# A Prospective, Randomized Study to Evaluate the Safety and Effectiveness of an AbluMinal Sirolimus CoatED Bio-Engineered StEnt (Combo Bio-Engineered Sirolimus Eluting Stent) Compared with a TAXUS® Liberté® Stent Control Arm for Treatment of Stenotic Lesions in Native Coronary Arteries

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The primary objective of this clinical trial is to demonstrate the safety and effectiveness of the Combo Bio-engineered Sirolimus Eluting Stent (Combo Stent) compared to the commercially available TAXUS® Liberté® Paclitaxel-Eluting Stent (DES) in…

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

## Summary

### ID

NL-OMON35675

**Source**
ToetsingOnline

**Brief title**
The REMEDEE Study

### Condition

- Coronary artery disorders

**Synonym**
angina pectoris, coronary atherosclerosis

**Research involving**
Human

## Sponsors and support

**Primary sponsor:** OrbusNeich Medical B.V.
**Source(s) of monetary or material Support:** de industrie (de sponsor: OrbusNeich)

## Intervention

**Keyword:** atherosclerosis, coronary, DES, stent

## Outcome measures

### Primary outcome

In-stent late lumen loss of the Combo Stent compared to the TAXUS® Liberté® DES

at 9 months post-procedure.

### Secondary outcome

1. All-cause and cardiac mortality at 30 days, 9 months, 1, 2, 3, 4, and 5

years;

2. Myocardial infarction: Q-wave and non Q-wave, cumulative and individual at

30 days, 9 months, 1, 2, 3, 4, and 5 years;

3. Major Adverse Cardiac Event (MACE) at hospital discharge, 30 days, 9 months,

1, 2, 3, 4 and 5 years post-procedure;

4. Vascular complications from index procedure through hospital discharge;

5. Rate of stent thrombosis, per ARC definitions, at 30 days, 9 months, 1, 2,

3, 4 and 5 years post-procedure;

6. Change in human anti-murine antibody (HAMA) plasma levels at 30 day and 9

month follow-up compared to baseline;

7. Device success, defined as attainment of <50% residual stenosis of the

target lesion using the Combo Stent;

8. Lesion success defined as attainment of < 50% residual stenosis using any

percutaneous method;

9. Procedure success defined as lesion success without the occurrence of

in-hospital MACE;

10. Clinically (ischemia)-driven target lesion revascularization at 30 days, 9

months, 1, 2, 3, 4 and 5 years.;

11. Clinically (ischemia)-driven target vessel revascularization at 30 days, 9

months, 1, 2, 3, 4 and 5 years;

12. Clinically (ischemia)-driven target vessel failure at 30 days, 9 months, 1,

2, 3, 4 and 5 years;

13. In-stent and in-segment angiographic binary restenosis at 9 months;

14. In-stent and in-segment minimum lumen diameter (MLD) at 9 months;

15. In-stent, proximal and distal late lumen loss at 9 months;

16. Neointimal hyperplasia volume and % in-stent volume obstruction at 9 months

as measured by intravascular ultrasound

(IVUS) for patients receiving angiographic/IVUS follow-up at 9 months;

17. Target lesion failure (TLF) at 30 days, 9 months, 1, 2, 3, 4 and 5 years.

# Study description

**Background summary**

The Combo Stent is indicated for restoring coronary flow in patients with de novo coronary lesions, with native coronary artery lesions of length <=20 mm,

and with a reference vessel diameter of 2.5 mm to 3.5 mm.

The Combo Stent has been designed to combine the pro-healing EPC capture technology found in the Genous* BIOENGINEERED R STENT* for rapidly achieving endothelial coverage and improved functionality along with abluminal sirolimus (aka rapamycin) sustained drug elution for control of neointimal proliferation. The Combo Stent is composed of the OrbusNeich R stent*, with an abluminal coating of a bioabsorbable polymer matrix formulated with sirolimus for sustained release, and an anti-CD34 antibody cell capture coating on the luminal surface.

**Study objective**

The primary objective of this clinical trial is to demonstrate the safety and effectiveness of the Combo Bio-engineered Sirolimus Eluting Stent (Combo Stent) compared to the commercially available TAXUS® Liberté® Paclitaxel-Eluting Stent (DES) in the treatment of single de novo native coronary artery lesions ranging in diameter from >=2.5 mm to <=3.5 mm and <=20 mm in length.

**Study design**

Prospective, multicenter, randomized study designed to enroll up to 180 patients who will be randomized 2:1 to the Combo Stent vs. TAXUS® Liberté® DES for treatment of stable native coronary artery disease.

**Intervention**

Stenting Procedure
Baseline angiography of the target vessel will be completed as per the Angiographic Core Laboratory Guidelines.
Subjects presenting without documentation of prior left ventricular ejection fraction assessment within previous 6 months that meets enrollment inclusion criteria (>=30%) will be required to undergo ejection fraction assessment to determine enrollment eligibility.
Pre-dilation to be performed per study stent labeling, but must be performed in the setting of calcified lesions.
Deployment of the Study Stent: Prior to use, the study stent (either Combo Stent or TAXUS® Liberté® DES according to randomization instruction) will be inspected per the Instructions for Use (IFU).
In all patients, the post-procedure target lesion angiography will be performed according to the Angiographic Core Laboratory Guidelines and must be captured in the similar manner used for the pre-procedure images.

9 months ± 30 days Follow-up
Angiographic follow-up on all subjects enrolled; IVUS follow-up in all subjects

in the IVUS sub-study (n=75; 50:25 Combo to TAXUS).

**Study burden and risks**

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. Known adverse events that may result from stent intervention include but may not be limited to: abrupt closure, acute myocardial infarction, allergic reaction or hypersensitivity to contrast agent or stainless steel, drugs (sirolimus or paclitaxel); and drug reactions to anti-platelet or anticoagulation drugs or contrast agent, aneurysm, arterial dissection, perforation, rupture or injury to the coronary artery, arterial rupture, arteriovenous fistula, atrial and ventricular arrhythmias (including bradycardia, tachycardia and fibrillation), bleeding complications which may require transfusions, cardiac or pulmonary or renal failure, cardiogenic shock, cardiac tamponade, coronary artery spasm, coronary artery or stent embolism, coronary artery or stent thrombosis, death, delayed endothelialization, distal emboli (air, tissue or thrombotic), emergent or non-emergent coronary artery bypass graft surgery, fever, hypertension, hypotension, immunologic reaction to murine antibodies, infection or pain at insertion site, ischemia (myocardial), myelosuppression, nausea and vomiting, palpitations, pericardial effusion, peripheral ischemia (due to vascular or nerve injury), pseudoaneurysm, restenosis of the stented segment of the artery, stroke/cerebrovascular accident (CVA), total occlusion of the coronary artery, unstable or stable angina pectoris, vasovagal reaction, vessel dissection, TIA, perforation of the heart/great vessels, infections/pyrogenic reactions, endocarditis, phlebitis, volume overload, anxiety, plaque
rupture/shift, and vascular complications including at the entry site which may require vessel repair including hematoma.

Potential Benefit
The Combo Stent can be expected to provide the same radial support as other coronary stents to minimize closure of a stenosed artery as is commonly indicated for coronary stenting. Additionally, the potential benefit of the Combo Stent is its effectiveness in inhibition of neointima while enhancing endothelial coverage that may reduce rates of restenosis without increasing rates of late and very late stent thrombosis compared to other commercially available DES.

# 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

General Inclusion Criteria
1. The patient must be >=18 and <= 80 years of age;
2. Symptomatic ischemic heart disease (CCS class 1-4, Braunwald Class IB, IC, IIB, IIC, IIIB, IIIC, and/or objective evidence of myocardial ischemia);
3. Acceptable candidate for CABG;
4. The Patient is willing to comply with specified follow-up evaluations;
5. The Patient or legally authorized representative has been informed of the nature of the study, agrees to its provisions and has been provided written informed consent, approved by the appropriate Medical Ethics Committee (MEC), Institutional
Review Board (IRB), or Human Research Ethics Committee (HREC). ;Angiographic Inclusion criteria:
6. Single de novo or non-stented restenotic lesion in the target vessel;
7. Patients with two-vessel coronary disease, may have undergone successful treatment (<20% diameter stenosis by visual estimate) of the non-target vessel with approved devices up to and including the index procedure but must be prior to the index target vessel treatment. Any non-target vessel or lesion intended
to be treated during the index procedure, cannot be an unprotected left main, ostial lesion, chronic total occlusion (CTO), heavily calcified, bifurcation, vein grafts, have angiographic

evidence of thrombus, be anything requiring atherectomy, thrombectomy, or pre-treatment with anything other than balloon angioplasty;
8. Target lesion located in a native coronary artery;
9. Target lesion (maximum length is 20 mm by visual estimate) covered by a single stent maximum 23 mm length for Combo Stent, and 24 mm in length for TAXUS® Liberté® (stent coverage including at least 3 mm of healthy vessel is recommended). The lesion length should be measured after pre-dilation procedure;
10. Reference vessel diameter must be >=2.5 to <= 3.5 mm by visual estimate. The vessel diameter should be measured after pre- dilation procedure and after intra-coronary nitroglycerin if spasm is suspected;
11. Target lesion >=50% and <100% stenosed by visual estimate.

## Exclusion criteria

General Exclusion Criteria
1. Pregnant or nursing patients and those who plan pregnancy in the period up to 1 year following index procedure. Female patients of child-bearing potential must have a negative pregnancy test done within 7 days prior to the index procedure per site standard test;
2. Patient has had a known diagnosis of acute myocardial infarction (AMI) within 72 hours preceding the index procedure (elevated troponin or CK-MB >=2 times upper limit of normal) or >72 hours preceding the index procedure and CK and CK-MB have not
returned to within normal limits at the time of procedure;
3. The patient is currently experiencing clinical symptoms consistent with new onset AMI, such as nitrate unresponsive prolonged chest pain;
4. Impaired renal function (serum creatinine >2.0 mg/dL or 177 µmol/l) or on dialysis;
5. Platelet count <100,000 cells/mm3 or >700,000 cells/mm3 or a WBC <3,000 cells/mm3;
6. Patient has a history of bleeding diathesis or coagulopathy or patients in whom anti-platelet and/or anticoagulant therapy is contraindicated;
7. Patient requires low molecular weight heparin (LMWH) treatment post-procedure or has received a dose of LMWH <=8 hours prior to index procedure;
8. Patient has received any organ transplant or is on a waiting list for any organ transplant;
9. Patient has other medical illness (e.g., cancer, known malignancy, or congestive heart failure) or known history of substance abuse (alcohol, cocaine, heroin etc.) that may cause non-compliance with the protocol, confound the data interpretation or is associated with a limited life expectancy (i.e., less than 1 year);
10. Patient has a known hypersensitivity or contraindication to aspirin, heparin/bivalirudin, clopidogrel/ticlopidine, prasugrel, stainless steel alloy, sirolimus, paclitaxel and/or contrast sensitivity that cannot be adequately pre-medicated;
11. Patient has previously received murine therapeutic antibodies and exhibited sensitization through the production of Human Anti-Murine Antibodies (HAMA);
12. Patient presents with cardiogenic shock;
13. Patient has current unstable cardiac arrhythmias that create hemodynamic instability;
14. Patient has extensive peripheral vascular disease that precludes safe 6 French sheath insertion;
15. Any significant medical condition which in the Investigator*s opinion may interfere with

the patient*s optimal participation in the study;
16. Currently participating in another investigational drug or device study or patient in inclusion in another investigational drug or device study during follow-up; ;Angiographic exclusion criteria:
17. Unprotected left main coronary artery disease with >=50% stenosis;
18. Ostial target lesion(s);
19. Totally occluded target vessel (TIMI flow 0);
20. Calcified target lesion(s) which cannot be successfully predilated;
21. Target lesion has excessive tortuosity unsuitable for stent delivery and deployment;
22. Angiographic evidence of thrombus in the target lesion(s);
23. Target lesion involving bifurcation with a side branch >=2.0 mm in diameter (either stenosis of both main vessel and major side branch or stenosis of just major side branch) that would require intervention of diseased side branch;
24. A significant (>50%) stenosis proximal or distal to the target lesion that cannot be covered by same single stent;
25. Diffuse distal disease to target lesion with impaired runoff;
26. Left ventricular ejection fraction (LVEF) <=30% (LVEF must be obtained within 6 months prior to the index procedure);
27. Pre-treatment with devices other than balloon angioplasty;
28. Prior stent within 10 mm of target lesion;
29. Intervention (PCI or bypass) of another lesion performed within 6 months before or planned within 30 days following the index procedure.

# Study design

## Design

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| 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

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|---|---|
| Recruitment status: | Recruitment stopped |
| Start date (anticipated): | 01-06-2010 |

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|---|---|
| Enrollment: | 20 |
| Type: | Actual |

### Medical products/devices used

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|---|---|
| Generic name: | coronary drug-eluting stent |
| Registration: | No |

## Ethics review

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|---|---|
| Approved WMO Date: | 22-03-2010 |
| Application type: | First submission |
| Review commission: | METC Universitair Medisch Centrum Utrecht (Utrecht) |

## 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 |
|---|---|
| Other | 2009-015539-34 |
| CCMO | NL29701.041.09 |