Prove ART (Abluminal Reservoir Technology) clinical benefIt in *all comers* patients.

Published: 15-05-2012
Last updated: 26-04-2024

Evaluate clinical performances of Cre8 in *all comer* population

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Coronary artery disorders
Study type	Observational invasive

Summary

ID

NL-OMON44679

Source
ToetsingOnline

Brief title
PARTICIPATE study

Condition

- Coronary artery disorders

Synonym
coronary artery desease, stenosis

Research involving
Human

Sponsors and support

Primary sponsor: CID S.p.A.
Source(s) of monetary or material Support: CID S.p.A.

Intervention

Keyword: Diabetic, Drug Eluting Stent, PCI, Polymer free

Outcome measures

Primary outcome

Incidence of clinical composite endpoint at 6 months:

Cardiac death / Target vessel MI / Clinically indicated TLR*

*Device oriented composite endpoint

Secondary outcome

- Incidence of clinical composite endpoints at 30 days, 1 year and yearly up to

5 years from the index procedure:

- Cardiac death / Target vessel MI / Clinically indicated TLR*

- All death / All MI / All Repeat Revascularization **

*Device oriented composite endpoint **Patient oriented composite endpoint

- Incidence of stent thrombosis throughout the study duration, classified

according to ARC definition;

- Angiographic measurements in-stent and in-segment (reference vessel diameter;

minimal lumen diameter; % diameter stenosis; binary restenosis; late lumen

loss) pre and post intervention and at 6-month follow-up, in the first 100

patients included in the pre-specified diabetic subgroup

Study description

Background summary

The development, clinical validation, and widespread use of drug-eluting stents (DES) have revolutionized the treatment of patients with coronary artery

disease. Large scale, prospective, multicenter double-blind randomized trials have provided strong evidence that sirolimus-eluting stents (SES), paclitaxel-eluting stents (PES), and zotarolimus-eluting stents (ZES) significantly reduce angiographic restenosis and enhance event-free survival compared with bare-metal stents (BMS) after implantation in native coronary arteries1-4. However, higher rates of late and very late stent thrombosis with SES and PES, likely due to delayed and incomplete endothelialization compared with BMS, have raised safety concerns with DES as a class5-8. Therefore, alongside clinical investigations, histopathological evaluations were conducted on the coronary arteries of patients who died after DES implantation to examine the healing status of the vessel. The evidence obtained suggested that the polymer components (especially stable polymers) used to carry the drug in the first generation of DES may be associated with a local inflammatory response, associated with localized hypersensitivity and eosinophil infiltration, with consequent alteration of the vessel wall and delay in the formation of the endothelium9-11.

Because specific stent design and/or polymer features may impact DES performance, numerous studies have focused on the comparative assessment of various DES, with conflicting results12-18.

The clinical need thus exists for enhanced stent designs which offer improved safety and efficacy profiles compared to the earlier stent platforms.

Thanks to numerous, consistent clinical evidences gathered on the first-generation DES, new technologies have been developed which have led to the creation of devices with delivery systems based on the use of more biocompatible or bioabsorbable (PLA) polymers and cytostatic drugs similar to sirolimus (Xience V device - everolimus; Endeavor Resolute device - zotarolimus, Biomatrix device - biolimus).

The clinical data obtained with this second generation have demonstrated, in all devices tested, no less efficacy than first-generation DES, and a better safety profile, although not statistically significant19 -21.

Concerning the most widely used second generation DES, EES (Xience V), after a small first-in-man trial (SPIRIT I), its safety and efficacy was further studied in larger randomized trials on patients with non-complex lesions in which EES was compared to PES (SPIRIT II and III)22, 23, proving its angiographic superiority and clinical non-inferiority. A step forward, in assessing the clinically significant differences among different DES, was done with a new randomized trial comparing EES versus PES, powered for testing superiority in clinical outcomes (SPIRIT IV) and of sufficient magnitude to provide data on patient subgroups, particularly patients with diabetes24.

At present, a third-generation of DES, developed to minimize the possible side effects related to the presence of the polymer, is being evaluated in humans. To avoid the presence of the polymer on the surface of the device, different platforms are being evaluated: those with a porous surface onto which the pure drug is placed (BioFreedom stent, Biosensor)25 and those with holes closed towards the intraluminal part by a bioabsorbable polymer, onto which the drug is loaded (Nevo stent, Cordis)26.

A third option to avoid the need of polymers has been used in the new CRE8 DES,

featuring a polymer free platform with abluminal reservoirs to release the Amphilimus formulation (Sirolimus formulated with organic fatty acid). This device has been tested against Taxus Liberté in a randomized clinical trial, to assess the non-inferiority angiographic efficacy results (see the Investigators* Brochure for detailed data).
Since the diabetic patients* subgroup was well represented in the study, a post-hoc analysis on diabetics has been conducted, showing that this high risk group could benefit from Cre8 implantation (6-month Late Lumen Loss 0.12±0.29 vs. 0.43±0.41 mm) 27.
Knowing that the presence of diabetes mellitus (particularly insulin requiring diabetes) has been a consistent, independent predictor of restenosis in most stent trials and registries and that some SES studies have raised questions regarding the relative efficacy of rapamycin analogue-eluting stents in patients with diabetes 28,29, the present study has been designed with a pre-specified sub-group analysis on diabetic subjects, including also an angiographic follow-up control on the first 100 diabetics included, to assess if the initial results obtained in the first in man trial are transposed also in the everyday clinical practice patients.

Study objective

Evaluate clinical performances of Cre8 in *all comer* population

Study design

Prospective, multicenter study

Study burden and risks

Clinical visit: 6-month follow-up.
Phone call: 30 days, yearly up to 5 years after procedure.
Angiographic control: 6-month follow-up in the first 100 enrolled diabetic patients.

Estimated enrolment complete: 12 months;
Estimated primary completion date: Q2 2013;
Estimated last patient out: Q4 2017

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

• Age > 18 years;
• Patients with symptoms of stable angina or documented silent ischemia;
• Patient with coronary artery disease ranging between 0 and 22 according to the Syntax score;
• Patients with acute coronary syndrome, including unstable angina, NSTEMI and STEMI;
• Patient is eligible for percutaneous coronary intervention (PCI) and is an acceptable candidate for surgical revascularization (CABG);
• Left ventricular ejection fraction > 30%;
• Target de-novo lesions with diameter stenosis > 50% (including total occlusion);
• Target lesion located in a target vessel with a diameter ranging from 2.5 to 4.0 mm;
• Patient has been informed of the nature of the study and agrees to its provisions and has provided written informed consent as approved by the Ethical Committee of the respective clinical site.

Exclusion criteria

• Female with childbearing potential or lactating;
• Known allergies to antiplatelets, anticoagulants, contrast media, sirolimus or cobalt

chromium;
• Acute or chronic renal dysfunction (defined as creatinine greater than 2.5 mg/dl or on dialysis);
• Thrombocytopenia (platelet count less than 100,000/mm³) or hypercoagulable disorder;
• Known significant gastro-intestinal or urinary bleeding within the past 6 months;
• Patient refusing blood transfusion;
• Patient currently under immunosuppressant therapy;
• Patient with planned surgery within 6 months from the index procedure unless dual antiplatelet therapy is maintained throughout the peri-surgical period;
• Co-morbidities that could interfere with completion of study procedures, or life expectancy less than 1 year;
• Participating in another investigational drug or device trial that has not completed the primary endpoint or would interfere with the endpoints of this study;
• Patient underwent target vessel revascularization with a DES within 3 months prior to the index procedure;
• Target lesion is located or supplied by an arterial or venous bypass graft.

Study design

Design

Study phase:	4
Study type:	Observational invasive
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	02-07-2012
Enrollment:	276
Type:	Actual

Medical products/devices used

Generic name:	Drug Eluting Stent - CRE8
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	15-05-2012
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	04-09-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	10-09-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	24-01-2018
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL39704.060.12