The CERC Chronicle

Issue No. 19 – December 2021

EDITORIAL

CRO Session @ Euro PCR

CERC has adopted a new corporate form integrating the concept of a company with a mission (Entreprise à Mission).

This new corporate form reaffirms CERC's founding principle, namely, improving public health, whilst embodying our dedication to achieving societal and environmental goals :

"With the patients' outcomes and quality of life as our ultimate purpose, our mission is to contribute to optimal healthcare via groundbreaking cardiovascular research. CERC is also committed to maintaining high standards of social and environmental corporate sustainability."

Our strong commitment to pursuing this mission is now reflected in our new corporate rules and regulations. Our progress will undergo regular assessment under the guidance of an in-house monitoring committee.
Finally, being able to join the quest for a third way in the corporate world is a great source of pride for CERC.

CERC DIRECTORS
MC Morice, A Neylons, P Garot, D Capodano

CERC New Members are joining us

DRAGICA PAUNOVIC

As a physician, I was always passionate about science and evidence. During the 27 years with Terumo, I was blessed with the opportunity to contribute to more than 100 clinical trials involving almost 100.000 patients.
Whenever a new product or a new scientific question emerged, the advice of practising physicians was indispensable to ensure that the study design was appealing, the hypothesis was correct, and the outcome would be valuable for the patients and clinical practice.
When CERC was established, I was fascinated with the concept, philosophy and wealth of knowledge and experience behind its founders. Since that time, CERC has become the place to go because CERC has everything I value the most, knowledge, passion, support, honesty, understanding, to name a few.
It is not surprising that I could not resist the opportunity to join this exceptional group of experts and the organization driving science that improves patient's care and shapes clinical practice.

Dragica Paunovic, MD, former Global Chief Medical Officer of Terumo Corporation, Interventional Systems

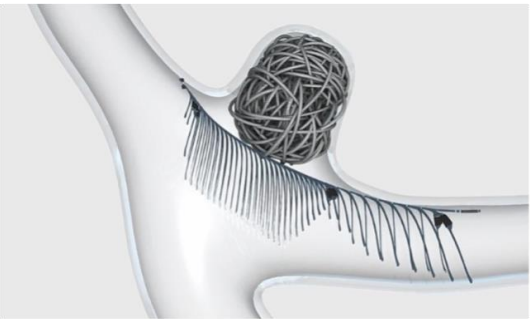
DIDIER TCHETCHE

I was eager to join the renowned community of CERC members who lead the way in the field of cardiovascular disease in Europe and beyond.
I strongly believe that learning more about these diseases is the best way to reduce disability and death.

Didier Techetche

SENIOR Trial

We are happy to begin our collaboration with CERC for a French post market trial evaluating the safety and efficacy of the eCLIPs device (eVasc) in the treatment of intracranial aneurysms.



An Bifurcation intracranial aneurysms are a potentially devastating disease in case of rupture and can be particularly complex to treat. In many instances surgical options cannot be considered, and percutaneous approaches can be at risk.
The population will consist of 120 patients having a saccular non-ruptured intracranial bifurcation aneurysm in the basilar tip or termino-carotid location. The eClips device is designed to allow for safe coiling of the aneurysm while protecting the patency of the bifurcation branches.

The trial will be conducted in 28 highly experienced French centers, the coordinating center being Hopital Fondation Rothschild in Paris where the principal investigator of the study Dr. Raphaël Blanc is working in the interventional neuroradiology department (Chairman Dr Michel Piotin).
The first investigator meeting was held during the French NeuroRadiology Society (SFNR) meeting in May 2021.

The primary endpoints are safety: proportion of patients with death or stroke within 30 days post procedure and efficacy: proportion of successful occlusion of the aneurysm without recurrence or re-intervention within 12 months.
Recruitment in the trial will begin before the end of the year and should take 24 months, each patient being followed during 2 years. The investigation has received support through the Forfait Innovation.

Dr Raphaël Blanc

EESIS-FR

Data management (DM) is involved in all aspects of clinical data processing using a range of computer, applications, database systems in accordance with regulatory standards to support collection, cleaning and management of trial data. The DM guarantees the reliability of the data.
The DM is involved in several steps during the course of the study:

- Case Report Form (CRF) review
- Data Management Plan and Data Validation Plan preparation
- Electronic Data Capture (EDC) design
- DM Status report
- Database snapshot/lock
- Data transfer

The CRF must contain all the data necessary to meet the objectives of the study. Once validated, the DM starts EDC design.
To validate the building of EDC, dummy data are entered to verify the compliance, logic and specifications validated in the CRF.
Before the go live, DM prepares two plans signed before the first patient inclusion:

- The Data Management Plan describes all Data Management activities
- The Data Validation Plan contains all database structure including the specifications and -checks

Every month, the DM prepares a DM status report for all the CERC studies, that offers an overview at a specific timepoint on:

- EDC signature status
- Follow-up tracking
- Any useful information helping the project team in the study success

At the end of the study or before an interim statistical analysis, the DM performs the database snapshot or lock. The data cannot be modified afterwards and the database is transferred for statistical analysis.

During the course of the study, the DM is responsible for many parallel tasks like EDC trainings, EDC accounts management, EDC updates…
In conclusion, the DM is here to ensure the quality of the data, but also to help to avoid manual actions that can be automated.

MASTER DAPT

The MASTER DAPT trial is the seminal clinical trial to define an optimal duration of dual antiplatelet therapy (DAPT) in unselected patients at high bleeding risk (HBR). It is an Investigator-initiated, multicenter, randomized, open-label, noninferiority trial with sequential superiority testing.

HBR patients represent a sizeable population in contemporary percutaneous coronary intervention (PCI) practice, for whom finding an optimal balance between prevention of ischemic events without triggering excessive bleeding is a challenge.

One month after PCI with Ultimaster™ DES implantation, 4579 patients, enrolled in 140 hospitals across 30 countries worldwide, were randomly assigned to discontinue dual antiplatelet therapy immediately (abbreviated therapy) or continue it for at least 2 additional months, depending on OAC status (standard therapy). The three ranked primary outcomes were NACE (a composite of death from any cause, myocardial infarction, stroke, or major bleeding), MACCE (a composite of death from any cause, myocardial infarction, or stroke), and major or clinically relevant nonmajor bleeding.

The study met all three co-primary endpoints and the results were presented by Dr. Valgimigli, the Co-PI of the study (primary endpoint), and Dr. Smits (a subset of patients on OAC therapy) at Hot Line session at the ESC congress and published simultaneously in NEJM and Circulation, respectively.

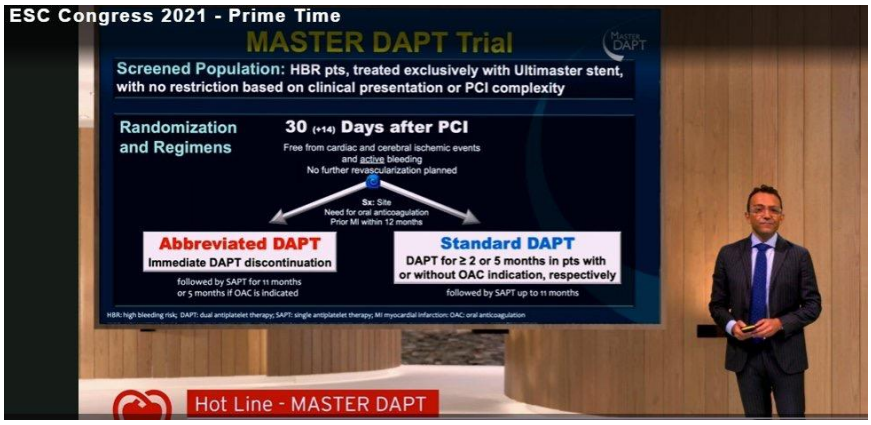
	Abbreviated	Standard	HR, 95%CI	p
NACE	**7.5%**	**7.7%**	**0.97 [0.78-1.20]**	**<0.001[1]**
MACCE	**6.1%**	**5.9%**	**1.02[0.86-1.30]**	**0.001[1]**
Bleeding	**6.5%**	**9.4%**	**0.68[0.55-0.85]**	**<0.001[2]**

1= non-inferiority; 2= superiority

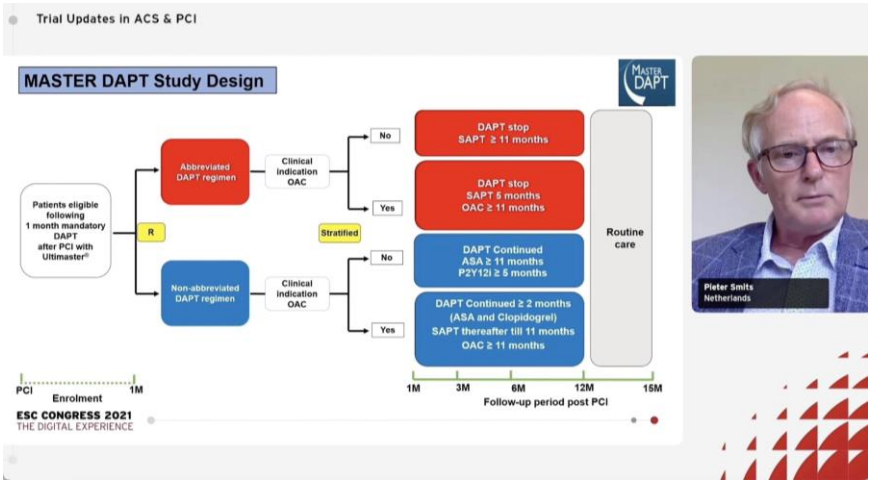
The main conclusions of the study are:

In patients at HBR who had undergone implantation of a biodegradable-polymer ULTIMASTER sirolimus-eluting stent, the abbreviated as compared to standard DAPT regimen was noninferior for NACE and MACCE and associated with a lower incidence of bleeding.

The results of this trial allow informed treatment decisions regarding DAPT at 1 month after PCI in HBR patients including patients at high ischemic risk.



The MASTER DAPT was a complex and demanding study from the initial approval process until the final stage when COVID struck. However, all major stakeholders of this study worked in harmony and with a spirit of inspiration and creativity, resulting in timely completion and almost 100% FU compliance!



We could accomplish this groundbreaking project thanks to the research grant provided by Terumo Corporation to the sponsor ECRI, the tireless work of CERC, Cardialysis, CvQuest and CTU Bern teams and an impressive dedication of our investigators and research personnel.

Our thanks go to all patients who generously agreed to take part in this important research.

Latest publications about our trials

Circulation

ORIGINAL RESEARCH ARTICLE

Abbreviated Antiplatelet Therapy in Patients at High Bleeding Risk With or Without Oral Anticoagulant Therapy After Coronary Stenting

An Open-Label, Randomized, Controlled Trial

Pieter C. Smits, MD, PhD; Enrico Frigoli, MD; Jan Tijssen, PhD; Peter Jüni, MD; Pascal Vranckx, MD, PhD; Yukio Ozaki, MD, PhD; Marie-Claude Morice, MD; Bernard Chevalier, MD; Yoshinobu Onuma, MD, PhD; Stephan Windecker, MD; Pim A.L. Tonino, MD; Marco Roffi, MD; Maciej Lesiak, MD; Felix Mahfoud, MD; Jozef Bartunek, MD, PhD; David Hildick-Smith, MD; Antonio Colombo, MD; Goran Stankovic, MD, PhD; Andrés Iñiguez, MD, PhD; Carl Schultz, MD, PhD; Ran Kornowski, MD; Paul J.L. Ong, MD, PhD; Mirvat Alasnag, MD, PhD; Alfredo E. Rodriguez, MD, PhD; Aris Moschovitis, MD; Peep Laanmets, MD; Dik Heg, PhD; Marco Valgimigli, MD, PhD; on behalf of the MASTER DAPT Investigators*

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 OCTOBER 28, 2021 VOL. 385 NO. 18

Dual Antiplatelet Therapy after PCI in Patients at High Bleeding Risk

M. Valgimigli, E. Frigoli, D. Heg, J. Tijssen, P. Jüni, P. Vranckx, Y. Ozaki, M.-C. Morice, B. Chevalier, Y. Onuma, S. Windecker, P.A.L. Tonino, M. Roffi, M. Lesiak, F. Mahfoud, J. Bartunek, D. Hildick-Smith, A. Colombo, G. Stanković, A. Iñiguez, C. Schultz, R. Kornowski, P.J.L. Ong, M. Alasnag, A.E. Rodriguez, A. Moschovitis, P. Laanmets, M. Donahue, S. Leonardi, and P.C. Smits, for the MASTER DAPT Investigators*

ORIGINAL STUDIES

WILEY

Polymer-free Biolimus-A9 coated thin strut stents for patients at high bleeding risk 1-year results from the LEADERS FREE III study

Franz R. Eberli MD[1] | Hans-Peter Stoll MD[2] | Philip Urban MD[3] | Marie-Claude Morice MD[3] | Philippe Brunel MD[4] | Luc Maillard MD[5] | Janus Lipiecki MD[6] | Stephane Cook MD[7] | Jacques Berland MD[8] | Thomas Hovasse MD[9] | Didier Carrie MD[10] | Diana Schütte PhD[2] | Sara Sadozai Slama MEng, MSc[2] | Philippe Garot MD[11]

jaa Just accepted article

EuroIntervention

Title: Impact of Clinical Presentation on Bleeding Risk after Percutaneous Coronary Intervention and Implications for the ARC-HBR Definition.

Authors: Felice Gragnano, M.D; Alessandro Spirito, M.D; Noé Corpataux, M.D; Lukas Vaisnora, M.D; Roberto Galea, M.D; Giuseppe Gargiulo, M.D, PhD; George C.M. Siontis, M.D, PhD; Fabien Praz, M.D; Jonas Lanz, M.D; Michael Billinger, M.D; Lukas Hunziker, M.D; Stefan Stortecky, M.D; Thomas Pilgrim, M.D; Sarah Bär, M.D; Yasushi Ueki, M.D; Davide Capodanno, M.D, PhD; Philip Urban, M.D; Stuart Pocock, PhD; Roxana Mehran, M.D; Dik Heg, PhD; Stephan Windecker, M.D; Lorenz Räber, M.D, PhD; Marco Valgimigli, M.D, PhD

CERC
7, rue du Théâtre
F 91300 Massy France
Tél : +33 (0)1 76 73 92 10
Fax : +33 (0)1 60 11 17 91
www.cerc-europe.org

@CERC_CRO @CERC