CLINICAL INVESTIGATION OF A DES (MISTENT* SYSTEM) WITH SIROLIMUS AND A BIOABSORBABLE POLYMER FOR THE TREATMENT OF PATIENTS WITH DE NOVO LESIONS IN NATIVE CORONARY ARTERIES

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The primary objective of this study is to demonstrate whether the MiStent Drug Eluting Coronary Stent System can safely and effectively improve coronary luminal diameter in patients with symptomatic ischemic heart disease due to discrete de novo...

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

Summary

ID

NL-OMON36775

Source
ToetsingOnline

Brief title
DESSOLVE II

Condition

- Coronary artery disorders

Synonym
coronary artery disease, stenosis

Research involving

Human

Sponsors and support

Primary sponsor: genae associates nv
Source(s) of monetary or material Support: Micell Technologies

Intervention

Keyword: Drug Eluting Coronary Stent System, Randomized trial, Sirolimus, Symptomatic ischemic heart disease

Outcome measures

Primary outcome

Primary Efficacy Endpoint: The primary endpoint is in-stent late lumen loss (LLL) measured by the angiographic core laboratory and calculated as a difference between the post-procedure minimal lumen diameters (MLD) in the treated segment (stented region) minus the MLD in the same region at follow-up. Angiographic analysis will be performed at 9 months.

Primary Safety Endpoint: The primary safety endpoint for this trial is the rate of Major Adverse Cardiac Events (MACE) defined as death, MI and target vessel revascularization (TVR) at 9 months post-procedure.

Secondary outcome

Secondary Endpoints:

1. Device success defined as stent deployment resulting in a final percentage diameter stenosis (DS) of less than or equal to 30% using the assigned stent;

2. Lesion success defined as attainment of <50% residual stenosis using any percutaneous method; 3. Procedural success defined as lesion success without an in-hospital

MACE event; 4. Total mortality (cardiac and non-cardiac);

5. Total MI (Q-wave and non-Q-wave) and total target vessel MI;

6. Clinically-driven target lesion revascularization (TLR) and target vessel revascularization

(TVR) rates;

7. Target vessel failure (TVF) and target lesion failure (TLF) at each follow-up visit. TVF and TLF defined as cardiac death, target vessel MI, or clinically-driven target vessel revascularization (or target lesion revascularization for TLF);

8. Stent thrombosis rates according to ARC classification post-procedure and at each follow-up visit;

9. Angiographic parameters: in-stent and in-segment late loss, percentage DS, MLD, and binary restenosis rates at 9 months;

10. Adverse events will be collected at each follow-up visit.

Subgroup Evaluations:

1. A subgroup of at least 30 patients (20 MiStent DES and 10 Endeavor controls) will undergo

OCT evaluation at procedure and at 9-months to assess the extent of strut coverage, stent malapposition, evidence of polymer absorption, tissue prolapse, dissections, and changes in stent and lumen area. Additionally, the presence of thrombus will be noted.

2. A subgroup of at least 42 patients (28 MiStent DES and 14 Endeavor DES controls) will undergo endothelial function testing by rapid atrial pacing at

9-months follow-up.

Study description

Background summary

Drug Eluting Stents (DES) have been introduced globally in the last several years. In most cases, DES manufacturers have modified existing bare metal stent designs (typically stainless steel or CoCr alloys) by applying a permanent polymer coating which elutes a drug intended to reduce the extent of restenosis. Delivery of drugs such as paclitaxel and sirolimus from such coated stents was developed to address restenosis caused by the growth and proliferation of neointima following stent implant. DES products currently have widespread clinical use; however, the potential local toxicity of these polymers and drugs continues to cause concern regarding their long-term effect on vessel healing, late thrombosis, and hypersensitivity. In order to address these concerns, Micell Technologies has developed the MiStent* Drug Eluting Coronary Stent System.
The MiStent* Drug Eluting Coronary Stent System consists of a CE Marked CoCr bare metal stent platform and delivery catheter, and a bioabsorbable polymer/drug coating containing sirolimus. This next-generation DES stent is intended to combine the long-term safety and stability characteristics of a bare metal stent with the demonstrated clinical advantages of a drug-eluting stent. Micell*s proprietary surface modification technology provides a unique drug delivery system through the use of bioabsorbable polymers and an approved drug with a well-known safety and efficacy profile (sirolimus).
The rapid-absorbing polymer/drug formulation is intended to control drug elution and the duration of polymer exposure precisely and consistently. As a result, Micell's coating is intended to deliver a precise therapeutic solution for coronary artery disease with the potential to avoid the long-term safety concerns associated with current drug-eluting stents.
Following stent implantation, this polymer/drug coating is deposited from the stent struts into the adjacent tissue. The deposited material continues to elute and deliver drug to the surrounding tissue as the polymer is absorbed by the tissue. It is expected, based on animal trials, that all of the polymer/drug material is absorbed within 90-days, leaving an inert BMS within the coronary artery.

Study objective

The primary objective of this study is to demonstrate whether the MiStent Drug Eluting Coronary Stent System can safely and effectively improve coronary luminal diameter in patients with symptomatic ischemic heart disease due to discrete de novo lesions of length < 27 mm in native coronary arteries with

reference vessel diameter between 2.5 mm and 3.5 mm. The patients will be followed for 5 years for major clinical events. Two important secondary objectives of this study are mechanistic in nature. Optical Coherence Tomography(OCT) evaluations and endothelial function testing will be conducted on subgroups of patients enrolled in the study. A subgroup of at least 30 patients (20 MiStent DES patients and 10 Endeavor DES control patients) at selected sites will undergo OCT evaluation at the index procedure and at 9-months to assess the extent ofstrut coverage, stent malapposition, evidence of polymer absorption, tissue prolapse, dissections, and changes in stent and lumen area. Additionally, the presence of thrombus will be noted. A subgroup of at east 42 patients (28 MiStent DES and 14 Endeavor DES controls) at selected sites will undergo endothelial function testing by rapid atrial pacing at 9-months follow-up. These two sub-studies will provide important information about the ability of the target vessel to heal with return of endothelial function after stent deployment. The return of normal endothelial function has been shown to be delayed with some drug-eluting stents with a non-erodible polymer coating and has been considered a risk factor for stent thrombosis. The MiStent DES has a coating that is completed absorbed within 3 months of stent deployment and as a result, may allow for more rapid and complete healing of the endothelium.

Study design

This is a prospective, single-blind, 2:1 unbalanced randomized, parallel group, controlled, multicenter superiority trial.
Enrollment of one hundred and seventy one (171) patients. As this is a 2:1 unbalanced randomization, it is anticipated that 114 patients will be treated with the MiStent* Drug Eluting Coronary Stent System and the remaining 57 patients will be treated with the control Endeavor DES stent system (Medtronic).

Intervention

Patients will be randomized into either the MiStent DES or Endeavor DES arm of the trial. This notification will be available through an interactive voice response system (IVRS) to inform the site as to which treatment group the patient is assigned after the baseline angiographic assessment confirms the target lesion matches enrollment criteria. Patients will not be informed of the treatment group they are assigned.

The intervention is done by a percutaneous coronary intervention. For patients randomized into the Endeavor DES arm, the Instructions for Use provided with the device should be followed. This is a well known device for the investigators which is CE approved. The MiStent DES implantation procedure is included in the Instructions for Use provided with the MiStent DES and is also described in Appendix A-4 of the protocol.

Study burden and risks

With any procedure there are risks and complications. Since the MiStent system is an investigational device, the risks associated with use are not entirely known, but are believed to be similar to the risks that are associated with current clinical practices using drug-coated stents to treat patients with symptomatic ischemic heart disease. In addition, the use of OCT and conducting endothelial function testing may cause additional risks. The following is a list of anticipated adverse events (in alphabetical order) that may result from the use of the device: COMMON - More than 10%
Angina pectoris, Bleeding or hematoma (bruising) at the access site, Pain at the catheter insertion site, Unstable angina
LESS COMMON - 2% to 9%
Acute myocardial infarction, Arrhythmias, Bradycardia, Hypotension, Restenosis of the stented arter,y Thrombus formation
RARE - 1% or less
Abrupt vessel closure, Allergic reaction to contrast media (dye), aspirin, heparin, clopidogrel bisulfate (Plavix), ticlopidine (Ticlid) or Prasurgrel (Effient), as prescribed Aneurysm, pseudoaneurysm or arteriovenous fistula, Cardiac tamponade, Cerebral vascular event, Coronary artery aneurysm, Damage to the stent or injury to the artery requiring emergency heart surgery, Death Device embolization Dissection, perforation, or rupture of the coronary artery, Embolism (air, tissue, thrombus or device), Hypersensitivity to cobalt-chromium, Hypersensitivity to sirolimus, Infection or fever, Pseudoaneurysm or fistula at the vascular access site, Stent misplacement, Stent thrombosis or occlusion, Stroke or transient ischemic attack (TIA), Thromboembolic events, Vascular trauma

The occurrence of the above listed complication(s) may lead to the need for repeat catheterization and/or PCI, emergency bypass surgery, myocardial infarction or death. This treatment may involve some additional risks, the nature of which is unknown.
Potential Risks associated with Sirolimus Following Oral Administration These are risks reported and associated with the oral administration (by mouth) of the drug, sirolimus. This drug will be eluted from the stent at a significantly lower dose compared to oral administration.
RARE - 1% or less
Abnormal liver function tests, Arthralgias, Diarrhea, Hypercholesterolemia, Hypersensitivity, including anaphylactic/anaphylactoid type reactions Hypertriglyceridemia Hypokalemia, Infections, Interstitial lung disease, Leukopenia, Lymphoma and other malignancies, Thrombocytopenia

Contacts

Public
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. 1. Male and female patients of age >=18 years and <=85 years;
2. Documented stable or unstable angina pectoris (Class I, II, III or IV), documented ischemia, or documented silent ischemia;
3. Planned single, de novo, types A, B1 or B2 coronary lesions (according to the ACC/AHA classification);
4. Target lesion located in a native coronary artery;
5. Target lesion in vessel with diameter ranging from 2.5 to 3.5 mm amenable to treatment (coverage) with a maximum 30 mm long stent;
6. Target lesion with >50% diameter stenosis;
7. If the patient has experienced a recent Q-wave (>72 hours) or non-Q-wave myocardial infarction, the CK, CK-MB levels should have returned to normal (8. Patients who are eligible for percutaneous coronary intervention (PCI);
9. Acceptable candidate for myocardial revascularization surgery (coronary artery bypass graft surgery);
10. A patient may have one additional critical non-target lesion. The target lesion is the only

lesion that must meet the study inclusion requirements. The non-target lesion may be treated at the time of the index procedure but must be successfully treated without complications before the target lesion. The non-target lesion will not be considered to be part of the study and does not require the follow-up evaluations defined in the protocol. If more than one lesion meets the inclusion criteria, only one lesion/vessel chosen by the Investigator should be treated with the study stent; the other lesion(s) should be treated outside the study with approved devices. An approved bare metal stent or another commercially available *limus* based DES product may be used in the non-target vessel.
11. The patient is judged to be capable of providing voluntary informed consent and has been fully informed of the nature of the study, is willing to comply with all study requirements and will provide written informed consent as approved by the Ethics Committee of the respective clinical site.
12. The patient is affiliated with a social security system (if required by individual country regulations).

Exclusion criteria

1. Female patients of childbearing potential who = do not have a confirmed negative pregnancy test at baseline and are not on some form of birth control;
2. Recent Q-wave myocardial infarction occurred within 72 hours prior to the index procedure.
3. Recent Q-wave or non-Q-wave myocardial infarction with still elevated levels of cardiac markers (e.g. CK; and CK-MB if the CK is elevated);
4. Left ventricular ejection fraction <30% (within the previous 6-months);
5. Patients in cardiogenic shock;
6. Cerebrovascular accident (CVA) or transient ischemic attack (TIA) within the past 6 months;
7. Active GI bleeding within past three months;
8. Any prior true anaphylactic reaction to contrast agents;
9. Patient is receiving or scheduled to receive chemotherapy within 30-days before or after the index procedure;
10. Patient is receiving oral or intravenous immunosuppressive therapy or has known life-limiting immunosuppressive or autoimmune disease (e.g., human immunodeficiency virus, systemic lupus erythematosus, but not including diabetes mellitus);
11. Renal dysfunction (creatinine > 2.0 mg/dL or 177 µmol/L);
12. Platelet count <100,000 cells/mm^3 or >700,000 cells/mm^3;
13. White blood cell count <3,000 cells/mm3;
14. Suspected or documented hepatic disease (including laboratorial evidence of hepatitis);
15. Heart transplant recipient;
16. Known contraindication to dual antiplatelet therapy (DAPT);
17. Known hypersensitivity to sirolimus (or its structurally related compounds), cobalt-chromium, or to medications such as aspirin, heparin and Angiomax® (bivalirudin), and all three of the following: clopidogrel bisulfate (Plavix), ticlopidine (Ticlid), and Prasugrel (Effient);
18. Concurrent medical condition with a life expectancy of less than 12 months;

19. Any major medical condition that, in the Investigator's opinion, may interfere with the optimal participation of the patient in this study;
20. Patient is currently participating in an investigational drug or another device study and has not completed the follow-up to the primary endpoint, or the patient in planning on participating in an investigational drug or another device study during the course of the present investigation prior to completing 12-months follow-up;
21. Target vessel has been treated within 10 mm proximal or distal to target lesion (by visual estimate) with any type of PCI (e.g., balloon angioplasty, stent, cutting balloon, atherectomy) or within a year prior to index procedure;
22. Planned or actual target vessel(s) treatment with an unapproved device, directional or rotational coronary atherectomy, laser, cutting balloon, or transluminal extraction catheter prior to stent placement;
23. Patient previously treated at any time with coronary intravascular brachytherapy;
24. Planned coronary angioplasty (with or without stenting) or CABG in the first 9 months after the index procedure or any other planned intervention within 30 days post index procedure;
25. Prior PCI of a non-target vessel must be at least 14 days prior to study enrollment;
26. The intent to direct stent the target lesion;
27. Angiographic Exclusion Criteria: To be assessed at the time of the index procedure catheterization prior to randomization and stent placement using visual estimate or online QCA, as appropriate;
27.1 In-stent restenotic target lesion;
27.2 More than one lesion requiring treatment in the target vessel (i.e. another lesion with >50% diameter stenosis (DS) proximal or distal to the target lesion);
27.3 Target vessel diameter <2.5 mm or >3.5 mm;
27.4 Long target lesion not amenable to treatment (coverage) with a 30 mm long stent;
27.5 Left main critical disease (>=50% DS);
27.6 Target lesion is located in a surgical bypass graft;
27.7 Total target vessel occlusion (TIMI flow grade 0-1);
27.8 Target lesion with ostial location (within 5 mm of ostium by visual assessment);
27.9 Target lesion at a bifurcation involving a lateral side branch >2.5mm or a lateral side branch that also requires stenting;
27.10 Calcified target lesion that anticipates unsuccessful/impracticable predilation;
27.11 Target vessel with excessive tortuosity or proximal angulation (>90 degrees);
27.12 Thrombus present in target vessel;
27.13 More than one non-target critical lesion;
27.14 Non-target lesion to be treated during the index procedure meets any of the following criteria:
27.14.1 Located within the target vessel;
27.14.2 Located within a bypass graft (venous or arterial);
27.14.3 Left main location;
27.14.4 Chronic total occlusion;
27.14.5 Involves a complex bifurcation (e.g., bifurcations requiring treatment with more than one stent).

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	26-04-2011
Enrollment:	50
Type:	Actual

Medical products/devices used

Generic name:	Coronary Stent System
Registration:	No

Ethics review

Approved WMO Date:	18-03-2011
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	02-05-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO Date:	26-05-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	17-06-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	08-07-2011
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	NL34640.100.10

Study results

Results posted: 05-12-2016

First publication
05-12-2016