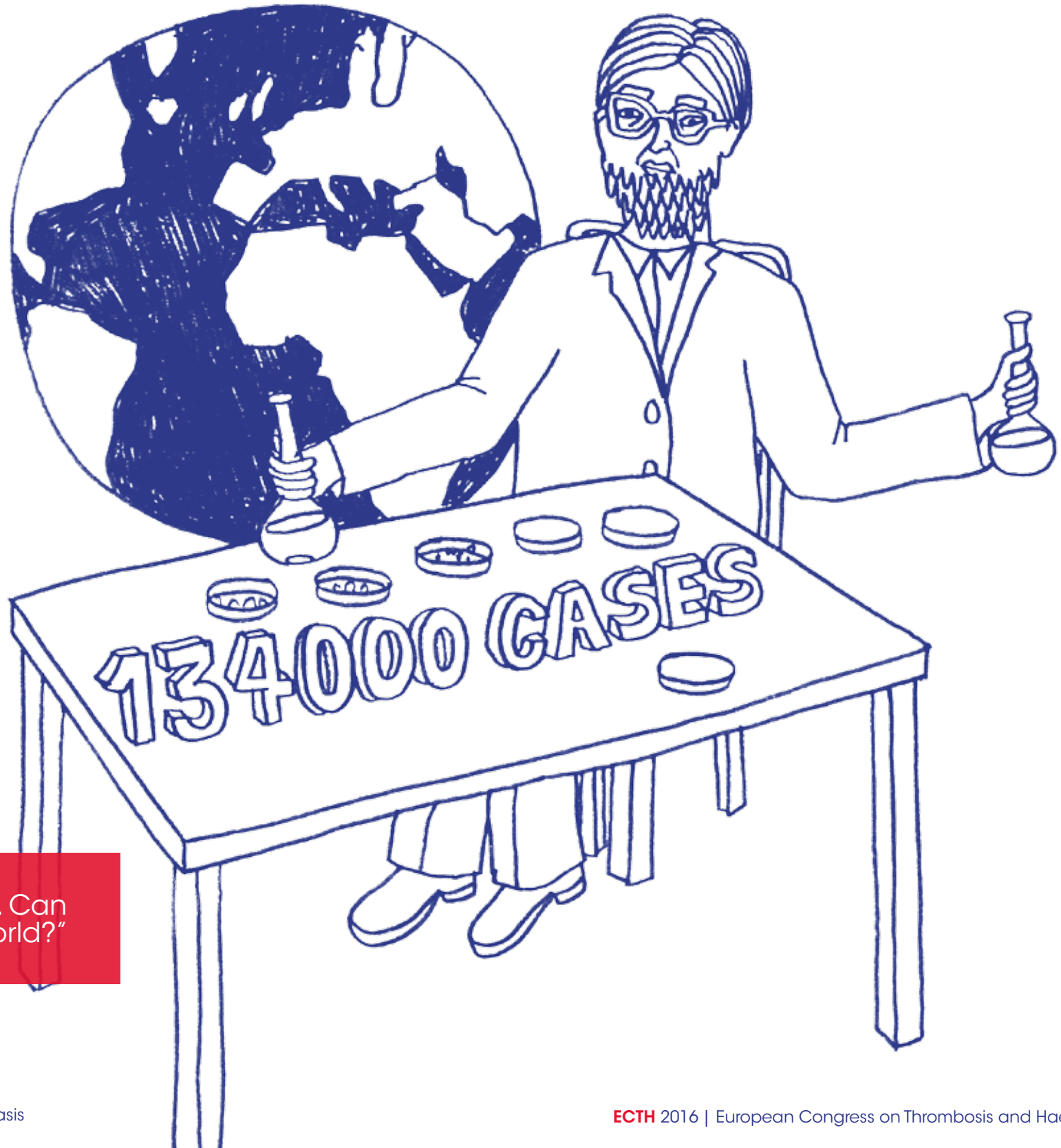
HARRY R. BÜLLER
Antithrombotic therapy: now and in the future

"I actually hate real world, because it suggests that what happens in the trials is not the real world."



"If it is true that with a simple addition of a statin, on top of anticoagulants, we are able to reduce the risk of recurrence by 25 to 30%, that would be really fantastic."

"In the DOAC period we have witnessed the battle of: "are you in favour of the thrombin inhibitor or are you a believer of the Xa inhibitor? This battle has now been set by the clinical data. But as we have already witnessed in the presentation by Thomas Renné, we are going to see a new era of anticoagulants in the next five to ten years and I can assure you, a new battle will arise, between factor XIa and XIIa."



"FDA studied 134,000 thrombosis cases. Can the results be reproduced in the real world?"

"If someone coughs up a cup of blood it is not a major bleed."

ECTH 2016 | European Congress on Thrombosis and Haemostasis

STATE OF THE ART

THOMAS RENNE
The contact pathway: an ideal target for antithrombotic therapy

"FXII-driven contact system is essential for (pathological) thrombus formation but has no function for haemostasis."

"FXII inhibition offers a safe strategy for prevention of thromboembolic disease with implications for ischaemic stroke, atherothrombosis, & cancer-associated VTE."

"Polyphosphate is an in vivo activator of the FXIIa-driven contact-system with implications for thrombotic (and allergic/ anaphylactic) diseases."

"Targeting platelet polyphosphate provides thromboprotection and does not affect bleeding, indicating that polyphosphate operates via FXII-contact activation in thrombosis in vivo."

"NAC prevents TTP signs in Adamts13-/- mice."

"NAC reduces HMW VWF multimers in Adamts13-/- mice."

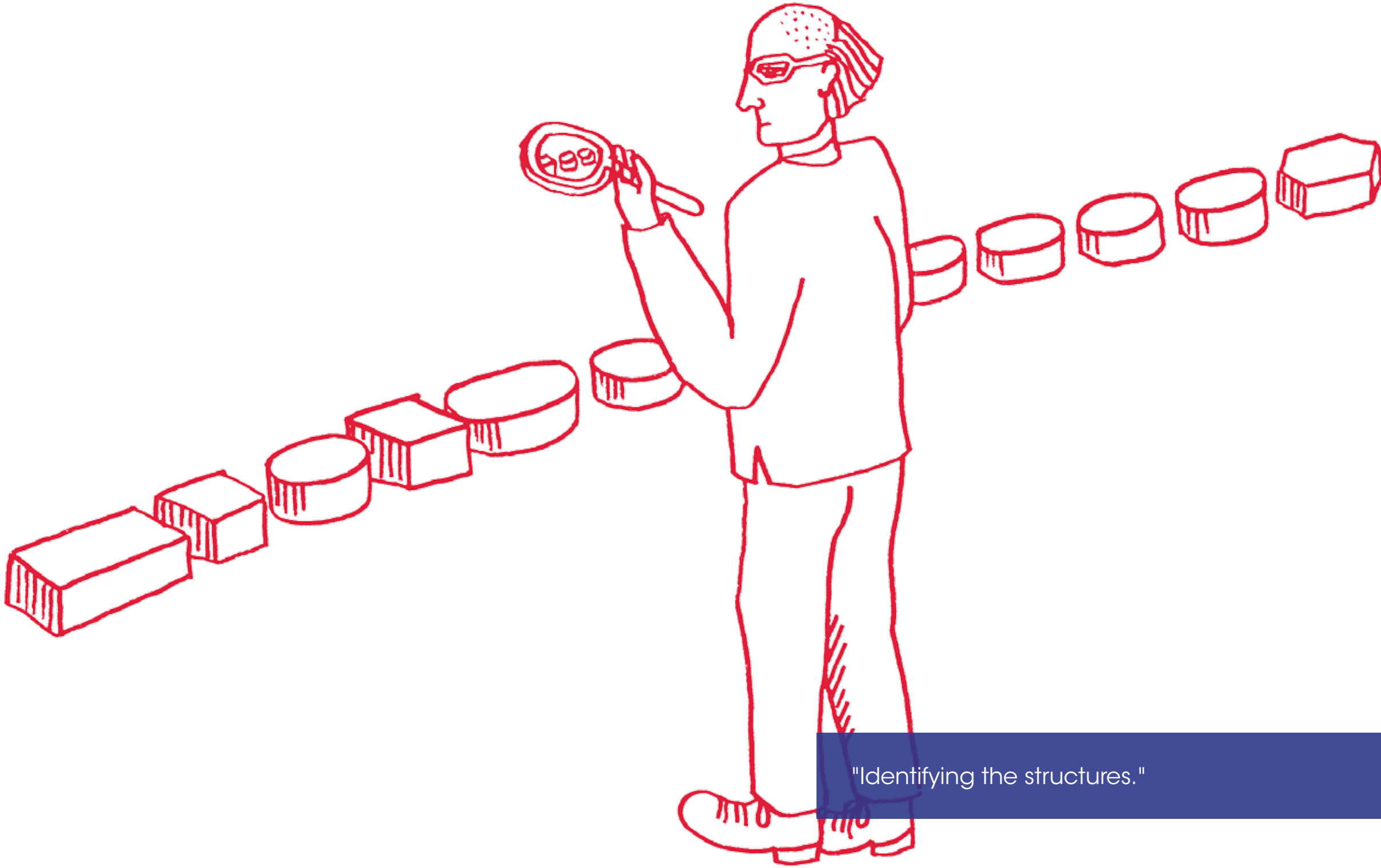
"NAC is not effective in reversing TTP signs in Adamts13-/- mice."

"NAC does not resolve TTP signs in a preclinical baboon model."

"NAC does not dissolve existing VWF-rich thrombi in vitro."

KAREN VANHOORELBEKE

Understanding ADAMTS13 and Thrombotic Thrombocytopenic Purpura



"Identifying the structures."

"We go to South Africa for experiments.
It`s very nice. Especially in the wintertime."

ECTH 2016 | European Congress on Thrombosis and Haemostasis

"Elevated circulatory platelet-oxLDL status corresponds with enhanced thrombotic function."

MEINRAD GAWAZ
Platelets and chemokines

JAVIER CORRAL
Congenital Thrombophilia: new factors and mechanisms

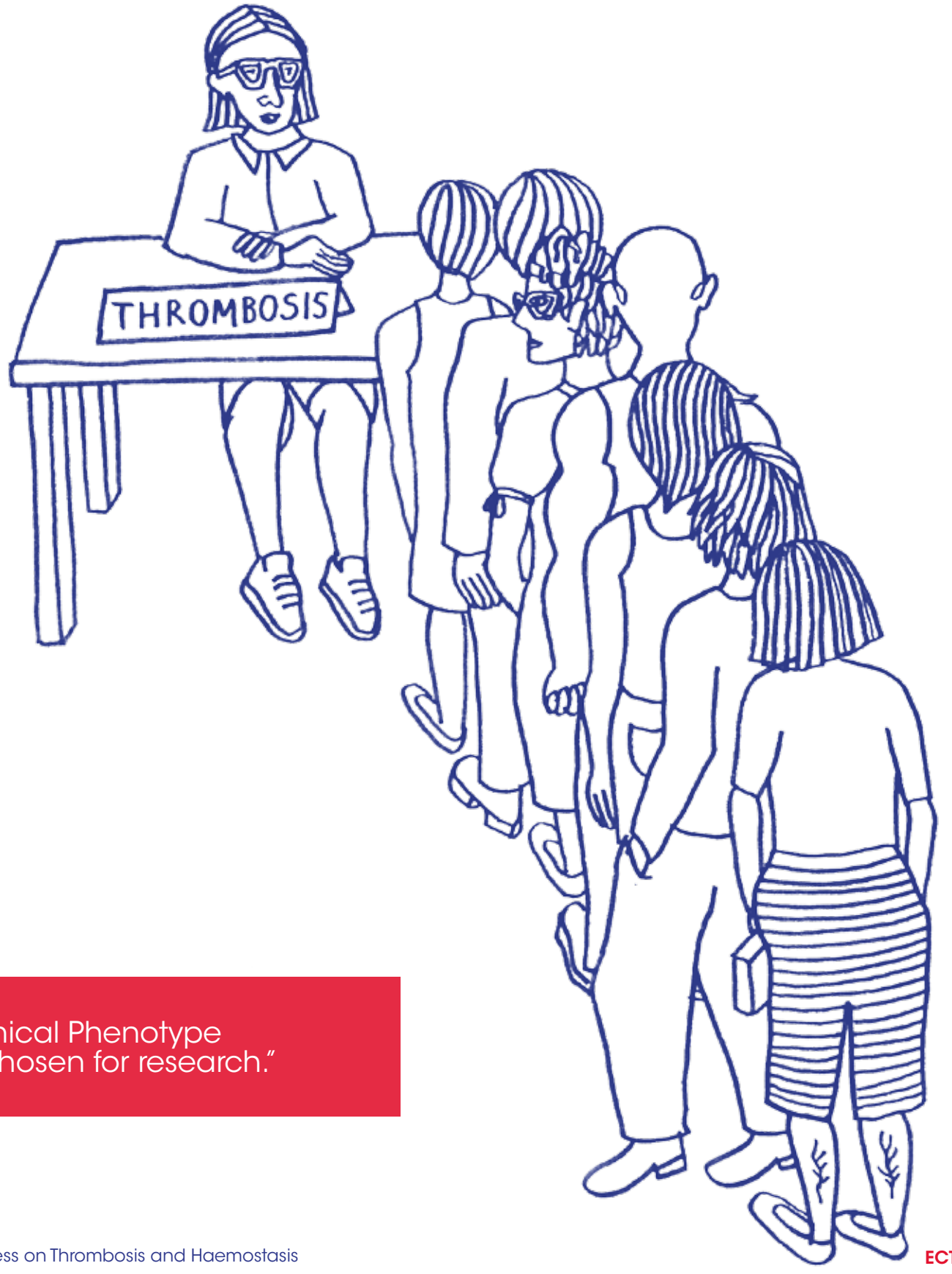
"The history of the identification of gene defects in venous thrombosis started 50 years ago. Strong mutations severely increased the risk of venous thrombosis. We now have to search new genetic risk factors by using different approaches and looking for new mechanisms."

"Thrombosis is a very complex disorder. What I try to show is that many different genes, not only those coding for proteins of the haemostatic system and also environmental factors, interacting with genetic defects play a relevant role in thrombosis."

"Probably the best example is that the identification of genes involved in the glycosylation pathway, together with alcohol intake, are important risk factors for venous thrombosis."

"There are no published results for thrombosis in 2016."

ECTH 2016 | European Congress on Thrombosis and Haemostasis



"30 Patients with Clinical Phenotype (thrombosis) were chosen for research."

ECTH 2016 | European Congress on Thrombosis and Haemostasis

ECTH 2016

Friday 30 September

SCIENCE, FAST & FURIOUS

JAN-JAAP VERHOEF
Platelet polyphosphate forms solid nanoparticles that are exposed on the cell surface and can trigger contact system activation

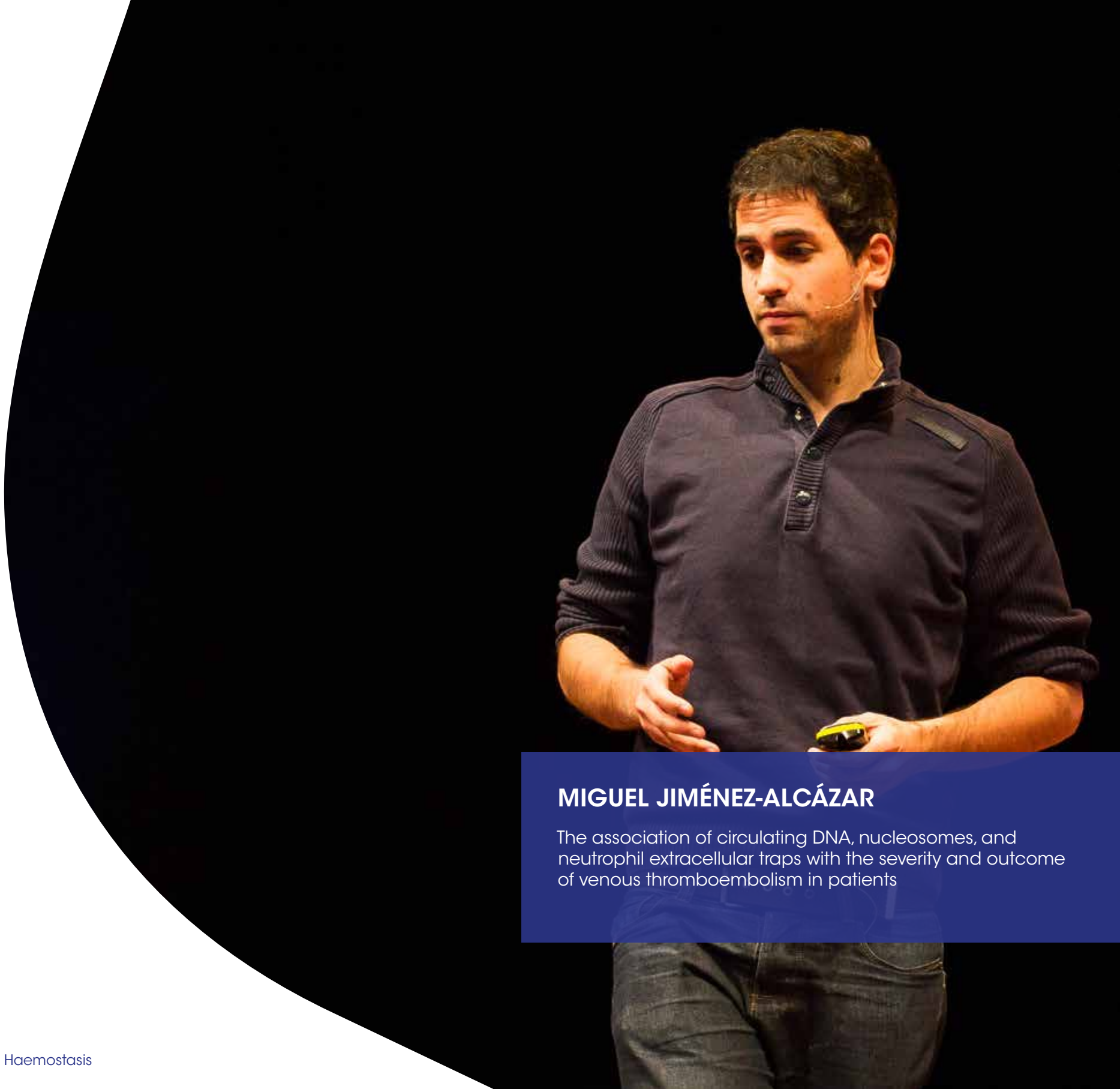
"We found new insights on how polyphosphate is composed within a dense granule blood platelet. Rather than a soluble molecule, we identified that poly-phosphate is complexed as a nanoparticle within blood platelets."

"It's this particulate state that is able to activate the contact system and is responsible for thrombus stability."

"Platelet polyphosphate forms solid nanoparticles that are exposed on the cell surface and can trigger contact system activation."

"The association of circulating DNA, nucleosomes and neutrophil extracellular traps with the severity and outcome of venous thromboembolism in patients."

"What we see is that NET-related markers based on DNA are increased in venous thromboembolism patients. Furthermore, these levels correlate with the extent of the disease, in particular DNA. Levels of DNA correlate with the mortality of patients within three years. We have established that DNA is a powerful and accurate predictive marker of mortality in VTE patients."



MIGUEL JIMÉNEZ-ALCÁZAR

The association of circulating DNA, nucleosomes, and neutrophil extracellular traps with the severity and outcome of venous thromboembolism in patients

MARJOLEIN BREKELMANS
Characteristics and treatment of vaginal bleeding in women with venous thromboembolism treated with apixaban of enoxaparin followed by warfarin

"I would like to raise awareness for this important and burdensome complication, that can affect women treated with oral anticoagulants."

If a bleeding event occurs it is significantly more likely to be of vaginal origin in apixaban treated women, as compared with warfarin."

"I know from my personal experience that women are reluctant to talk about vaginal bleeding complications of oral anticoagulant treatment. Even if I ask them directly they sometimes provide avoiding answers. It is therefore important to provide a safe and trustworthy environment to discuss this issue as it may influence the quality of life.

"There are 17,000,000 people who yearly suffer from a stroke, of which 80% is ischaemic stroke. However, a therapy is not that adequate, since only 5% of patients is helped with this strategy."

"It is important to know the composition of thrombi that cause ischaemic stroke and one particular factor involved are the neutrophil extracellular traps or NETs. It is important to investigate their involvement in stroke thrombus formation, because it could improve current thrombolytic treatment."

ELODIE LARIDAN

Neutrophil extracellular traps in thrombi from patients with acute ischaemic stroke

STATE OF THE ART

"Several coagulation factors and inhibitors have minor splicing variants with unique functional properties."

"The expression of these splicing isoforms varies among individual's and may contribute to shape the individuals risk of VTE."

"Antisense approaches aimed at increasing the relative expression of splicing variants with anticoagulant properties might represent a new strategy to restore the haemostatic balance in thrombophilic individuals."

ELISABETTA CASTOLDI

Modulation of alternative splicing of coagulation genes: a new approach to prevent venous thrombosis

"The behavior of thrombin is eventually altered."

ECTH 2016 | European Congress on Thrombosis and Haemostasis

CECILIA BECCATTINI
Key points in the diagnosis and treatments of venous thromboembolism

"I believe that we can conclude that we have solid data on the need to tailor our diagnostic and treatment strategy and we now have agents that are easy to use and probably safer than conventional treatment of venous thrombotic embolism. And please consider that duration of treatment should probably be individualised, based on the risk for recurrence."

"Haemophilia treatment is likely to be very different in 10 years time."

"Long term outcomes are not just about what treatment is given. How treatment is used is at least as important."

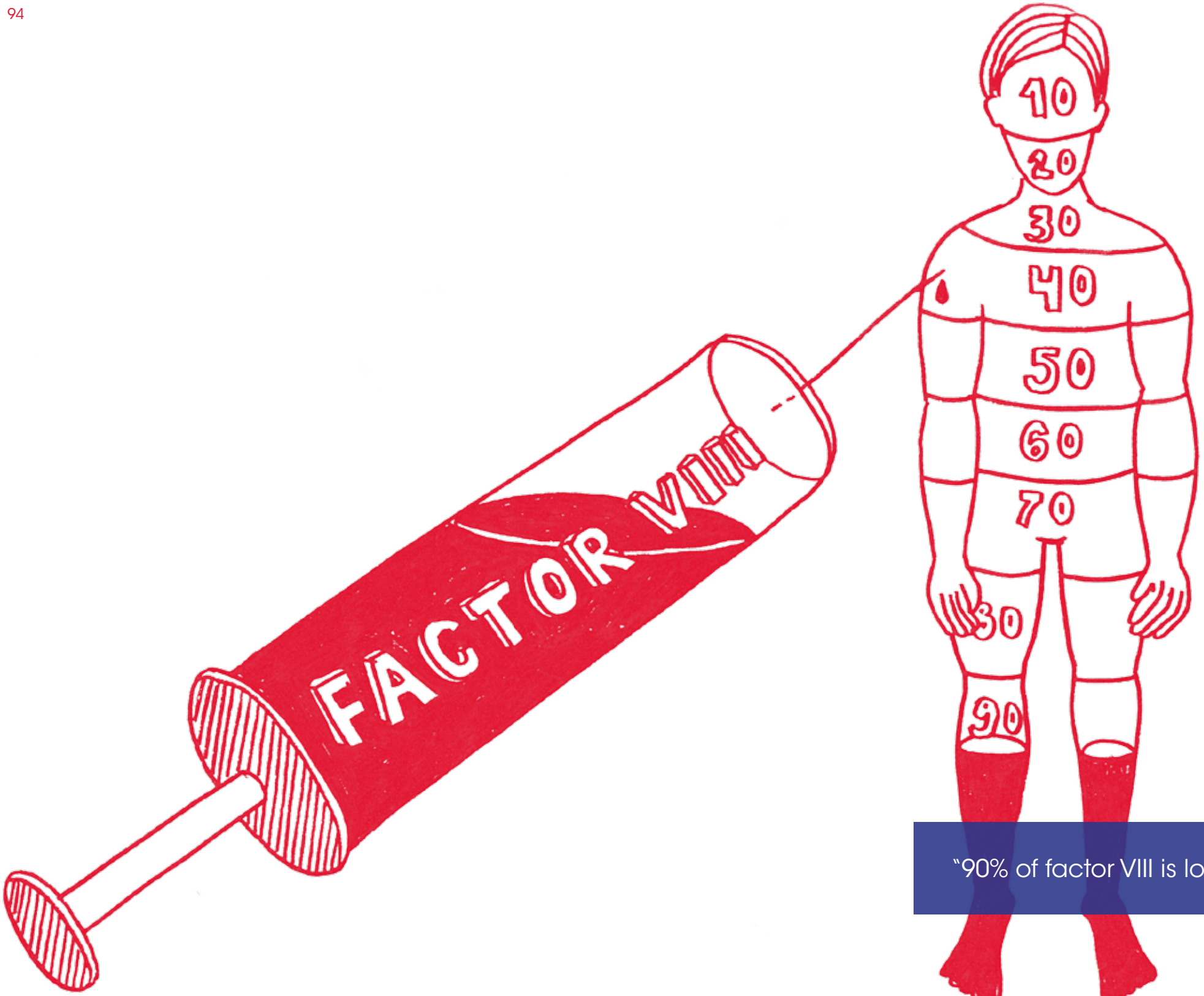
PETER COLLINS
Advancing therapeutics in haemophilia

"Haemophilia A is due to the absence of factor VIII. To correct the bleedings the most effective therapy is to inject therapeutic factor VIII."

"But up to 30% of the patients develop inhibitory immune response, to date. The reasons for the immunogenicity are not understood and what I will discuss are the first steps of the immune response, which is how factor VIII is captured by antigen presenting cells."

"Mannose ending glycans charged residues in the C1 and C2 domains of factor VIII have been shown to play a role in the uptake process in vitro. However, the situation is more complex in vivo because von Willebrand factor interferes with these mechanisms."

SÉBASTIEN LACROIX-DESMAZES
The immune response to factor VIII



"90% of factor VIII is lost after injection."

"All the described experiments were conducted under static conditions."

ECTH 2016 | European Congress on Thrombosis and Haemostasis

"I want to give you an overview of where the field gene therapy and haemophilia currently stands. Wat are the challenges? And where are we going from here?"

"Is gene therapy a magic bullet? Is it going to cure haemohilia, is it going to be the ultimate treatment without any side effects? That's what we hope, but I think that we have to be cautious."

THIERRY VANDENDRIESSCHE

Emerging gene therapy strategies in haemophilia

"What inspired me to go into gene therapy is the fact that when a child is born with a point-mutation in his or her genome, it has to bear the burden of that mutation for the rest of his or her life. It's like a Sword of Damocles hanging above the patient's heads and sooner or later the patient will suffer from that very mutation."

"If you have a mutated or broken gene, with conventional gene therapy, and I can't believe I am using this term because here is nothing conventional about gene therapy, one can just add a gene and this functional gene will compensate for the defects of the broken gene.

"The moral of the story is that we can try to improve the technology of gene therapy on different levels. When these are combined in the most optimal configuration, you can then conceive a clinical trial with low vector dosis that will also hopefully be safe enough."

ECTH 2016 | European Congress on Thrombosis and Haemostasis

"If you inject factor VIII into mice, they will develop antibodies."

ECTH 2016 | European Congress on Thrombosis and Haemostasis

ECTH 2016

Interviews

ATTENDEES IMPRESSIONS

RUIFANG LI

From China | PhD at LUMC Leiden, Clinical Epidemiology

Ruifang Li is studying the risk factors for the first occurrence and recurrence of venous thrombosis.

"I hope to learn about what others are doing in this field, and to keep up to date about the progress that's being made. We are looking for some new risk factors that might be reported about during this congress. And of course I'd like to meet people working in the same field and find possible collaborations."

AMANDA BOK

From Belgium | CEO European Haemophilia Consortium

"It was an excellent conference, with strong speakers and good science. There were 760 participants, which is amazing, but it still feels like a nice format, not too big, where you can sink your teeth in the sessions and still have access to speakers and participants. I really like seeing so many young people.

Normally, you tend to see quite many high-level people. It is nice to hear young voices, and their perspectives, because they are the future and that we invest in our talent."

ANNE DEMULDER

From Belgium | Medical doctor, working in the lab at the Center of Haemophilia, HEMOWAB in Brussels

"I liked the State of the art sessions and the presence of many young people. The talk on polyphosphate, in one of the State of the art sessions gave me some new insights. It was very educational. In general, it was highly interactive, especially in the "meet the expert sessions". One improvement could be to use more small rooms that are suitable for networking."

BRIAN O'MAHONY

President of EHC

"A lot of stuff is not factual but subjective, so it's good to hear different speakers talking about new developments, with a different audience asking different questions who have different interpretations of the same data."

MOHAMMED KHAN

From The United Kingdom | Clinical haematologist. Works in Aberdeen Royal Infirmary

"It's a good blend of both clinical medicine and science. The updates on haemophilia treatment were very good. There were some good science based talks. I enjoyed the fast and furious sessions. You got very succinct presentations, because it gives you a small amount of insight into an area that you might want to expand your knowledge base on. There were some problems with the app and the conference book could have been more detailed. Overall, I go home feeling informed."

FRITS ROSENDAAL
Epidemiologist | Connected to the Leiden University Medical Center and University Leiden, where he works as a professor of Clinical Epidemiology

TILMAN HACKENG
Professor and chairman of Biochemistry at the Cardiovascular Research Institute of the University Maastricht

INTERVIEW ROSENDAAL & HACKENG

With this first edition of ECTH, Board members Frits Rosendaal and Tilman Hackeng are filling a gap in the existing meetings on thrombosis and haemostasis. What will be the added value of this congress?

"We have our national societies doing their thing, next to the large international meetings, bringing all these different societies together", says Frits Rosendaal. "What is missing is the "in between", the regional meeting of different nationalities. We have learned that it creates added value to have more people from different countries. In Europe we have a large concentration of people, in a relatively small area of high-level research. So in that way it's very efficient and affordable for attendees to gather in Europe."
Tilman Hackeng: *"Especially young scientists cannot always afford to travel overseas in order to attend an international congress. That's why we also reduced the fee, and in combination with local low airfare it is more accessible to those younger scientists."*

You also wanted to experiment with the traditional format of a congress. How will attendees notice this?

Hackeng: *"In part, because of the Science, Fast and Furious talks, which are modelled according to the successful format of the so called TEDx talks.*

Rosendaal: *"Traditionally, the style of presentation is always less exciting than the content. We wanted to leave the beaten track of 15 slides, with the standard format of introduction, methods, results and discussion and do something different."*

Hackeng: "We took the eight most high-scoring abstracts and contracted Jean-Paul Toonen, curator of TEDx Maastricht, who coached the speakers in presenting their research in a more exciting fashion."

Rosendaal: *"this is important because most of science is funded by tax money and so society deserves its scientist to explain their research in an understandable way.*

Hackeng: *"We want to anticipate on this development and be the first to experiment with the way of presenting data. The overal goal that Jean-Paul Toonen has set: A great talk should stick with the audience for at least two years."*

"The congress will also be spectacularly different from regular meetings, because we skipped the exhibition of industry sponsors", says Hackeng. "Plus, the industry can also participate in the scientific program, because their research is actually excellent, but sometimes also a bit under the radar. Integrating industry research into the scientific program on an invited basis is revolutionary."

What are your expectations and hopes for the event? How should it impact the field?

"That a lot of people get what they want from a congress", says Rosendaal. "To learn, to network, meet people and be inspired. We want people go home with a bit more knowledge and inspiration and to mobilise the existing structure of scientists in the field. Furthermore, we are trying to find ways to make the congress more useful and pleasant, which is an experiment for both of us."

ECTH 2016

Our partners

ACKNOWLEDGEMENTS

ECTH wishes to express gratitude to the following companies which, through their generosity, have helped to make this congress possible:

★★★

Bristol-Myers Squibb

Pfizer

Daiichi-Sankyo

CSL Behring
Biotherapies for Life™

★★

NOVARTIS

★

ARYOGEN
آریوژن فارمد

Boehringer Ingelheim

GRIFOLS

HYPHEN BioMed
A Company of Sysmex Group

KEDRION BIOPHARMA

LFB
ETHICAL COMMITMENT

sobi
Pioneer in Rare Diseases

Stago

ECTH 2016 | European Congress on Thrombosis and Haemostasis

CENTENARY CELEBRATION 2016

CELEBRATING 100 CSL™
Parent Company of CSL Behring

CSL has, this year, marked 100 years of delivering on our promise for patients

Achieving this milestone is a testament to our values, science, people and the patients we serve — yesterday, today and tomorrow.

Few organisations have the vision, focus and agility to accomplish such a feat. Fewer still have such a rich heritage with an even brighter future ahead. In many ways, we're just getting started; delivering on promises is what we do at CSL.

We're a patient-centred organisation with a unique combination of R&D focus, operational excellence and commercial strength that enables us to consistently identify, develop, and deliver innovations that patients with life-threatening conditions, such as haemophilia, need.

We have grown into a global biotherapeutics leader. Today, we provide innovative biotherapies to people in more than 60 countries. Our 16,000 people are driven by a deep passion and commitment to serve the thousands of patients who depend on our medicines to help them to live their lives to the full.

We've been able to sustainably deliver on our promise because innovation is at the heart of everything we do. It is at the heart of how we safely and effectively produce medicines for a range of serious medical conditions and it is led by the 1,100 dedicated R&D experts who focus on solving patients' unmet needs every day.

Emerging innovations, such as treatments for haemophilia A and B, along with support programmes, promise to provide new opportunities to improve patient well-being, unlike at any other time in history. But there's more to be achieved — especially in helping to raise awareness of serious diseases and the importance of early diagnosis. For example, 75% of the people with blood disorders in the world are either undertreated or not treated at all.

So, we work closely with the patient advocacy community, including the European Haemophilia Consortium, to find ways to raise awareness of serious medical conditions and encourage the right conversations with healthcare professionals to prompt early diagnosis and timely treatment.

CSL is the parent company of CSL Behring. As we begin our second century, our promise to save lives and protect the health of people gets stronger by the day.

For more information about CSL Behring, please visit:
www.cslbehring.com

Date of preparation: September 2016 PO-005-160829

ECTH 2016 | European Congress on Thrombosis and Haemostasis

ECTH 2016 | European Congress on Thrombosis and Haemostasis

CHOOSE ELIQUIS® FOR YOUR PATIENTS WITH DVT / PE[1–3]

Start with ELIQUIS

for your patients with acute DVT / PE

(10 mg BD initiation for first 7 days, followed by 5 mg BD for at least 3 months):[2*†]

- The AMPLIFY trial demonstrated **comparable efficacy** with **significantly less major bleeding** vs. standard of care (enoxaparin / warfarin) at 6 months[1‡]
- No initial injections or bridging with LMWH required[2]

Stay with ELIQUIS

for the prevention of recurrent DVT / PE

(2.5 mg BD initiated after 6 months of treatment with ELIQUIS 5 mg BD or another anticoagulant):[2†]

- The AMPLIFY-EXT trial demonstrated **superior efficacy**, with a **comparable major bleeding** rate to placebo[2,3§]
- A licensed dose which is lower for prevention of recurrent VTE than for VTE treatment[2]

* As per available medical guidelines, short duration of treatment (at least 3 months) should be based on transient risk factors (e.g., recent surgery, trauma, immobilisation).[2]

† The duration of overall therapy should be individualised after careful assessment of the treatment benefit against the risk for bleeding.[2]

Not all patients who start on ELIQUIS for acute DVT / PE will stay on ELIQUIS; some acute DVT / PE patients who receive treatment do not require treatment for the prevention of recurrent DVT / PE. Other patients may be prescribed ELIQUIS for the prevention of recurrent VTE after initial treatment for acute DVT / PE with another anticoagulant.[2] This is a decision for the prescribing clinician together with patient involvement in the decision-making.

Twice-daily dosing across the VTE treatment phases[2]

Freedom from INR monitoring and dietary restrictions, with the choice to take with or without food[2]

‡ AMPLIFY: Phase III, randomised, double-blind trial in 5,395 patients with DVT and / or PE.[1] The duration of the trial was 6 months.[1] The primary efficacy endpoint was rate of recurrent VTE / VTE-related death vs. enoxaparin / warfarin.[1] Efficacy analyses based on ITT population for whom the outcome status at 6 months was documented; safety analyses based on patients who had at least one dose of study drug.[1]

§ AMPLIFY-EXT: Phase III, randomised, double-blind trial in 2,482 patients with DVT or PE who had completed 6 to 12 months of anticoagulation therapy.[3] The duration of the trial was 12 months.[3] Efficacy analyses based on ITT population for whom the outcome status at 12 months was documented; safety analyses based on patients who had at least one dose of study drug.[3]

Prescribing information can be found overleaf.

ELIQUIS® (apixaban) 2.5 mg & 5 mg Film-coated Tablets Prescribing Information

Consult summary of product characteristics (SmPC) prior to prescribing and for full list of adverse reactions. **PRESENTATION:** Film-coated tablets; 2.5mg and 5mg apixaban. **INDICATION:** Prevention of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation (NVAF) with one or more risk factors, such as prior stroke or transient ischaemic attack (TIA), age ≥75 years, hypertension, diabetes mellitus or symptomatic heart failure (NYHA Class ≥II). Treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE), and prevention of recurrent DVT and PE in adults (see Special warnings and precautions for information on haemodynamically unstable PE patients). Prevention of venous thromboembolic events (VTE) in adult patients who have undergone elective hip or knee replacement surgery (2.5 mg only). **DOSAGE AND ADMINISTRATION:** Oral. Taken with water, with or without food. *Prevention of stroke and systemic embolism in patients with NVAF:* The recommended dose is 5 mg taken twice a day. Patients who meet at least two of the following criteria: serum creatinine ≥1.5 mg/dL (133 micromole/l), age ≥80 years, or body weight ≤60 kg should receive the lower dose of Eliquis, 2.5 mg twice daily. All patients with severe renal impairment (creatinine clearance 15-29 ml/min) should receive the lower dose of Eliquis 2.5 mg twice daily. Therapy should be continued long term. *Treatment of DVT, treatment of PE and prevention of recurrent DVT and PE (VTE):* The recommended dose for the treatment of acute DVT and treatment of PE is 10 mg taken twice daily for the first 7 days followed by 5 mg taken twice daily. As per available medical guidelines, short duration of treatment (at least 3 months) should be based on transient risk factors (e.g. recent surgery, trauma, immobilisation). The recommended dose for the prevention of recurrent DVT and PE is 2.5 mg taken twice daily. When prevention of recurrent DVT and PE is indicated, the 2.5 mg twice daily dose should be initiated following completion of 6 months of treatment with Eliquis 5 mg twice daily or with another anticoagulant. The duration of overall therapy should be individualised after careful assessment of the treatment benefit against the risk for bleeding. *Prevention of VTE (VTEp): elective hip or knee replacement surgery:* The recommended dose is 2.5 mg taken twice a day. The initial dose should be taken 12 to 24 hours after surgery. In patients undergoing hip replacement surgery, the recommended duration of treatment is 32 to 38 days. In patients undergoing knee replacement surgery, the recommended duration of treatment is 10 to 14 days. *Missed Dose for All Indications:* If a dose is missed, Eliquis should be taken immediately and then continue with twice daily dose as before. *Switching:* switching treatment from parenteral anticoagulants to Eliquis (and vice versa) can be done at the next scheduled dose. These medicinal products should not be administered simultaneously. *Switching treatment from VKA therapy to Eliquis:* warfarin or other VKA therapy should be discontinued and Eliquis started when the international normalized ratio (INR) is <2. *Switching treatment from Eliquis to VKA therapy:* administration of Eliquis should be continued for at least 2 days after beginning VKA therapy. After 2 days of co-administration of Eliquis with VKA therapy, an INR should be obtained prior to next scheduled dose of Eliquis. Co-administration of Eliquis and VKA therapy should be continued until the INR is ≥2. *Renal impairment:* No dose adjustment in mild or moderate renal impairment. Eliquis is to be used with caution in severe renal impairment (creatinine clearance 15-29 mL/min) as there may be an increased risk of bleeding. For the prevention of stroke and systemic embolism in patients with NVAF and severe renal impairment, patients should receive the lower dose of Eliquis 2.5 mg twice daily. Patients with NVAF and serum creatinine ≥1.5 mg/dL (133 micromole/L) associated with age ≥80 years or body weight ≤60 kg should also receive the lower dose of Eliquis 2.5 mg twice daily for stroke/systemic embolism prevention. In patients with creatinine clearance <15 mL/min, or in patients undergoing dialysis, there is no clinical experience therefore Eliquis is not recommended. *Hepatic impairment:* Contraindicated in patients with hepatic disease associated with coagulopathy and clinically relevant bleeding risk. Not recommended in patients with severe hepatic impairment. Use with caution in patients with mild or moderate hepatic impairment (Child Pugh A or B). No dose adjustment is required in patients with mild or moderate hepatic impairment. Use with caution in patients with elevated liver enzymes (ALT/AST >2 x ULN) or total bilirubin ≥1.5 x ULN. Prior to initiating Eliquis, liver function testing should be performed. *Cardioversion* (NVAF): Patients can stay on Eliquis while being cardioverted. *Paediatric population*: Eliquis is not recommended in children and adolescents below the age of 18 **CONTRAINDICATIONS:** Hypersensitivity to the active substance or to any of the excipients listed in SmPC, active clinically significant bleeding, hepatic disease associated with coagulopathy and clinically relevant bleeding risk, lesion or condition if considered a significant risk factor for major bleeding (refer to SmPC). Concomitant treatment with any other anticoagulant agent except under specific circumstances of switching anticoagulant therapy or when unfractionated heparin is given at doses necessary to maintain an open central venous or arterial catheter (refer to SmPC). **SPECIAL WARNINGS AND PRECAUTIONS:** *Haemorrhage risk:* Carefully observe for signs of bleeding. Use with caution in conditions with increased risk of haemorrhage. Discontinue administration if severe haemorrhage occurs. *Interaction with other medicinal products affecting haemostasis:* Concomitant treatment with any other anticoagulant is contraindicated (see contraindications). The concomitant use of Eliquis with antiplatelet agents increases the risk of bleeding. Care is to be taken if patients are treated concomitantly with non-steroidal anti-inflammatory drugs (NSAIDs), including acetylsalicylic acid. Following surgery, other platelet aggregation inhibitors are not recommended concomitantly with Eliquis. In patients with atrial fibrillation and conditions that warrant mono or dual antiplatelet therapy, a careful assessment of the potential benefits against the potential risks should be made before combining this therapy with Eliquis. *Use of thrombolytic agents for the treatment of acute ischemic stroke:* there is very limited experience with the use of thrombolytic agents for the treatment of acute ischemic stroke in patients administered Eliquis. *Patients with prosthetic heart valves:* safety and efficacy of Eliquis have not been studied in patients with prosthetic heart valves, with or without atrial fibrillation. Therefore, the use of Eliquis is not recommended in this setting. *Surgery and invasive procedures:* Eliquis should be discontinued at least 48 hours prior to elective surgery or invasive procedures with a moderate or high risk of bleeding. This includes interventions for which the probability of clinically significant bleeding cannot be excluded or for which the risk of bleeding would be unacceptable. Eliquis should be discontinued at least 24 hours prior to elective surgery or invasive procedures with a low risk of bleeding. This includes interventions for which any bleeding that occurs is expected to be minimal, non-critical in its location or easily controlled. If surgery or invasive procedures cannot be delayed, appropriate caution should be exercised, taking into consideration an increased risk of bleeding. This risk of bleeding should be weighed against the urgency of intervention. Eliquis should be restarted after the invasive procedure or surgical intervention as soon as possible provided the clinical situation allows and adequate haemostasis has been established (see SmPC). *Temporary discontinuation:* Discontinuing anticoagulants, including Eliquis, for active bleeding, elective surgery, or invasive procedures places patients at an increased risk of thrombosis. Lapses in therapy should be avoided and if anticoagulation with Eliquis must be temporarily discontinued for any reason, therapy should be restarted as soon as possible. *Spinal/epidural anaesthesia or puncture:* When neuraxial anaesthesia (spinal/epidural anaesthesia) or spinal/epidural puncture is employed, patients treated with antithrombotic agents for prevention of thromboembolic complications are at risk of developing an epidural or spinal haematoma which can result in long-term or permanent paralysis. The risk of these events may be increased by the post-operative use of indwelling epidural catheters or the concomitant use of medicinal products affecting haemostasis. Indwelling epidural or intrathecal catheters must be removed at least 5 hours prior to the first dose of Eliquis. The risk may also be increased by traumatic or repeated epidural or spinal puncture. Patients are to be frequently monitored for signs and symptoms of neurological impairment (e.g., numbness or weakness of the legs, bowel or bladder dysfunction). If neurological compromise is noted, urgent diagnosis and treatment is necessary. Prior to neuraxial intervention the physician should consider the potential benefit versus the risk in anticoagulated patients or in patients to be anticoagulated for thromboprophylaxis. There is no clinical experience with the use of Eliquis with indwelling intrathecal or epidural catheters. In case there is such need and based on the general PK characteristics of Eliquis, a time interval of 20-30 hours (i.e. 2 x half-life) between the last dose of Eliquis and catheter withdrawal should elapse, and at least one dose should be omitted before catheter withdrawal. The next dose of Eliquis may be given at least 5 hours after catheter removal. As with all newer anticoagulant medicinal products, experience with neuraxial blockade is limited and extreme caution is therefore recommended when using Eliquis in the presence of neuraxial blockade. *Haemodynamically unstable PE patients or patients who require thrombolysis or pulmonary embolectomy:* Eliquis is not recommended as an alternative to unfractionated heparin in patients with pulmonary embolism who are haemodynamically unstable or may receive thrombolysis or pulmonary embolectomy since the safety and efficacy of Eliquis have not been established. *Patients with active cancer:* efficacy and safety of Eliquis in the treatment of DVT, treatment of PE and prevention of recurrent DVT and PE (VTEt) in patients with active cancer have not been established. *Renal impairment:* see dosage and administration section. *Elderly patients:* increasing age may increase haemorrhagic risk. Also, the co-administration of Eliquis with ASA in elderly patients should be used cautiously because of a potentially higher bleeding risk. *Body weight:* low body weight (< 60 kg) may increase haemorrhagic risk. *Hepatic impairment:* see dosage and administration section. *Interaction with Inhibitors of CYP3A4 and P-gp:* The use of Eliquis is not recommended in patients receiving concomitant systemic treatment with strong inhibitors of both CYP3A4 and P-gp, such as azole-antimycotics (e.g., ketoconazole, itraconazole, voriconazole and posaconazole) and HIV protease inhibitors (e.g., ritonavir). These medicinal products may increase Eliquis exposure by 2-fold or greater in the presence of additional factors that increase Eliquis exposure (e.g. severe renal impairment). *Interaction with Inducers of CYP3A4 and P-gp:* Eliquis should not be used for the treatment of DVT and PE in patients receiving concomitant systemic treatment with strong inducers of both CYP3A4 and P-gp since efficacy may be compromised. In patients receiving concomitant systemic treatment with strong inducers of both CYP3A4 and P-gp, Eliquis should be used with caution for the prevention of VTE in elective hip or knee replacement surgery, for the prevention of stroke and systemic embolism in patients with NVAF and for the prevention of recurrent DVT and PE, though no dose adjustment for Eliquis is required during concomitant therapy with such medicinal products. *Hip fracture surgery:* Eliquis has not been studied in clinical trials in patients undergoing hip fracture surgery to evaluate efficacy and safety in these patients. Therefore, it is not recommended in these patients. *Laboratory parameters:* Clotting tests (PT, INR, and aPTT) are affected as expected by the mechanism of action of apixaban. Changes observed in these clotting tests at the expected therapeutic dose are small and subject to a high degree of variability (see SmPC). *Information about excipients:* Eliquis contains lactose. Patients with galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take Eliquis. **DRUG INTERACTIONS:** Medicinal products associated with serious bleeding are not recommended concomitantly with Eliquis, such as: thrombolytic agents, GPIIb/IIIa receptor antagonists, thienopyridines (e.g. clopidogrel), dipyridamole, dextran and sulfinpyrazone. Due to an increased bleeding risk, concomitant treatment with any other anticoagulants is contraindicated. Administration of activated charcoal reduces Eliquis exposure. Also see contraindications and special warnings and precautions section; Consult SmPC (contraindications, special warnings and precautions and drug interactions) for full details on interactions. **PREGNANCY AND LACTATION:** *Pregnancy:* Not recommended during pregnancy. *Breastfeeding:* Discontinue breastfeeding or discontinue Eliquis therapy. **UNDESIRABLE EFFECTS:** Increased risk of occult or overt bleeding from any tissue or organ, which may result in post haemorrhagic anaemia. The signs, symptoms, and severity will vary according to the location and degree or extent of the bleeding. *Prevention of VTE in adult patients who have undergone elective hip or knee replacement surgery (VTEp):* Common (≥1/100 to <1/10): anaemia, haemorrhage, haematoma, nausea, contusion. Uncommon (≥1/1,000 to <1/100): thrombocytopenia; specific haemorrhage such as gastrointestinal, post procedural, incision site, operative; haematochezia. Rare (≥1/10,000 to <1/1,000): hypersensitivity, allergic oedema and anaphylaxis; specific haemorrhage such as eye (including conjunctival), rectal, muscle; haemoptysis. *Prevention of stroke and systemic embolism in adult patients with NVAF, with one or more risk factors (NVAF):* Common (≥1/100 to <1/10): specific haemorrhage such as eye (including conjunctival), gastrointestinal, rectal; haemorrhage, haematoma, epistaxis, gingival bleeding, haematuria, contusion. Uncommon (≥1/1,000 to <1/100): hypersensitivity, allergic oedema and anaphylaxis; specific haemorrhage such as brain, intra-abdominal, abnormal vaginal, urogenital, traumatic, post procedural, incision site; haemoptysis, haematochezia. Rare (≥1/10,000 to <1/1,000): specific haemorrhage such as respiratory tract, retroperitoneal. *Treatment of DVT and PE, and prevention of recurrent DVT and PE (VTEt):* Common (≥1/100 to <1/10): haemorrhage, haematoma, epistaxis; specific haemorrhage such as gastrointestinal, rectal; gingival bleeding, haematuria, contusion. Uncommon (≥1/1,000 to <1/100): specific haemorrhage such as eye (including conjunctival), abnormal vaginal, urogenital, traumatic, post procedural, incision site; haemoptysis, haematochezia. Rare (≥1/10,000 to <1/1,000): specific haemorrhage such as brain, respiratory tract. Please refer to the SmPC for further details of adverse reactions including other types of haemorrhage. **LEGAL CATEGORY:** POM. **PACKAGE QUANTITIES AND BASIC NHS PRICE:** Carton of 10 film-coated tablets 2.5mg £9.50, 20 film-coated tablets 2.5mg £19.00, 60 film-coated tablets 2.5mg £57.00, 56 film-coated tablets 5mg £53.20, 28 film-coated tablets 5mg £26.60. **MARKETING AUTHORISATION NUMBERS:** EU/1/11/691/001-3, EU/1/11/691/008, EU/1/11/691/014 **MARKETING AUTHORISATION HOLDER:** Bristol-Myers Squibb/Pfizer EEIG, BMS House, Uxbridge Business Park, Sanderson Road, Uxbridge, Middlesex, UB8 1DH. Telephone: 0800-731-1736. **DATE OF PI PREPARATION:** March 2016 432UK1600117-01-01 ELQ1118

Adverse events should be reported.
Reporting forms and information can be found at www.mhra.gov.uk/yellowcard.
Adverse events should also be reported to Bristol-Myers Squibb Pharmaceuticals Ltd Medical Information on 0800 731 1736 or medical.information@bms.com

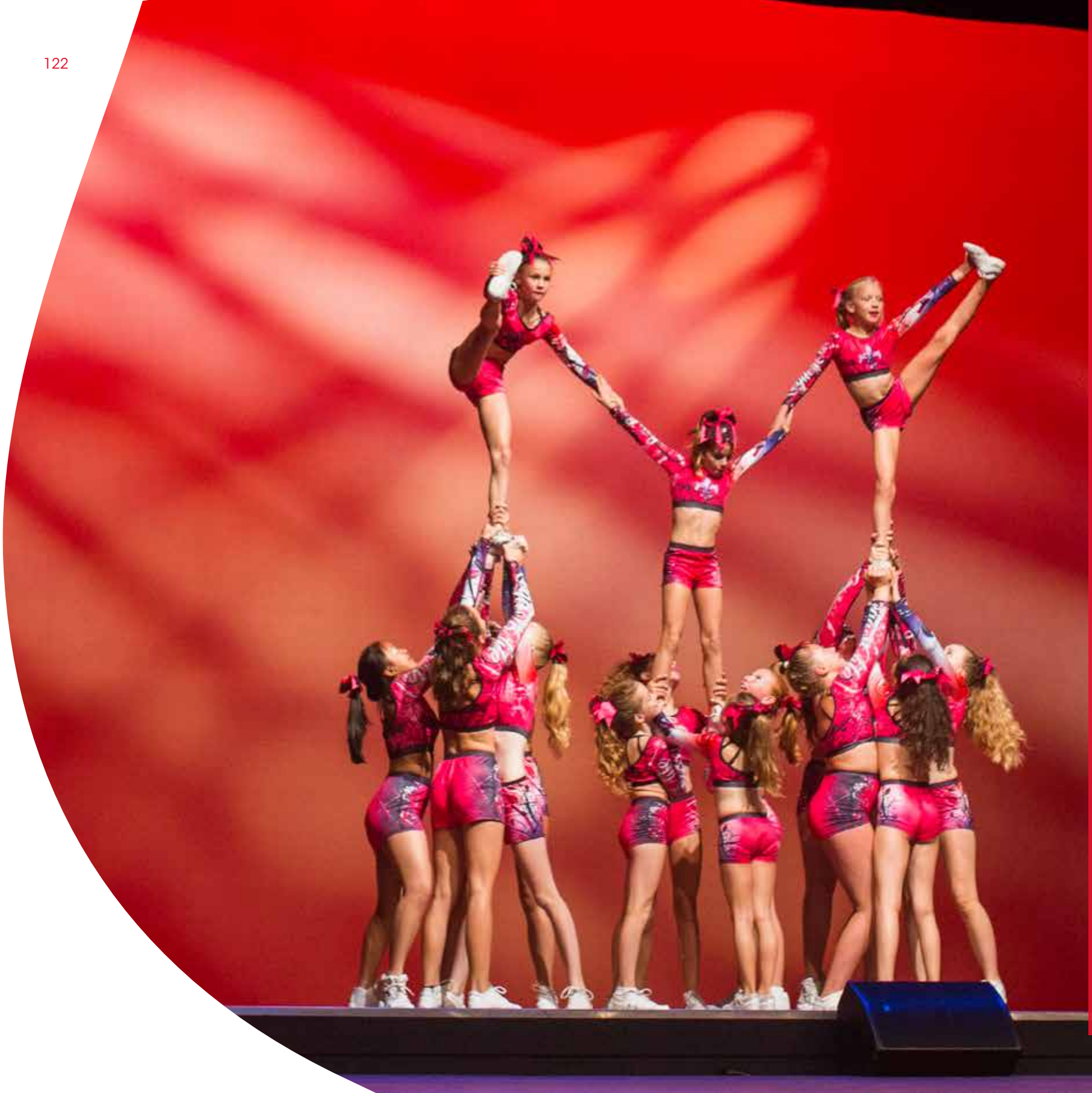
Please refer to your country's adverse event reporting system. Prices apply to the UK only. Please refer to your country's medical information department for information on local prices.

BD = Twice Daily DVT = Deep Vein Thrombosis
INR = International Normalised Ratio ITT = Intention To Treat
LMWH = Low Molecular Weight Heparin NOAC = Non-vitamin K antagonist Oral Anticoagulant PE = Pulmonary Embolism
VTE = Venous Thromboembolic Events

References: 1. Agnelli G *et al.* N Engl J Med 2013; 369: 799–808.
2. ELIQUIS® (apixaban) Summary of Product Characteristics. Available at http://www.medicines.org.uk. Last accessed 1st September 2016.
3. Agnelli G *et al.* N Engl J Med 2013; 368: 699–708.

Date of preparation: October 2016 **Job code:** PP-ELI-EUR-0509
www.eliquisglobal.com

Bristol-Myers Squibb Pfizer Eliquis® apixaban



COLOFON

ORGANISATION TEAM:

SPECIAL THANKS TO:

AUTHORS:
Romy Willems - Magazine Design
Charlotte Porskamp - Art Direction
Daukanté Subaciute - Illustration
Amar Inderdjiet - Photography
Kitty Arends - Text

VISUAL REPORT:
Visuele Notulen
www.visuelenotulen.nl

With a team of creative professionals Visuele Notulen has cared for the visual report of this event. As an organization we aim to get a longer hold of the message and engage people more closely in the content of the day.

visuele notulen

Rendez-vous à Marseille

ECTH 2018

European Congress on
Thrombosis and Haemostasis

Marseille, France

24 - 26 October