pro-COAG meeting

18.30-21.00h, Thursday 28th February 2019
Hilton Gendarmenmarkt, Berlin,
Germany

This Expert Meeting is organised and
funded by Roche Diagnostics International Ltd.

Chair's welcome

I am delighted to welcome you to this Roche-sponsored meeting entitled:
Roche pro-COAG taking place on Thursday 28th February 2019 in Berlin, Germany.

Coagulation laboratories face the challenge of keeping up with the continual advances and developments in the field. The introduction of new agents, such as direct oral anticoagulants (DOACs), to the anticoagulant armoury and the rapidly growing number of patients with bleeding disorders receiving novel therapies worldwide has required modifications of existing assays and the development of new ones for their measurement. However, the resources, funding and knowledge required for some of the current specialist assays are not available to all laboratories.

This meeting will provide insights and updates in coagulation diagnostics and will explore how treatment monitoring can be optimised through the use of proper diagnostics. Following this, we will highlight the current unmet needs and challenges in coagulation diagnostics and develop perspectives for future assays.

At the end of the presentations, we will host a Q&A session in order to discuss the evolving landscape of coagulation diagnostics in more detail and to promote scientific exchange between attending delegates.

I hope that you find this event engaging, and that you contribute your thoughts on the future of coagulation diagnostics.

Carl-Erik Dempfle
Coagulation Center, Mannheim, Germany

Faculty

Carl-Erik Dempfle (Chair)
University Hospital Mannheim, Mannheim, Germany

Erik Klok
Leiden University Medical Center, Leiden, Netherlands

Johanna Kremer
Bern University Hospital, University of Bern, Switzerland

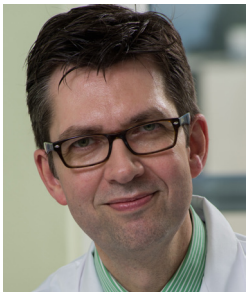
Jens Müller
University Clinic Bonn, Bonn, Germany

Giuseppe Lippi
University Hospital of Verona, Verona, Italy

Elena Riester
Labor Augsburg MVZ GmbH, Augsburg, Germany

Agenda

TIME	SESSION	PRESENTER
18:30	Chair's Welcome	Carl-Erik Dempfle, Mannheim, Germany
18:35	D-Dimer thresholds in diagnosis of acute PE: implications from the YEARS study	Erik Klok, Leiden, Netherlands
19:00	Upcoming biomarkers in coagulation: ADAMTS13, a proteolytic marker to identify CV risk and sepsis	Johanna Kremer, Bern, Switzerland
19:25	Assay challenges with emicizumab for the treatment of haemophilia A	Jens Müller, Bonn, Germany
19:50	Advancements with the cobas t 711 fully automated coagulation analyser ▪ Results from the first investigator-initiated study of cobas t 711: analytical performance of key coagulation assays ▪ An observational workflow comparison between cobas t 711 and other coagulation analysers	 Giuseppe Lippi, Verona, Italy Elena Riester, Augsburg, Germany
20:30	Panel discussion / Q&A	Carl-Erik Dempfle
21:00	Meeting close & refreshments	



Carl-Erik Dempfle (Chair)
IMD Coagulation Center Mannheim
University of Heidelberg
University Hospital Mannheim
Mannheim, Germany

Biography

Professor Carl-Erik Dempfle currently serves as Medical head of the IMD Coagulation Center Mannheim (Germany), and Associate Professor for Internal Medicine at University Hospital Mannheim, University of Heidelberg (Germany). Previously, he has served as head of the Clinical Hemostasis Unit at Mannheim University Hospital, including the central blood coagulation laboratory, research laboratory, outpatient service and clinical consultation service. In 2011, he was awarded the Alexander Schmidt-Prize of the Gesellschaft für Thrombose- und Hämostaseforschung (GTH).

Prof. Dempfle is a member of several professional societies including the International Society on Thrombosis and Haemostasis (ISTH), GTH and the International Fibrinogen Research Society. He served as co-chairman of the ISTH scientific subcommittees on fibrinolysis and disseminated intravascular coagulation, and as co-editor of *Thrombosis Research* and *Thrombosis and Haemostasis*. Prof. Dempfle has published over 150 scientific publications.

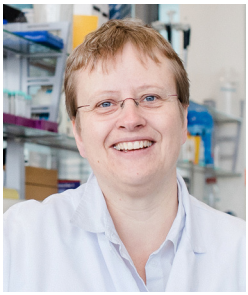
Erik Klok
Leiden University Medical Center
Leiden
Netherlands

Biography
Dr. Erik Klok is an Internist Vascular Medicine Specialist from Leiden University Medical Center, Leiden (Netherlands). His research interests include all aspects of venous thromboembolism. He combines clinical work in Leiden with a scientific position as visiting Professor at the Center for Thrombosis and Hemostasis, Mainz (Germany).

Presentation summary: D-Dimer thresholds in diagnosis of acute PE: implications from the YEARS study
Current guidelines support the systematic application of a diagnostic algorithm consisting of pre-test probability determination, a highly sensitive D-dimer test and computed tomography pulmonary angiography (CTPA) for all patients with suspected pulmonary embolism (PE); it has been shown to be safe, reduce the number of required imaging tests and be cost-effective. Importantly, there is still room for improvement of this algorithm since up to 75% of patients are still referred for CTPA with associated exposure to ionizing radiation and contrast material. With only one in four CTPA scans indicative of PE, the specificity of the algorithm needs to be optimised.

In this lecture, the results of the YEARS and ARTEMIS studies will be discussed. In these two studies, a novel diagnostic algorithm was successfully tested in a general population of patients with suspected PE, and in pregnant women with suspected PE, respectively. The strength of this algorithm lies in the pre-test probability dependent D-dimer threshold and the simultaneous assessment of the pre-test probability and D-dimer concentration. This allows for a large reduction in the number of required imaging tests as well as in turn-around time at the emergency ward.

'This meeting touches upon unmet needs and provides solutions for our daily clinical practice.'



Johanna Kremer
Department of Hematology & Central Hematology Laboratory (UKH-HZL)
Inselspital
Bern University Hospital
University of Bern, Switzerland

Biography

Professor Johanna Kremer Hovinga is the Head of the Reference Center for Hemophilia for Adults/European Hemophillia Comprehensive Care Center (EHCCC) Bern University Hospital. She is also the Deputy Head of Coordinated Haematological Research Management System (CHARMS) at the same institute. During the past 15 years her research has focussed on VWF and its size regulator ADAMTS13 in health and various disease states, primarily thrombotic microangiopathies.

Presentation summary: Upcoming biomarkers in coagulation: ADAMTS13, a proteolytic marker to identify CV risk and sepsis

Low levels of ADAMTS-13, a Zn-metalloprotease enzyme that cleaves VWF during blood clotting, are associated with an increased risk of arterial thrombosis, MI and CV disease. Whilst ADAMTS-13 is not a biomarker of sepsis itself, it is related to the response of other sepsis biomarkers and its level is inversely correlated to that of IL-6. Several assays are available to investigate the levels of ADAMTS-13; however, additional information is needed to determine the prognostic value of these assays in terms of using ADAMTS-13 as a biomarker for identifying and assessing sepsis and CV risk.

'ADAMTS-13 is a novel proteolytic biomarker of value in the field of coagulation, especially thrombotic microangiopathies and with further research, it can potentially be used to identify CV risk and for prognosis in sepsis.'

Jens Müller
Institute of Experimental Haematology and Transfusion Medicine (IHT)
University Clinic Bonn
Bonn, Germany

Biography
Dr. Jens Müller currently serves as technical supervisor of both the HLA and Coagulation laboratories at the IHT (University of Bonn, Germany).

Presentation summary: Assay challenges with emicizumab for the treatment of haemophilia A
Emicizumab (Hemlibra®) is a bispecific antibody that binds to activated factor IX and factor X and mimics the function of activated FVIII. Although emicizumab and FVIIIa show functional similarities, structural differences artificially shorten the clotting times in aPTT-based laboratory assays when conducted in the presence of emicizumab, which can result in misinterpretation of results. Plasma levels of emicizumab can be accurately measured using a modification of the FVIII one-stage clotting assay. Since emicizumab does not bind to bovine factors IX and X, a chromogenic FVIII assay based on bovine factors can be used for the measurement of plasma FVIII:C levels even in the presence of emicizumab. The use of such an assay also allows the detection of neutralizing anti-FVIII-antibodies by the Nijmegen-Bethesda-Assay in the presence of emicizumab.

'New anticoagulant agents have different impacts on currently available assays. Thus, test systems must be verified accordingly to provide reliable and accurate results in order to ensure optimal treatment for patients.'

Giuseppe Lippi
Professor of Clinical Biochemistry, University of Verona
Director, Laboratory of Clinical Chemistry and Hematology,
University Hospital of Verona
Verona, Italy

Biography

Professor Giuseppe Lippi currently serves as Professor of Clinical Biochemistry and Molecular Biology at the University of Verona (Italy), and Director of the Clinical Chemistry and Hematology laboratories at the University Hospital of Verona (Italy).
Professor Lippi is Editor-in-Chief of *Annals of Translational Medicine* and *Journal of Laboratory and Precision Medicine* and also serves as Associate Editor of *Clinical Chemistry and Laboratory Medicine*, *Seminars in Thrombosis and Hemostasis* and *Diagnosis*.

Presentation summary: Results from the first investigator-initiated study of cobas t 711: analytical performance of key coagulation assays

We evaluated the analytical performance of the cobas t 711 analyser on the imprecision and linearity of PT, aPTT, fibrinogen, AT and D-dimer. Results were compared with two other coagulation analysers (Instrumentation Laboratory [ACL TOP 700] and Stago STA-R MAX). Methods comparison studies revealed PT, APTT and fibrinogen results on cobas t 711 are globally aligned with those obtained on Instrumentation Laboratory ACL TOP 700 and Stago STA-R MAX. Results of this preliminary evaluation demonstrate that the cobas t 711 coagulation analyser displays excellent performance for routine measurement of PT, aPTT, fibrinogen, AT and D-dimer in clinical laboratories.

'Since laboratory diagnostics have become a mainstay for the diagnostic and therapeutic approach of haemostasis disorders, the availability of rapid, accurate, precise, automated and relatively inexpensive, laboratory tests is becoming increasingly important.'

Elena Riester
Head of Clinical Chemistry/Haematology/Coagulation Division
Labor Augsburg MVZ GmbH,
Augsburg, Germany

Biography
Dr. Elena Riester is the Head of Clinical Chemistry/Haematology/Coagulation Division at Labor Augsburg MVZ GmbH (Germany). She has trained at the University of Ulm (Germany), obtaining a PhD at the Institute of Microbiology and Biotechnology, and a Master of Biochemistry prior to that.

Presentation summary: An observational workflow comparison between cobas t 711 and other coagulation analysers
With increasing requirements for analysers used in hemostasis labs, there is growing interest in automated coagulation systems. In addition to optimal diagnostic performance, efficient workflow should address issues emerging from budget restrictions and skill shortages.

The coagulation analyser, cobas t 711 coagulation analyzer (Roche) was compared with the competitive test systems – Sysmex CS-5100 (Siemens), STA-R MAX (Stago), and ACL Top (Instrumentation Laboratory) – for efficient workflow. A fixed series of test protocols were developed to compare these devices reagent management, device maintenance and test automation based on quantitative and qualitative data.

For basic routine parameters (PT, aPTT, Fib), only minor differences in cycle time were observed between the devices. In contrast, cobas t 711 showed best performance for cycle time in extended routine (PT, aPTT, Fib, AT, D-Dimer, TT). Comparison of the maintenance procedure showed the shortest time requirements for the Siemens analyser; however, cobas t 711 showed a significantly lower hands-on interaction and cycle time for reagent management compared with other tested devices.

'Sharing knowledge, ideas and concepts between scientists, laboratories and clinicians is essential to improve therapies for patients.'

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