2024 euroPCR

The CERC Chronicle

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CERC at EuroPCR 2024

CERC, as a long-standing partner of EuroPCR, is very proud to participate in and contribute to its exciting educational program, through the results of **eight** clinical trials, **five** of which will be presented at the Late Breaking Clinical Trials Sessions.

CERC Clinical Trials Presentation Program

May 14th 15:15-16:45

Théâtre Havane Hotline session

BIOADAPTOR-RCT
Two-years clinical outcomes
S. Saito

ABILITY DG
Randomised comparison of Ablaminus DES+ sirolimus-eluting stents in coronary artery disease patients with diabetes mellitus global
R. Mehran

SELUTION
Patient and procedure characteristics for 1000 Selution SLRTM sirolimus-eluting balloon procedures
S. Eccleshall

May 15th 8:30-10:00

Théâtre Havane LBT Session

KISS
Keep bifurcation Single stenting Simple
B. Chevalier

LANDMARK
Early outcomes of a randomized non-inferiority trial comparing TAVI devices
P. Serruys

May 16th 8:30-10:00

Poster Lab

REFORM
Biolimus A9 DEB for the treatment of in-stent restenosis: one-year outcomes
R. Durand

Room 341

DAPT
1-month DAPT after biodegradable-polymer everolimus-eluting stent in high-bleeding risk patients
G. Stefanini

Room 352A

PINNACLE
Hertz contact intravascular lithotripsy: primary outcomes
S. Verheye

Meet CERC Board Members

We would be delighted to connect with you and dive into the latest developments in cardiovascular research. Let's explore cutting-edge ideas for innovative trials together and share our thoughts on unmet needs to improve patient care.

CERC New Studies

Celic Meril	Myval Young
CM Concept Medical	Magical SV
ENDORON VASCULAR SUTURING	SEAL
AuriGen MEDICAL	ZENITH
restore medical	CARDIAC CT
BioME	BioME

Come and meet us
Booth M6 Level 2

Academic Research Consortium Initiatives

CAD Frontiers ACTION A2D2

By Antoinette Nylon

CERC was very proud to attend the Atherosclerotic CT imaging Outcome CoNsortium: Accelerating Atherosclerosis Drug Development meeting in Washington this year.

This is the second international consortium meeting of researchers, clinicians, policy experts, and industry partners to discuss and move forward candidate CCTA surrogates of coronary artery disease for accelerating translation of novel therapies and expanding indications for existing therapies.

Let us not forget that up to 25% of first myocardial infarctions in under 45-year-olds occur in those without Standard Modifiable cardiovascular Risk Factors (SMuRF-less CAD), and this patient group has excess mortality compared to those with traditional risk factors. Because humans are essentially the only mammals that spontaneously develop atherosclerosis pre-clinical models are extremely limited thus the urgency for surrogates to translate novel therapies.

Given the negative experience in cardiovascular medicine with surrogates in the past (PVC suppression in the CAST trial) cardiovascular trials have adopted rigorous standards focused on MACE outcomes in clinical trials. However, such trials become extremely difficult in primary prevention cohorts due to low event rates and required patient years follow up. New pathways to approval using imaging surrogates in mechanistic phase II trials and to 'de-risk' large scale phase III trials need to be pursued. Such use of imaging surrogates is highly established in the oncology field and now in cardiovascular medicine with the advances in cardiac CT we could do the same for atherosclerosis.

CCTA is a rapidly growing field and volume in Europe has increased up to 5-fold over the last 3 years. CT coupled with AI gives us unprecedented insights into plaque morphology, inflammation, and hemodynamics. While several candidate surrogate measures were discussed at the forefront is total non-calcified plaque volume (NCVP) and there are several approved plaque quantification tools available as stand-alone software or cloud-based solutions available to quantify this. While there is still discussion as to what the NCPV threshold should be and how it should be measured what is required is consistency and rigor in acquisition and analysis. Other key areas where CCTA imaging can be applied are in trial enrichment - to identify high risk groups with higher event rates to decrease sample size and in mechanistic phase II trials as evaluation of treatment response.

We must adhere to the ARC mission "to create dynamic, transparent and collaborative forum for stakeholders to develop consensus definitions and standard nomenclature in pivotal clinical trials of medical devices and to disseminate such definitions and recommended processes into the public domain". The leadership of the ACTION A2D2 to bring together these stakeholders is outstanding. CROs have an important role to play in the promotion of NCPV as a CCTA endpoint across trials to continue the work of building the case for validated surrogate endpoints.

CROs will also play an important role in site selection and assuring consistency in image quality.

Imaging protocols are central as scan parameters have a meaningful impact on plaque composition.

Our patients are being left behind. Cardiovascular treatments only correspond to 3% of drug Cardiovascular launches in Europe and the US over the last 5 years. We urgently need to address the hurdles and work together towards validating imaging surrogates as a pathway to the translation of new safe and effective treatments.

VARC – HBR

By Philippe Garot

We are thrilled to announce that the **"VARC-HBR consensus document"** is now published in EuroIntervention (DOI:10.4244/EIJ-D-23-01020, online in the EuroPCR Issue).

VARC-HBR is a CERC-driven Academic Research Consortium Initiative (ARC) focusing on High Bleeding Risk (HBR) in patients with aortic stenosis requiring TAVI. This document represents the first pragmatic approach to a consistent definition of HBR evaluating the safety and effectiveness of procedures, devices and drug regimens for patients undergoing TAVI. To better characterize the profile of HBR patients with valve disease, VARC-HBR combined the contributions of experts from the VARC, BARC and ARC-HBR groups, including worldwide physicians, representatives of the U.S. Food and Drug Administration and the Japanese Pharmaceuticals and Medical Devices Agency, and observers from the pharmaceutical and medical device industries.

The **VARC-HBR Board**: Philippe Garot, Marie-Claude Morice, Roxana Mehran and Davide Capodanno.

Latest Milestones of CERC Trials

Enrollment Completed

1. TARGET FIRST
2. PROVE

85% of Target Enrollment Reached

1. SELUTION DeNovo

50% of Enrollment Reached

1. EVERGREEN

25% of Target Enrollment Reached

1. GLYCAR
2. REVERSE

Enrollment Started

1. All Women
2. MENA TAVI
3. RNS by DWP

Other milestones

1. First 1000 patients enrolled in e-ULTRA 10K

Seeing is Believing: Intracoronary Imaging for Lipid-Lowering Therapy Trials

By Davide Capodanno

Intracoronary imaging offers a valuable opportunity to investigate the effect of novel lipid-lowering therapy drugs on several plaque characteristics, including plaque volume, plaque burden, plaque composition, and vulnerable plaque features.

Some examples of emerging endpoints for intracoronary imaging studies of lipid-lowering drugs include coronary plaque regression, change in plaque composition, reduction in vulnerable plaque features, reduction in stenosis. These "mechanistic" endpoints can provide additional information on the effectiveness of pharmacologic interventions in reducing cardiovascular disease beyond traditional measures such as blood pressure, lipid levels, and glucose levels.

At CERC, we are equipped with state-of-the-art technology and adhere to rigorous quality standards to analyze intracoronary imaging data accurately. Our core-lab facilities ensure meticulous evaluation, while our network of European sites ensures rapid trial execution.

For pharmaceutical companies seeking to understand how their lipid-lowering drugs work in vivo, intravascular imaging endpoints offer valuable insights. By utilizing CERC's expertise such companies can gain a deeper understanding of the mode of action of their drugs, thus refining their therapeutic approaches and advancing cardiovascular research.

In lipid-lowering therapy trials, through the lens of intravascular imaging, we at CERC can uncover the complexities of cardiovascular disease and drive innovation in trial design.

Think of CERC for your next trial in this space!

MYVAL YOUNG STUDY

By Philippe Garot

CERC & MERIL are very happy to announce a new innovative trial in the TAVI field!

"**MYVAL YOUNG**" will study the performance of the Myval Balloon expandable THV system (Meril, Gujarat, India) in patients aged 65 to 75 years with symptomatic aortic stenosis (mean gradient≥40mmHg and/or peak velocity>4m/s). The outcomes of consecutive 65 to 75-year-old patients treated with Myval THV will be compared to that of the PARTNER 3 trial that used Sapien 3 THV (Edwards, Irvine, California, USA). A total of 550 patients will be enrolled in up to 50 sites in 10 countries in Europe and Asia. This is a non-inferiority trial testing the hypothesis that the outcomes of "young" patients treated with the Myval balloon-expandable THV system are equivalent to outcomes of patients treated with Sapien 3.

The **primary endpoint** of the trial is the rate of all-cause death, stroke and rehospitalization at 1 year after the index TAVI procedure. **Secondary endpoints** encounter the components of the primary endpoint, TAVI failure at 5 years, a CT Corelab at 30 days after the procedure with a specific goal of evaluating the technical feasibility of a future redo-TAVI procedure and an echocardiography corelab at discharge, 30 days, 1 year, 3 year and 5 years to explore Myval hemodynamics and durability over time. Important predefined subgroups focusing on patients with bicuspid aortic valves and patients with a large annulus will be of special interest.

In the spirit of CERC's designed studies, MYVAL YOUNG is disruptive with a very innovative device and the aim to reach upgraded recommendations thanks to scientifically proven evidence. The primary investigators of the study are Dr. Didier Tchétché (Clinique Pasteur, Toulouse, France) and Dr. Philippe Garot (Institut Cardiovasculaire Paris-Sud, Massy, France). The study will be managed and monitored by CERC (full CRO services from study design to result presentation and study close-out). Enrollment will start in September 2024 and is scheduled to finish in September 2025. The primary endpoint of the study will be available in early 2026 and could be presented at EuroPCR 2026.

How does the future of bioresorbable scaffolds looks like?

By Peter Smits

Coronary vascular scaffolds, such as ABSORB and MAGMARIS, have garnered significant interest in the field of interventional cardiology due to their potential to overcome limitations associated with traditional metallic stents.

These bioresorbable scaffolds are designed to provide temporary support to the coronary artery post-angioplasty, gradually resorbing over time and leaving behind a healed vessel without any permanent implant.

The ABSORB bioresorbable vascular scaffold was one of the first of its kind to receive regulatory approval. However, its usage has been associated with concerns regarding scaffold thrombosis and adverse clinical outcomes (ABSORB 4, AIDA, COMPARE-ABSORB). The increased rate of thrombosis has been attributed predominantly to the relatively large strut thickness (157 µm) of the device compared to the second-generation DES from the same manufacturer (81 µm).

MAGMARIS, a magnesium alloy bioresorbable scaffold, demonstrates promising safety and efficacy. While initial studies suggest sufficient vessel support, the first-generation MAGMARIS exhibited relatively high late lumen loss (Haude et al, BioMAG-1 study).

Despite early challenges, ongoing advancements in bioresorbable scaffold technology, like Abbott's 100-micron strut ESPRIT PLLA scaffold, are enhancing their effectiveness, as evidenced by positive results in trials such as LIFE-BTK, for below-the-knee applications based on which it was just approved by FDA.

Meril's MeREs PLLA scaffold boasts a thin strut (100 µ) and shorter resorption time, delivering promising outcomes up to 3 years FU in coronary artery disease patients (Asok Seth, MeRes-1 trial).

The Firesorb PLLA scaffold from Microport has two different strut thicknesses, depending on the diameter (100 micron up to 2.75 mm and 125 microns for the 3.0- and 4.0-mm scaffolds). In the randomized study of 433 patients, it showed similar late lumen loss as the metallic CoCr-EES comparator, 0.17+/-0.27 versus 0.19+/-0.37 ($p<0.001$ for non-inferiority) at 1 year. (Song et al. FUTURE -II)

The FANTOM Encore is Tyrosine derived polymer scaffold with strut thickness ranges between 95 to 115 microns, depending on the diameter. The scaffold is radiopaque and showed promising results in the recent published 240 patients' single arm FANTOM-II study (Lutz et al, EuroIntervention 2024).

The magnesium scaffold of Biotronik has undergone several modifications and its current DREAM 3G scaffold version shows good results and is ready to be evaluated in a pivotal 1859 patients randomized BIOMAG-II trial.

However, there is one important point to put the 'leave nothing behind' concept in perspective. Both with bioresorbable scaffolds and drug-eluting balloons the long-term 'vascular restoration' promise of reducing target vessel related late events compared to metallic DES has still to be proven. Only in a meta-analysis of the 5 ABSORB studies with 5-year follow-up there is weak signal that beyond 3 years the risk on TLF is decreasing (Powel et al. Final report ABSORB program, CRT 2024). Second, up to now, BRS studies are limited to 5-year FU and only the COMPARE-ABSORB trial will report 7-year follow-up outcomes of ABSORB compared to Xience. Unsure if the future for BRS looks bright. Let's hope Jean-Jacques Rousseau was right with his saying 'patience is bitter, but its fruit is sweet'.

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THE BEAUTY OF COLLABORATIVE WORK:
The Story of Partnership in the ABILITY Diabetes Global Trial

By Julie FAURE

This Chronicle explores the collaborative journey of Mount Sinai and CERC, the two organizations that stand at the forefront of innovation and clinical research. The shared vision and synergy of their leaders Marie Claude Morice and Roxana Mehran and their teams coupled with the recognition of this value by Dr Manish Doshi, the Founder & Managing Director of Concept Medical, are at the origin of the Ability Diabetes Global Trial. The trial enrolled 3000 patients with diabetes in 100 centers worldwide. As the story unfolds, it becomes evident that the partnership between Mount Sinai and CERC was not merely a union of resources, but a fusion of complementary strengths. Through the ABILITY Diabetes Global Trial, the combined expertise in clinical investigations, safety, data management, and analysis, and biostatistics ensured seamless integration, accelerating the pace while upholding rigorous standards. Drawing upon respective strengths, the two organizations orchestrated a seamless integration of preclinical results, international regulatory compliance, patient recruitment strategies, safety boards, and data collection/analysis. Throughout the strenuous journey of clinical development and execution, both organizations maintained an unwavering commitment to transparency, communication, and mutual respect. Regular meetings and joint decision-making processes fostered a culture of trust and accountability, laying the foundation for a truly symbiotic relationship.

However, the journey was not without its challenges. From regulatory hurdles to unforeseen setbacks in patient recruitment, the road to success was paved with obstacles. Yet, it was precisely during these moments of adversity that the strength of the partnership shone brightest. Through resilience, adaptability, creativity, and a shared commitment to the mission, CERC and Mount Sinai navigated through stormy seas and emerged stronger, and more determined than ever to fulfill the expectation.

As the chapter closes on this remarkable journey of collaboration, the legacy of Mount Sinai and CERC, remains an example of inspiration in the field of clinical research. It also serves as a testimonial to the transformative power of partnership, reminding us that by joining forces and pooling our collective talents, we can overcome the greatest of challenges and achieve the proudest of goals for the betterment of the patients we serve.