BioNIR Ridaforolimus Eluting Coronary Stent System (BioNIR) In Coronary Stenosis Trial

Published: 21-01-2014
Last updated: 24-04-2024

1) The BioNIR is non-inferior to the Resolute for the primary clinical endpoint of target lesion failure (TLF) (defined as the composite of cardiac death, target vessel-related MI, or ischemia-driven TLR) at 12 months2/ The BioNIR is non-inferior to...

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

Summary

ID

NL-OMON47650

Source
ToetsingOnline

Brief title
BIONICS

Condition

- Coronary artery disorders

Synonym
coronary artery disease, coronary artery stenosis

Research involving
Human

Sponsors and support

Primary sponsor: Medinol Ltd.
Source(s) of monetary or material Support: Medinol Ltd.

Intervention

Keyword: BioNIR, Coronary artery stenosis, PCI

Outcome measures

Primary outcome

Target Lesion Failure (TLF) at 12 months defined as the composite of cardiac death, target vessel-related myocardial infarction, or ischemia-driven target lesion revascularization.

Secondary outcome

Clinical Secondary Endpoints to be evaluated at 30 days, 6 months, and 1, 2, 3, 4 and 5, except as noted:

* Device, Lesion, and Procedure Success at time of baseline procedure

* TLF at 30 days, 6 months, and 2, 3, 4 and 5 years defined as the composite of cardiac death, target vessel-related MI, or ischemia-driven TLR.

* Major adverse cardiac events (MACE; the composite rate of cardiac death, any MI or ischemia-driven TLR)

* Target vessel failure (TVF; the composite rate of death, target vessel related MI or ischemia-driven TVR)

* All-cause mortality

* Cardiac death

* Myocardial Infarction

* Target Vessel Related MI

* Ischemia-driven TLR

* Ischemia-driven TVR

* Stent Thrombosis (ARC definite and probable)

Angiographic Sub-Study Secondary Endpoint to be evaluated at 13 months:

* Angiographic in-stent and in-segment late loss

IVUS Sub-Study Secondary Endpoint to be evaluated at 13 months:

* In-stent percent neointimal hyperplasia

* Stent mal-apposition

Study description

Background summary

Percutaneous Intervention (PCI) is part of the standard treatment for coronary artery stenoses and has been shown to relieve ischemia and angina in stable coronary disease and improve outcomes in acute coronary syndromes particularly in patients with ST elevation myocardial infarction (STEMI). Stents, originally developed in the 1980s, have almost entirely replaced balloon angioplasty with the advantage of greater procedural success with reduced risk of abrupt closure as well as reduced rates of restenosis. Bare metal stents, however, were still limited by up to 30% restenosis rate due to neointimal proliferation. The advent of drug eluting stents (DES) which released anti-proliferative medications into the stented region markedly reduced the restenosis rate, thereby reducing the rate of repeat revascularization. Concern emerged, however, over late and very late stent thrombosis with the use of DES. Stent thrombosis has been linked to delayed and incomplete endothelialization as well as stent mal-apposition and strut breakage. Additional issues with DES include a local inflammatory reaction, allergic reactions to the stent components, and impairment of endothelial function.
Different DES have been shown to have differing rates of angiographic late loss as well as different rates of clinical events such as target lesion failure (TLF) and stent thrombosis. Different stent design, polymer features, and anti-proliferative drug used may impact these important clinical endpoints. The overall low event rate, however, has necessitated large scale clinical trials to evaluate new stents. Registration studies have also been limited by strict enrollment criteria which have excluded many patient and lesion types which are typically treated in clinical practice including complex lesions and patients with acute coronary syndromes.
The BioNIR is a new DES which uses a closed-cell design and an improved delivery system and therefore may improve outcomes compared to other drug eluting stents. The present trial is aimed at assessing the safety and efficacy

of the BioNIR in comparison to a second generation DES, the Zotarolimus-eluting Resolute stent (Medtronic).
The aim of the present trial is therefore to evaluate the BioNIR in comparison to the Resolute in a clinically diverse population representative of contemporary stent use. The trial will enroll a broad population including patients with ACS (unstable angina, NSTEMI, and STEMI) as well as complex lesions. The inclusion of patients with AMI and particularly STEMI is justified given that the majority of PCIs are in patients with ACS with STEMI accounting for up to 30% of ACS cases. In order to reduce the potential for confounding, patients with STEMI will be enrolled only after 24 hours have elapsed from their initial hospital presentation. Typically such patients will have already undergone primary PCI of the culprit lesion. Stent thrombosis is increased in the setting of primary PCI mostly in the first 24 hours. Therefore, confounding is unlikely and furthermore subjects will be stratified in the trial by ACS vs. non-ACS status.

Study objective

1) The BioNIR is non-inferior to the Resolute for the primary clinical endpoint of target lesion failure (TLF) (defined as the composite of cardiac death, target vessel-related MI, or ischemia-driven TLR) at 12 months
2/ The BioNIR is non-inferior to the Resolute for the secondary endpoint of angiographic in-stent loss at 13 months
3. The BioNIR is more cost-effective than the Resolute

Study design

This BIONICS study is a prospective, multi-centre, single-blind, two-arm, randomized clinical study comparing two drug eluting stents, i.e. the non-CE marked investigational device: the BioNIR Ridaforolimus Eluting Coronary Stent System and the comparator CE marked device: the Resolute Zotarolimus Eluting Coronary Stent System.

Clinical follow-up will be performed at 30 days, 6 months and 1, 2, 3, 4 and 5 years post-enrolment.

The BIONICS study will take place in the USA, Canada and a number of European countries (Belgium, Germany, Italy, Netherlands, Poland and Spain) and in Israel. Applications for clinical study approval have begun in Israel and Canada and are expected to be submitted to all other countries by December 2013.

The study will involve approximately 1906 patients who will be randomized 1:1 to each study arm (953 per study arm). In North America, 200 of these patients will be consented for follow-up repeat angiography at 13 months; 100 of these patients will also be consented for IVUS (intravascular ultrasound) at baseline

and at 13 months

Intervention

Alle subjects will undergo coronary angiography and PCI with study stent implantation (BioNIR or Resolute). The stent will remain implanted during the follow-up period, in total 5 years.

Study burden and risks

Anticipated Clinical Benefits
The potential benefit of the study stent is its effectiveness in inhibition of neointimal growth while enhancing endothelial coverage. The study stent has the potential to reduce rates of restenosis without increasing rates of late and very late stent thrombosis compared to other commercially available DES.

Anticipated Adverse Device Effects
It is expected that the adverse device effects for BioNIR would not differ from the anticipated adverse device effects based on years of clinical experience with rapid exchange DES implantations.

Residual Risks Associated with Investigational Device
Foreseeable adverse events that may result from stent intervention can be found in Section 14.6 as well as the IB section 5.3.

Risks Associated with Participation in the Clinical Investigation
There is extensive clinical and commercial experience worldwide with cardiac catheterization and interventional procedures and it is expected that the surgical and procedural risks will not be significantly different in this clinical trial. For the subset of subjects who participate in the angiographic and/or IVUS evaluation at 13 months post-procedure, the risks of non-clinically indicated diagnostic angiography are the same or less as clinically indicated angiography. Please note that this subset of subjects is not relevant to the EU participating subjects.

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

1. Age * 18 years.
2. Patient with an indication for PCI including angina (stable or unstable), silent ischemia (in absence of symptoms a visually estimated target lesion diameter stenosis of *70%, a positive non-invasive stress test, or FFR *0.80 must be present), NSTEMI, or recent STEMI. For STEMI the time of presentation to the first treating hospital, whether a transfer facility or the study hospital, must be >24 hours prior to randomization and enzyme levels (CK-MB or Troponin) demonstrating that either or both enzyme levels have peaked.
3. Non-target vessel PCI are allowed prior to randomization depending on the time interval as follows:
a. During Baseline Procedure:
i. PCI of non-target vessels performed during the baseline procedure itself immediately prior to randomization if successful and uncomplicated defined as: <50% visually estimated residual diameter stenosis, TIMI Grade 3 flow, no dissection * NHLBI type C, no perforation, no persistent ST segment changes, no prolonged chest pain, no TIMI major or BARC type 3 bleeding.
b. Less than 24 hours prior to Baseline Procedure:
i. Not allowed (see exclusion criteria #2).
c. 24 hours-30 days prior to Baseline Procedure:
i. PCI of non-target vessels 24 hours to 30 days prior to randomization if successful and uncomplicated as defined above.
ii. In addition, in cases where non-target lesion PCI has occurred 24-72 hours prior to the baseline procedure, at least 2 sets of cardiac biomarkers must be drawn at least 6 and 12

hours after the non-target vessel PCI.
iii. If cardiac biomarkers are initially elevated above the local laboratory upper limit of normal, serial measurements must demonstrate that the biomarkers are falling.
d. Over 30 days prior to Baseline Procedure:
i. PCI of non-target vessels performed greater than 30 days prior to procedure whether or not successful and uncomplicated.
4. Patient or legal guardian is willing and able to provide informed written consent and comply with follow-up visits and testing schedule.;Angiographic inclusion criteria (visual estimate)
5. Target lesion(s) must be located in a native coronary artery or bypass graft conduit with visually estimated diameter of *2.5 mm to *4.25 mm.
6. Complex lesions are allowed including calcified lesions (lesion preparation with scoring/cutting and rotational atherectomy are allowed), presence of thrombus, CTO, bifurcation lesions (except as noted in exclusion criteria #30), ostial RCA lesions, tortuous lesions, bare metal stent restenotic lesions, protected left main lesions, and saphenous vein graft lesions.
7. Overlapping stents are allowed.

Exclusion criteria

1. STEMI within 24 hours of initial time of presentation to the first treating hospital, whether at a transfer facility or the study hospital or patients in whom enzyme levels (either CK-MB or Troponin) have not peaked.
2. PCI within the 24 hours preceding the baseline procedure.
3. Non-target lesion PCI in the target vessel within 12 months of the baseline procedure.
4. History of stent thrombosis.
5. Cardiogenic shock (defined as persistent hypotension (systolic blood pressure <90 mm/Hg for more than 30 minutes) or requiring pressors or hemodynamic support, including IABP.
6. Subject is intubated.
7. Known LVEF <30%.
8. Relative or absolute contraindication to DAPT for 12 months (including planned surgeries that cannot be delayed, or on or indicated for chronic oral anticoagulant treatment).
9. Calculated creatinine clearance <30 mL/min using Cockcroft-Gault equation (<40 mL/min for subjects participating in the angiographic follow-up sub-study).
10. Hemoglobin <10 g/dL.
11. Platelet count <100,000 cells/mm3 or >700,000 cells/mm3.
12. White blood cell (WBC) count <3,000 cells/mm3.
13. Clinically significant liver disease.
14. Active peptic ulcer or active bleeding from any site.
15. Bleeding from any site within the prior 8 weeks requiring active medical or surgical attention.
16. If femoral access is planned, significant peripheral arterial disease which precludes safe insertion of a 6F sheath.
17. History of bleeding diathesis or coagulopathy or will refuse blood transfusions.
18. Cerebrovascular accident or transient ischemic attack within the past 6 months, or any

permanent neurologic defect attributed to CVA.
19. Known allergy to the study stent components, whether in the BioNIR or Resolute, e.g. cobalt, nickel, chromium, molybdenum, Carbosil®, PBMA, Biolinx polymer, or limus drugs (ridaforolimus, zotarolimus, tacrolimus, sirolimus, everolimus, or similar drugs or any other analogue or derivative or similar compounds).
20. Known allergy to protocol-required concomitant medications such as aspirin, or DAPT (clopidogrel, prasugrel, ticagrelor), or heparin and bivalirudin, or iodinated contrast that cannot be adequately pre-medicated.
21.Any co-morbid condition that may cause non-compliance with the protocol (e.g. dementia, substance abuse, etc.) or reduced life expectancy to <24 months (e.g. cancer, severe heart failure, severe lung disease).
22. Patient is participating in or plans to participate in any other investigational drug or device clinical trial that has not reached its primary endpoint.
23. Women who are pregnant or breastfeeding (women of child-bearing potential must have a negative pregnancy test within one week before treatment).
24. Women who intend to procreate within 12 months after the baseline procedure (women of child-bearing potential who are sexually active must agree to use a reliable method of contraception from the time of screening through 12 months after the baseline procedure).
25. Patient has received an organ transplant or is on a waiting list for an organ transplant.
26. Patient is receiving or scheduled to receive chemotherapy within 30 days before or any time after the baseline procedure.
27. Patient is receiving oral or intravenous immunosuppressive therapy or has known life-limiting immunosuppressive or autoimmune disease (e.g., HIV). Corticosteroids are allowed.;Angiographic Exclusion Criteria (visual estimate)
28. More than 100 mm planned stenting in the entire coronary tree.
29. Unprotected left main lesions *30%, or planned left main intervention.
30. Ostial LAD or LCX lesions (stenting of any diseased segment within 5 mm of the unprotected left main coronary artery).
31. Bifurcation lesions with planned dual stent implantation.
32. Stenting of lesions due to DES restenosis.
33. Another lesion in a target or non-target vessel (including all side branches) is present that requires or has a high probability of requiring PCI within 12 months after the baseline procedure.

Study design

Design

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):	28-04-2014
Enrollment:	119
Type:	Actual

Medical products/devices used

Generic name:	Drug Eluting Stent (DES) - BioNIR
Registration:	No

Ethics review

Approved WMO Date:	06-03-2014
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	19-06-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	29-11-2019
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
ClinicalTrials.gov	NCT01995487
CCMO	NL46831.101.13