LIVER FAILURE & INFLAMMATION

Recommendations for Clinical Practice & New Developments

September 06th – 08th, 2019
Rostock - Hohe Düne, Germany

Steffen Mitzner & Jan Stange
Department of Medicine
University of Rostock
Welcome Address

Ladies and gentlemen, friends and family,

it is our pleasure to welcome you at our annual Liver Support Meeting in Rostock-Warnemuende, at the Marina in Hohe Düne between September 6th and 8th, 2019.

20 years ago, on September 11th 1999, the first International Liver Dialysis Symposium was opened by Reinhardt Schmidt and chaired by Roger Williams. The program addressed the use of albumin dialysis in acute liver failure and also, the first randomized trial investigating albumin dialysis in hepatorenal syndrome was presented.

The term "acute on chronic liver failure" was used to summarize complications of decompensation of chronic liver disease that might potentially benefit from liver dialysis, such as hepatic encephalopathy (HE), hemodynamic instability and hepatorenal syndrome (HRS). Before that, the term had been used in the indexed literature 1995 by Ohnishi H, Sugihara J, Moriwaki H and Muto Y in a Japanese journal named "Ryokiketsu Shokogun Shirizu".

After albumin dialysis offered a new mechanism to interfere with the pathophysiology of acute decompensation of chronic liver failure, articles using the term for naming a potential indication for liver support therapy were published increasingly; the first one by Schmidt L, Svendsen LB, Romming S, Hansen BA and Stolze Larsen F on Cerebral Blood Flow effects of MARS in AoCLF in Liver Transplantation 2001(7).

Fin was a visitor of the very first Liver Dialysis Symposium and we are very glad to have him visiting our 20th anniversary. In addition, it was the ground breaking article by Sambit Sen, Roger Williams and Rajiv Jalan, “The pathophysiological basis of acute-on-chronic liver failure” in Liver 2002(22) which laid out a hypothesis that AoCLF is a distinct syndrome. We are equally excited to have both, Roger and Rajiv visiting our 20th anniversary of the Rostock Liver Support Meeting.

Christian Steiner, the then Medical Director of the first company commercializing albumin dialysis laid the foundation for the Albumin Dialysis Registry, inspired by the ECMO Registry maintained by the Extracorporeal Life Support Organization (ELSO) under the leadership of Robert Bartlett.

The trio of Rajiv Jalan, Vicente Arroyo (who later spearheaded the Chronic Liver Failure Consortium-CLIF) and Patrick Kamath (one of the pioneers who published the MELD score in 2001) met at an international liver conference following an invitation by Christian and outlined first thoughts about an AoCLF database.

Until today, those efforts resulted into the formation of three geographic societies, the Chronic Liver Failure Consortium-CLIF (http://www.ecfl.org), the North Atlantic Consortium for the Study of End stage Liver Disease NACELD (https://naceld.org/) and the Asian Pacific Association for the Study of the Liver ACLF (http://www.aclf.in/). Highly competitive, they all have contributed to tremendous progress in understanding, defining and classifying AoCLF which is the pre-requisite to develop, study and approve new therapeutic approaches towards AoCLF, including extracorporeal liver support.
Regulatory agencies, such as the FDA and the EMA are now appreciating and adopting the terminology. From a technological perspective, the first introduction of extracorporeal albumin dialysis using MARS inspired the use of similar technologies, such as Single Pass Albumin Dialysis (SPAD), Advanced Organ Support (ADVOS) and finally Open Albumin Dialysis (OPAL). Competitively, apheresis-like technologies such as Fractionated Plasma Separation and Adsorption (FPSA, later commercialized as Prometheus), Large Volume Plasma Exchange (LVPE), Selective Plasma Exchange Therapy (SEPET), Albumin Exchange Therapy and Endotoxin Adsorption (DIALIVE) and full blood adsorption technologies such as CytoSorb have entered clinical research phases to investigate the efficacy in AcCLF. The latest efforts to develop cell-based therapies have not resulted into commercially available products yet but have already contributed significantly further to better understand the syndrome of liver failure and potential mechanisms of actions. Therefore, we reserved a special spot for an update on cellular/bioartificial therapies.

As in any other area of medicine where progress is made in the interest of patients, industry and academia must and are working in a dialectic partnership. However, we shall never forget that at the end the achievements must result into patient’s benefit. An estimated number of over 50,000 treatments have been applied since the advent of albumin dialysis and over a thousand indexed papers have been published, an indicator that the field is only growing, although we must remain vigorous in our efforts to ensure every patient who needs bridging due to liver failure can have access to liver support therapy.

Therefore, we also want to give our special thanks to the multiple governmental bodies that have supported this research, from the EU-commission over the Federal Government of Germany and the State Government of Mecklenburg-Western Pomerania.

Also, we fondly want to thank the former chair of the University of Rostock’s Department of Internal Medicine and a past president of numerous academic societies for artificial organs, Horst Klinkmann for creating an environment of inspiration and research in the area of organ support in Rostock, without which extracorporeal albumin dialysis would not have seen the light of the day.

We also would like to thank our clinical mentor, Wolfgang Ramlow for encouraging us during our very first patient treatments with an archaic version of early MARS.

Special thanks also go to our dean, Emil Reisinger who continues the tradition of encouraging research to develop even better systems for organ support and the president of our University, Wolfgang Schareck who has helped not only as a devoted transplant surgeon.

Last but certainly not least, this year’s meeting needs also to be a meeting to celebrate. It is the 20th anniversary. But it will not be the last.

Yours sincerely,

Steffen Mitzner
Jan Stange
## Scientific Program

**Saturday, September 7th, 2019**

**Ballsaal**

- **from 07:30 am**  
  Registration  
  Foyer Ballsaal

- **08:00 – 08:10 am**  
  Steffen Mitzner & Jan Stange (Rostock, Germany)  
  20 Years of Albumin Dialysis & Liver Support Meetings

- **08:10 – 09:40 am**  
  **Morning Session I**  
  Albumin Dialysis as Liver Support Therapy: Past, Present & Future  
  **Chairs:** Roger Williams (London, UK)  
  Horst Klinkmann (Rostock, Germany)

  - **08:10 – 08:40 am**  
    Tarek Hassanein (San Diego, USA)  
    20 Years of Experiences with Albumin Dialysis as Liver Support Therapy

  - **08:40 – 09:10 am**  
    Faouzi Saliba (Paris, France)  
    Lessons from multiple Clinical Studies & Consequences for future Trials

  - **09:10 – 09:40 am**  
    Jan Stange (Rostock, Germany)  
    The Future of Liver Support Therapy - Technology, Monitoring, Diagnostics

- **09:40 – 10:00 am**  
  Coffee Break

- **10:00 – 12:00 pm**  
  **Morning Session II**  
  Detoxification Efficacy & its Monitoring  
  **Chairs:** Markus Busch (Hannover, Germany)  
  Janos Fazakas (Budapest, Hungary)

  - **10:00 – 10:20 am**  
    Valentin Fuhrmann (Muenster, Germany)  
    A Proposal for Practice Guidelines - who, when and how long to treat

  - **10:20 – 10:40 am**  
    Aleksandra Jung (Krakow, Poland)  
    Monitoring Metabolites for Kinetic Modeling of Liver Support

  - **10:40 – 11:00 am**  
    Katja Waterstradt (Berlin, Germany)  
    Use of Albumin-Functionality-Test as an Efficacy Endpoint

  - **11:00 – 11:20 am**  
    Michael Hinz (Rostock, Germany)  
    Albumin-binding Function as a Biomarker for Extracorporeal Support Studies

  - **11:20 – 11:40 am**  
    Ivano Riva (Bergamo, Italy)  
    Comparison of Blood Purification of different Liver Support Therapies

  - **11:40 – 12:00 pm**  
    Steffen Mitzner (Rostock, Germany)  
    Discussions & Summary

- **12:00 – 01:30 pm**  
  Lunch & Poster Session

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<tr>
<th>Time</th>
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| 01:30 – 03:40 pm | Afternoon Session I  
  Inflammation & Liver Failure | Rajiv Jalan (London, UK)  
  Rudolf Staub (Graz, Austria)  
  Janos Fazakas (Budapest, Hungary)  
  Fin Stolze Larsen (Copenhagen, Denmark)  
  Markus Busch (Hannover, Germany)  
  Tung Yu Tsui (Rostock, Germany)  
  Tarek Hassanein (San Diego, USA)  
  Roger Williams (London, UK)  
  Horst Klinkmann (Rostock, Germany)  
  Markus Busch (Hannover, Germany)  
  Janos Fazakas (Budapest, Hungary)  
  Fin Stolze Larsen (Copenhagen, Denmark)  
  Markus Busch (Hannover, Germany) |
| 04:00 – 06:00 pm | Afternoon Session II  
  Future of Extracorporeal Liver and Immune Support | Nikolaos Pyrsopoulos (New Jersey, USA)  
  Jens Alrichter (Rostock, Germany)  
  Pedro Baptista (Zaragoza, Spain)  
  Christian Steiner (Berlin, Germany)  
  Tung Yu Tsui (Rostock, Germany)  
  Tarek Hassanein (San Diego, USA)  
  Roger Williams (London, UK)  
  Horst Klinkmann (Rostock, Germany)  
  Markus Busch (Hannover, Germany)  
  Janos Fazakas (Budapest, Hungary)  
  Fin Stolze Larsen (Copenhagen, Denmark)  
  Markus Busch (Hannover, Germany) |
20th Anniversary of ISAD
The International Liver Support Meeting Rostock

★ 20 YEARS ★
OF THE ISAD MEETING IN ROSTOCK
20th Anniversary of ISAD
The International Liver Support Meeting Rostock

We would like to thank all sponsors and donators of the 20th anniversary of the ISAD in Rostock-Hohe Düne!

With your support and innovations, the congress will be a great event!

Social Program
Saturday, September 7th, 08:00 pm
Join us for a great Night on a lovely Boat on the Warnow River!
Please register!
Price: € 30.00

Social Program
Sunday, September 8th, 10:00 am
Sailing Trip (by Invitation)

Contact
Meeting Coordinator
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Venue
Yachthafenresidenz Hohe Düne
Am Yachthafen 1
18119 Rostock-Warnemünde
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Hemoadsorption in isolated conjugated hyperbilirubinemia after extracorporeal membrane oxygenation support. Cholestasis of septa: A case report and review of the literature on differential causes of jaundice in ICU patient

Paweł Piekarzyk(1), Paweł Kitkiew, Beata Potięcz-Stucka(1), Justyna Sylaska-Stawiarska(1), Edyta Rudyk(1), Michal Borys(1) and Miroslaw Czuczwar(2) | 1 III Department of Anesthesiology and Intensive Care, Medical University of Lublin, Lublin, Poland | 2 Student’s Scientific Association, III Department of Anesthesiology and Intensive Care, Medical University of Lublin, Lublin, Poland | Int J Artif Organs 2019, 42(5): 263 - 8

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Albutec GmbH

Albutec GmbH was founded 2004 by Sebastian Klammt, Norbert Boehl and Katrin and Jan Stange, one of the inventors of MARS™ as a device for Extracorporeal Albumin Dialysis. The goal was to provide better dialysate albumin by removing the stabilizers from commercial albumin since the stabilizers (Caprylate and N-Acetyl-Tryptophan) occupy binding sites and reduce the efficacy of albumin dialysis. The technology is used to improve the binding function of intravenous albumin and to improve the efficacy of albumin in extracorporeal albumin dialysis.

The lead product is the Hepalbin™ Adsorbent, which is part of the OPAL® System for Extracorporeal Albumin Dialysis (ECAD), marketed by HepaNet GmbH.

In 2019, Sponholz et. al. presented the significant improvement of patient’s albumin binding function assessed by ESR using the Hepalbin™ Adsorbent, while the use of conventional adsorbents failed in this study, the latter observation confirming data published before by Jalan et al., which also suggested that albumin binding function detected by ESR may be a surrogate marker for outcome in Acute on Chronic Liver Failure (AoCLF).

Albutec is committed to further develop extracorporeal albumin dialysis in order to improve the outcome of liver failure.

Albutec is DIN EN ISO 13485 certified. It has authorisation for wholesale trade in medical products in accordance with § 52 AMG (German Medicines Act). The company has received funding by the Government of Mecklenburg-West Pomerania, the federal Government of Germany and the European Union.

Albutec thanks its loyal US and German Investors.

References:
ARTCLINE GmbH
A Clinical Stage Company at the Crossover of Medical Device and Biotech Industry
Established in 2007 as a spin-off of Rostock University Medicine, ARTCLINE has developed a patented therapy system employing dialysis equipment and immune cells to treat sepsis patients.
Positive results of two clinical trials have been published already. ARTCLINE currently develops the serial product to be tested in a pivotal study.
ARTCLINE is a clinical stage company having developed the patented ICE therapy. The ICE therapy is somehow similar to dialysis employing immune cells from healthy blood donors to treat patients with severe infections. Main indication is sepsis, a whole-body inflammation and infection, killing annually more than 200,000 patients in the US and more than 50,000 patients in Germany (www.world-sepsis-day.org). The costs for sepsis patients in the US are about US$ 20 billion annually and in Germany € 4 billion annually.
The ICE therapy of ARTCLINE uses human white blood cells, mainly granulocytes which represent the first defense line of our immune system. In order to avoid side effects, these cells are not infused into the patient but instead the blood is treated extra-corporeally in a dialysis-like system. Positive clinical results have been achieved and published. ARTCLINE currently develops the serial product in order to receive CE mark and start sales in Europe.
ARTCLINE is the only company world-wide employing human immune cells for treating sepsis. Basis is a range of granted patents. In principle an ICE treatment consists of three products: a modified dialysis machine, a disposable set made of tubes and filters, and the immune cells.
ARTCLINE is located with its headquarters and R&D facilities directly adjacent to the University Medicine Rostock.
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EASL
EASL, The European Association for the Study of the Liver, is a medical association dedicated to pursuing excellence in liver research and clinical practice of liver disorders. Also, we aim to provide education to all those interested in hepatology. Most importantly, while the roots of the association date back in Europe in 1966, EASL continues to engage globally with all stakeholders in the liver field wherever they are working. Therefore, our aim is to spread knowledge and expertise in best practices and the latest scientific breakthroughs in hepatology.
EASL’s mission is to be the Home of Hepatology. Therefore, all involved with treating liver disease can realize their full potential to cure and prevent it. As a result, the purpose of the association is to promote communication between European workers interested in the liver and its disorders. Most importantly, the association shall:
• Promote research concerning the liver
• Promote education of physicians, scientists and public awareness of liver diseases and their management
• Act as an advisor to European and national health authorities concerning liver diseases, provision of clinical services and the need for research funding
• Foster European multicentre controlled trials
• Facilitate scientific exchange
• Facilitate participation of young investigators at its meetings

BioCon Valley Mecklenburg-Vorpommern e.V.
Health Economy – a success story supported by BioCon Valley
BioCon Valley Initiative is the partner of the health economy in the german federal state Mecklenburg-Western Pomerania. As a central contact and service provider, the company and the association supports the players in the industry and contributes to the economic and scientific profile of the location. BioCon Valley is actively involved in networking and branch monitoring, project initiation and support, internationalisation, support of start-ups and marketing of the health industry.
Within this framework, the initiative organizes more than 70 specialist and thematic events per year – starting with small-format industry meetings with a specialist audience, workshops, the „Healthy Age(s)?“ forum, the „Health Parliament“, the “Board of Trustees for Health Economy” with currently 70 members and the National Conference on Health Economy with around 700 participants. The repertoire oft the initiative also includes the realisation of business delegations with high-ranking political support and participation in leading international trade fairs.
BioCon Valley has 16 employees and is represented at two locations in Greifswald and Rostock.
ANNIVERSARY

20th ISAD

The International Liver Support Meeting Rostock

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