2023 euroPCR

The CERC Chronicle

Issue No. 24 – May 2023

15th CERC Anniversary

CERC at EuroPCR 2023

CERC, as a long-lasting partner of EuroPCR, the World-Leading Course in Interventional Cardiovascular Medicine, is very proud to be part of and to contribute to its exciting educational program, through the results of numerous clinical trials, six of which will be presented during the Late Breaking Clinical Trials Sessions.
Furthermore, many of our experts will actively participate in educational sessions as speakers, moderators or operators.

Late Breaking Clinical Trials Sessions

May 16th 12:00-13:30 Room Maillot Chairs: A. Neylon & D. Capodanno	**EBC II** Five-year follow-up - Provisional vs. culotte for coronary bifurcations: S. Arunothayaraj
	KISS Provisional stenting in bifurcation lesion: benefit of side branch intervention : B. Chevalier
	EBC MAIN Left main coronary stent study: three-year follow-up: Dr. Hildick-Smith
May 17th 14:45-16:15 Room Maillot Chairs: S. Windecker & R. Waksman	**BIOADAPTOR-RCT** 12-month primary endpoint outcomes: S Saito
	LEADERS FREE III Clinical outcomes at three years from first-in-man: F Eberli
	REFORM Randomised trial of biolimus DEB for in-stent restenosis: R Byrne
May 17th 14:45-16:15 Room 341 Facilitators: E. Cerrato & M. Sabate	**BioFreedom** One-year results of the Asian STEMI registry: P Ong

Meet CERC CEO and Directors

We are delighted to meet you and discuss the newest trends in the cardiovascular field, new ideas for clinical research and share the innovations we are bringing to this area.

Upcoming Clinical Trials at CERC !!!

Ceric / Biosensors International	ALL WOMAN
TERUMO	NAGOMI PMCF
VENUSMEDTECH	VITAE System
Elixir Medical Corporation	DynamX Sprint BTK RCT
核心医疗 Core Medical	LVAD Coreheart
German Heart Center Munich	Symphony Registry IIT

Come and meet us
Booth M6 Level 2

An Interview with Roxana Mehran, MD, FSCAI

A Mount Sinai Professor in Cardiovascular Clinical Research and Outcomes and director of interventional cardiovascular research and clinical trials at The Zena and Michael A. Weiner Cardiovascular Institute at The Icahn School of Medicine at Mount Sinai, New York, NY.

By Dragica Paunovic

Professor Mehran, it is a great honor and a privilege to have you contributing to CERC Chronicle. Given this unique opportunity, please allow me to ask you a few questions.

Q1. What was the most important driving force behind your passion for clinical research?

For me it has always been the curiosity to answer questions clinicians face and patients care about. And this has led me to clinical research focused on outcomes of patients. I also wanted to be there at the table to be sure that we had fair assessment of our devices, procedures, and new therapies, with good clinical equipoise. These were fundamental to me.

Q2. Clinical research has evolved over the years, but could we do more to accelerate innovation in clinical trials?

We must and can do better. We need to be more inclusive in our patient enrollment and trial criteria, more innovative with our approach, more pragmatic with our questions, and how we answer them, and more applicable to daily practice. This means that we have a finite time to evaluate therapies for given conditions, using comparative effectiveness methodology to answer the questions, with current technologies to speed up the trial timelines. Otherwise, our work and final results will not be applicable.

Q3. How can we all mobilize to improve diversity in clinical trials?

To improve diversity requires intentional work with real results, and not just window dressing for our trials. If we want diverse patients, we should include diverse investigators who serve those patients often not included in our trials. Trial leadership will also need to be more diverse, and our methodology can also be curtailed to make sure we have diverse patients included. This can be done through capping certain populations and focusing on women and minorities until we have met our quotas, there are many ways. We must find the way.

Q4. As we are so close to gender equality, could you briefly tell us how you and Marie Claude came up with the idea to found the Women as One initiative?

I have always admired and looked up to Prof Morice. She was the true "Trailblazer" of our time Early in the years PCI and new devices were being examined, she was the only one who led the way for other women. She and I had a discussion, and she was all in... We wanted an organization that was completely focused on a simple mission of promoting talented women in medicine. And this is how Women as One was born. Simple, doable, provocative, and most importantly intentional.

Q5. You are a great friend and supporter of CERC. Is it about your admiration for our founder, Marie Claude, CERC's DNA to embrace and unconditionally support trials with a hypothesis to change clinical practice and improve patient care?

I love the concept of CERC, clinical trials by clinicians in practice who answer questions for patients through collaboration and Inclusion. A dream come true.

CERC is completely transparent, collaborative, and effective in delivering the answers that matter for clinicians, and patients. CERC is also a beacon for regulatory trials and provides the best and most comprehensive services, that is topline, with highest quality and with the best efficient and timely delivery?

Q6. Finally, what is the hottest research subject in your mind right now?

Well, the fact that DCB is still not approved in the US and not on our shelves is something to deal with, and we now have several trials that hopefully will prove them to be safe and effective. There is much excitement in heart failure therapies, which are device based. Also, in the valve arena, there are many important new devices on the horizon. The current wearable technologies are giving us many important opportunities to follow patients for important endpoints, and even think about tech-based enrollment in trials. Primary and secondary prevention on top of device/interventional /surgical therapies will be reducing the burden of disease and improve outcomes. Finally, Artificial Intelligence will be front and center in choosing best possible ways forward.

ALL WOMEN Clinical Trial

Bridging the Gender Gap in Heart Disease Care

By Nozomi Watanabe & Ghada Khoury Martin

Imagine a world where women receive equitable medical care, where their unique needs and concerns are not ignored or overlooked. The ALL WOMEN clinical trial aims to move us closer to this vision by "bridging the gap" at the study leadership level by both a woman and a man: Prof. **Alaide Chieffo** and Prof. **Ignacio Cruz-Gonzaléz.** Almost exclusively conducted by female experts, ALL WOMEN focuses on female patients over 75 years old with severe aortic stenosis (AS). Although AS affects both genders, historically, women have been denied surgical treatment more often than men mainly because of late presentation and perceived greater peri-procedural complications. With the introduction of transcatheter aortic valve implantation (TAVI), the leading generalized treatment option for aortic valve stenosis, the gender disparity has decreased. Despite that, gender-specific studies are essential to assess the safety and efficacy of devices in specific scenarios such as smaller annulus, hypertrophic and small left ventricle.... The ALL WOMEN randomized trial aims to demonstrate that a new, self-expanding, ALLEGRA valve (Biosensors International), provides lower mean trans-aortic gradient to balloon expandable valves.
Ultimately, this newly launching study promises to optimize outcomes and advance the field of interventional cardiology by tailoring treatment to women's specific characteristics.
By addressing a previously invisibilized category, highlighting the importance of women's wellbeing, and showcasing the value of female medical expertise, the ALL WOMEN trial represents a significant step towards achieving true gender equality in healthcare.

"Equality consists in the same treatment of similar persons".
Aristotle

CERC and ARC initiatives

By Philippe Garot & Davide Capodanno

The Academic Research Consortium (ARC) is a collaborative forum of stakeholders founded in 2006 to develop and disseminate consensus definitions for pivotal clinical trials of medical devices. Under the auspices of ARC, CERC is coordinating two initiatives in the domains of structural and coronary interventions.

VARC-HBR Initiative - The Valve Academic Research Consortium (VARC) is an ARC derivative devoted to the field of heart valve interventions. Recently, the VARC-3 provided an overview of risk assessment after TAVI that included definitions of bleeding, but factors contributing to this risk were not discussed. Standardized bleeding definitions for cardiovascular clinical trials were previously introduced by the Bleeding Academic Research Consortium (BARC). The risk of major bleeding after TAVI is non-negligible and has been consistently associated with an increased risk of mortality. Compared to percutaneous coronary intervention (PCI), TAVI is more invasive and is directed to older patients with frequent comorbidities that make them at high bleeding risk (HBR). Although conditions associated with bleeding related to PCI have been defined by the ARC-HBR initiative in 2019 (another CERC managed initiative!), they remain insufficiently explored after TAVI. A recent post-hoc analysis of the SCOPE-2 trial demonstrated that patients with and without HBR according to the ARC definition for PCI experience similar rates of BARC bleeding type 3 or 5. HBR criteria should, therefore, be defined in a way that is specific to TAVI patients, especially for risk assessment prior to the selection of the strategy and for the selection of post-TAVI antithrombotic regimens based on individualized bleeding risk profiles. To better characterize the profile of HBR patients with valve disease, CERC has designed a new ARC initiative, named VARC-HBR, mixing contributions of experts from the BARC, VARC and ARC-HBR groups, including worldwide physicians, representatives of the US Food and Drug Administration and the Japanese Pharmaceuticals and Medical Devices Agency, as well as observers from the pharmaceutical and medical device industries. Factors contributing to higher risk of severe bleeding are consensually discussed and will be determined in early 2023.

Language around DAPT – an ARC initiative – In patients undergoing PCI, the use of antiplatelet therapy comes at the expense of an increased risk of bleeding complications. Finding the optimal intensity of platelet inhibition needed according to the clinical presentation of atherosclerotic cardiovascular disease and individual patient factors is a daily clinical challenge. Modulation of antiplatelet therapy is a medical action that is frequently performed in practice to balance the risk of thrombotic or ischemic events and the risk of bleeding. This goal may be achieved by reducing (i.e., de-escalation) or increasing (i.e., escalation) the intensity of platelet inhibition by changing the type, dose or number of antiplatelet drugs. Because de-escalation or escalation can be achieved in different ways, with a number of emerging approaches, confusion arises with terminologies that are often used interchangeably.

To address this issue, this ARC collaboration will provide an overview of different strategies of antiplatelet therapy modulation for patients with coronary artery disease, including but not limited to those undergoing PC, and consensus statements on standardized definitions.

Lost in MDR Translation? CERC can help!

By Ute Windhövel & Dragica Paunovic

The announcement of the EU Medical Device Regulation (EU 2017/745) (MDR) several years back has delighted academia and medical practitioners as it promised increased scrutiny of patient safety, extensive and meaningful clinical evidence, and support for innovations. The medical device has embraced these Regulation goals in the hope of streamlined processes and complete transparency about the requirements for placing devices on the EU market. All European stakeholders hoped that the MDR would consolidate and strengthen this market, ensure patient safety, and preserve sufficiently fast access to innovation for patients. As time passed, and as the Regulation was implemented, key gaps and uncertainties emerged, contributing to collective anxiety about the MDR transition period's feasibility and the future of EU healthcare system.

The medical device industry has committed significant resources to comply with new requirements and make a success of the new regulatory system. Still, lack of clarity and lack of certification capacity by Notified bodies, forced many companies to prioritize their portfolio leading to shortages of many legacy devices. Furthermore, manufacturers' R&D, clinical and regulatory resources were drained into the ongoing MDR recertification processes, reducing new developments and innovation. The small and highly innovative companies changed their strategies by prioritizing markets with more unpredictable regulatory processes, leaving European patients in a long queue for their innovative, sometimes life-changing or lifesaving, products.

CROs and Academic research organizations after years of delivering ground-breaking science found themselves in a paradoxical situation to assist the industry and healthcare system to continue benefiting from the devices, sometimes on the market for more than 20 years with an excellent safety and performance track record. This new type of research, mainly single-arm observational registries, besides being scientifically unattractive are changing the real meaning of clinical research, meant to find new and better ways to detect, diagnose, treat, and prevent disease. The cost of those registries is not negligible, reducing the medical device industry's resources to support academia in further developing strong and more impactful clinical evidence that would contribute to advancing patient care and medical practice in general. By extending the deadlines for the re-certification, the recent MDR amendment (2023/607) gave some breath to the manufacturers, but its spirit and requirements stayed the same.

To ease the burden of our medical device industry partners, CERC developed a comprehensive, cost effective, all-in-one, PMCF strategy fully compliant with MDR requirements. Furthermore, benefitting from our strong cardiovascular therapeutic area expertise, we offer a full partnership in developing clinical evaluation strategy, clinical evaluation plan and reports throughout product life cycle.

An Interview with Marie-Claude Morice, MD, FESC, FACC, CERC CEO

By Simon Hazout & Ghada Khoury Martin

*Dr. Morice, we are thrilled and thankful to have your contribution to this Chronicle on **CERC's 15th anniversary**. With this exceptional opportunity, allow us to ask you a few questions.*

Q1: As the CEO of CERC, could you please share with us your background and how it has contributed to your role today ?

It's a long story. When I became an interventional cardiologist, I was immediately attracted to clinical research, and it has since become completely intertwined with my work. This specialty is constantly evolving, with new technologies, devices, and treatments emerging all the time. Naturally, all these innovations need to be thoroughly tested, and that's where clinical research comes in. Research and practice have always been linked in my work, and when the time came for me to retire from patient practice, it was a wonderful opportunity to focus solely on clinical research. This way, I could continue to fulfill the commitment I made to myself as a young girl: to help people live better.

Q2: As CERC's 15th anniversary draws near, what would you say is the company's most notable achievement or milestone to date?

Honestly, I feel that the CERC team, along with all the CERC founders and our industry partners, achieved a lot. We conducted truly important and impactful trials. When we established CERC, our goal was to improve patient outcomes and increase the visibility of European research. Through our numerous trials, we achieved that objective. Of course, there is still more work to be done, but I believe that one of our significant accomplishments, in addition to all the trials we are collectively proud of, is that we are part of the ARC Consortium. This nonprofit organization, led by clinical researchers, regulators, and industry partners, aims to unify trial definitions and designs so that they can be comparable and poolable. I believe that was a major achievement.

Q3: I've heard that CERC has a unique management structure in both operational and medical aspects. Could you elaborate about this and explain how it benefits both the company and its partners?

CERC is a unique research organization because it was created and driven solely by doctors. As a result, we strive in our trials not only to meet regulatory requirements for new devices approval, but also to address unmet patient needs. All this sets us apart and makes CERC a unique organization

Q4: How does CERC stay at the forefront of new developments and technologies in medical research?

The CERC team includes many experts from various fields, and it is a challenge to mention them all. We have Dr. Mylotte, Dr. Tchetche, Dr. Garot... specialists in structural heart disease, including Aortic, Mitral, and Tricuspid valves, LAA... Our team also includes Dr. Smits, Dr. Hildick-Smith, and other incredible experts in coronary artery disease, Dr. Mehran, Dr. Steg.. leaders in the research of drugs and drug-device combination treatment. Dr. Paunovic, with years of experience as chief medical officer for Terumo, brings valuable industry perspectives and trends. Furthermore, our team has physicians such as Dr. Capodanno, Dr. Chevalier... skilled in clinical trial design and innovation. Dr. Mahfoud's expertise in renal denervation and heart failure and Dr. Neylon's in imaging enrich our collective knowledge. With many other experts in our CERC family, we are confident to always be at the forefront of innovation and covering all fields of cardiovascular disease, clinical research, regulatory requirements, and industry trends.

Q5: Can you share with us any exciting projects or partnerships that CERC is currently working on?

At CERC, we nourish diversity and inclusion, be it for clinical projects types, population studied, or geography. We have many exciting projects underway. For instance, we are leading the most significant trial on DeNovo lesions treated with the drug-eluting balloon (DEB) versus DES, a highly relevant topic. We have exclusive TAVI programs tailored for women or the Middle East region. Thanks to our branch in Singapore, CERC Asia, we are conducting a significant randomized trial on Asian populations, comparing DEB versus DES. Our commitment to diversity and exploring new areas is reflected in our partnerships with innovative, emerging companies. We appreciate the trust bestowed upon us by our industry partners.

Q6: With the upcoming Euro PCR conference, what are CERC's goals and expectations for its participation to this event?

EuroPCR is a major scientific event for CERC every year. This year is fascinating as we have six trials accepted for the hotline sessions, all conducted by our team. We're proud of this accomplishment and will attend the presentations with project leaders, CRAs, and our entire team. The conference offers a unique opportunity to network with industry partners, investigators, and study coordinators. We anticipate a dynamic and engaging atmosphere at our booth and will host various meetings within and outside the formal conference schedule.

Q7: What's your take on the future of medical research and CERC's role in shaping it?

I am very proud to have worked on clinical research with our team over the past 15 years and with our accomplishments. With the reinforcement of our management team, the new generation of our clinical research team will be even more efficient and carry out more trials with an equally significant impact.

As we look to the future of research, we are facing some challenges with European regulations, which, I am confident, will soon be corrected and bring Europe back to the center of innovation. Additionally, with the advent of artificial intelligence, we will have the opportunity to gather much more data and conduct even more effective research than we do today.

The future of innovation and clinical research in Europe will be bright again!

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