# The OPTIMIZE Trial to Assess the Procedural and Clinical Value of the Svelte IDS and RX Sirolimus-Eluting Coronary Stent Systems for the Treatment of Atherosclerotic Lesions in a Randomized Study

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The study objective is to assess the safety and efficacy of the Svelte DES-IDS and the Svelte DES-RX compared to a commercially available Xience or Promus Drug-Eluting Stent in subjects with up to three de novo coronary artery lesions in up to two...

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

## Summary

### ID

NL-OMON48597

**Source**
ToetsingOnline

**Brief title**
OPTIMIZE

### Condition

- Coronary artery disorders

**Synonym**
coronary artery stenosis - narrowing of the coronary artery

**Research involving**

Human

## Sponsors and support

**Primary sponsor:** Svelte Medical Systems, Inc.
**Source(s) of monetary or material Support:** Svelte Medical Systems

## Intervention

**Keyword:** Coronary Artery Disease, Coronary Stent, Drug Eluting Stent

## Outcome measures

### Primary outcome

Non-inferiority of Target Lesion Failure (TLF) at 12 months post-procedure defined as: Cardiac Death, Target Vessel Myocardial Infarction (TVMI) (Q wave and non-Q wave) or clinically driven Target Lesion Revascularization (TLR) by percutaneous or surgical methods

### Secondary outcome

• TLF at 6 months post-procedure and annually from 2-year through 5-year follow-up.

• TVF at 6 and 12 months post-procedure, and annually through 5-year follow-up defined as cardiac death, TVMI, or clinically-driven TVR by percutaneous or surgical methods.

• TLR and TVR total and clinically-driven at 6 and 12 months post-procedure and annually through 5-year follow up.

• MACE at 6 and 12 months post-procedure and annually through 5-years follow-up, defined as all-cause mortality, TVMI and clinically- driven TLR.

• Total Death (cardiac and non-cardiac) at 6 and 12 months post-procedure and annually through 5-year follow up.

• TVMI at 6 and 12 months post-procedure and annually through 5-year follow up.

• ST at 30 days, 6 and 12 months post-procedure, and annually through 5-year follow up using the ARC definitions.

• Acute success rates:

• Device Success: Attainment of < 30% final residual stenosis of the target lesion using only the randomized stent;

• Lesion Success: Attainment of < 30% final residual stenosis of the target lesion using any stent with or without other interventional devices;

• Procedure Success: Lesion success and no in-hospital Major Adverse Cardiac Event (MACE).

• Direct Stent Strategy Success: Attainment of < 30% final residual stenosis of the target lesion without pre-dilatation if the operator had originally chosen to proceed using a direct stent approach;

• Procedure time: Begins with placement of the introducer sheath and ends with removal of all interventional and diagnostic devices

• Intervention time: Begins with the time the guiding catheter is inserted into the subject until it is removed

• Device time: Begins with the time the guide wire tip exits the guiding catheter until the time the guide wire tip is fully retrieved back into the guiding;

• Puncture site complications, need for transfusion, hematoma formation

• For each subject, contrast volume (mL) and exposure to fluoroscopy (time and grays) is to be recorded at the beginning of the PCI (i.e., at the time of guiding catheter insertion). In the case of ad-hoc PCI, if contrast volume and

exposure to fluoroscopy cannot be recorded beginning only with PCI, then these

data points

are to be collected for the entirety of the diagnostic and interventional

procedure.

# Study description

### Background summary

Different studies comparing 'direct stenting' with conventional stenting (with predilation) demonstrate a high degree of technical and procedural success with direct stenting, including a significant reduction in the procedure time, radiation exposure, contrast use and cost. Direct stenting (such as with the Svelte system) offers the possibility of reducing risk factors, which is especially important in high risk patients (elderly, multiple blood vessels, chronic renal disease and peripheral arterial disease).

This study has been designed to gather further information on the safety and the performance of the Svelte Integrated Delivery System for the treatment of de novo stenotic lesions in native coronary arteries.

Although studies have shown that the use of drug-eluting stents (especially sirolimus eluting) provide better outcomes than bare metal stents, there are concerns about the biocompatibility of the polymers which carry the drug. As these polymers can cause inflammation, leading to restenosis and possibly thrombosis, there is great interest in developing bioerodible,non-inflammatory polymers (as used with the Svelte system).

### Study objective

The study objective is to assess the safety and efficacy of the Svelte DES-IDS and the Svelte DES-RX compared to a commercially available Xience or Promus Drug-Eluting Stent in subjects with up to three de novo coronary artery lesions in up to two native coronary artery vessels.

### Study design

A prospective, single-blind, randomized, active-control, multi-center clinical trial comparing the safety and efficacy of the Svelte Sirolimus-Eluting Coronary Stent Integrated Delivery System (Svelte DES-IDS) and Svelte Sirolimus-Eluting Coronary Stent Rapid Exchange Delivery System (Svelte DES-RX)

to that of the commercially available Abbott Vascular Xience or Boston Scientific Promus Drug-Eluting Coronary Stents. In this study, subjects will have stents placed for primary treatment of symptomatic ischemic heart disease. One thousand six hundred and thirty (1630) subjects (1:1 randomization Svelte DES-IDS or DES-RX to Xience or Promus DES) will be treated in up to one hundred twenty (120) sites in the United States, Europe and Japan to establish non-inferiority in the primary endpoint of Target Lesion Failure (TLF). Follow-up contacts post procedure will be made for clinical assessments at 30-days, 6 months, 12 months and annually through 5 years.

**Intervention**

Angiography and coronary angioplasty

**Study burden and risks**

Svelte has conducted risk analysis for the Svelte Sirolimus-Eluting Coronary Stent Integrated Delivery System (DES-IDS) and Svelte Sirolimus-Eluting Coronary Stent Rapid Exchange System (DES-RX) and concluded that from a technology, construction, material, application and design perspective intolerable risks were either not inherent to the design of the device or were successfully mitigated. The Svelte DES obtained CE Mark and is commercially available in select accounts in Europe, utilizing either a radial and femoral approach.

Potential or Anticipated Adverse Events Adverse events may be associated with the use of any coronary stent in native coronary arteries:
• Access site pain, hematoma, hemorrhage or infection
• Allergic reaction to contrast, antiplatelet therapy, CoCr, PEA or sirolimus
• Aneurysm, pseudoaneurysm or arteriovenous fistula (AVF)
• Arrhythmias
• Cardiac tamponade
• Coronary artery spasm, abrupt closure, occlusion, perforation or dissection
• Coronary stent dislodgement or embolism
• Coronary stent thrombosis
• Death
• Embolism - air, tissue or thrombus
• Emergent or non-emergent peripheral vascular or coronary artery bypass graft surgery
• Fever or infection
• Hypotension / hypertension

Intervention due to:
• Failure to deliver stent
• Stent deformation, collapse or fracture
• Stent migration or embolization

• Myocardial ischemia or infarction
• Peripheral ischemia / peripheral nerve injury, renal insufficiency or failure
• Restenosis of stented artery
• Stroke / TIA
• Thrombosis - stent or other
• Unstable or stable angina The following additional side effects/complications may be associated with, but not limited to, the use of sirolimus and poly(ester amides):
• Anemia
• Diarrhea
• Dry mouth and/or dry skin
• Headache
• Pain - abdominal or arthralgia
• Rash

## 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. Subject is >= 18 years old;
2. Subject (or subject*s legal representative) understands the study requirements, the treatment procedures and provides written informed consent before any study-specific tests or procedures are performed;
3. Japan only: for subjects < 20 years of age, the subject and the subject*s legal representative must provide written informed consent before any study specific tests or procedures are performed;
4. Subject is an eligible candidate for PCI;
5. Subject has symptomatic coronary artery disease with objective evidence of ischemia or silent ischemia;
6. Subject has clinical symptoms or ECG changes consistent with non-ST elevation MI (NSTEMI), is clinically and hemodynamically stable and has cardiac enzymes documented to be decreasing prior to the study procedure (CK-MB is preferred, but if troponin is assessed, enzymes decreasing, stable or elevated up to 20% over the prior assessment are acceptable);
7. Subject is an acceptable candidate for CABG;
8. Subject agrees to comply with specified follow-up evaluations.;Angiographic Inclusion Criteria (visual estimate):
1. Subject has <= 3 de novo target lesions in <= 2 native coronary artery vessels, with <= 2 lesions in a single vessel, each meeting the angiographic criteria and none of the exclusion criteria.
2. Target lesion(s) must be located in a native coronary artery with RVD >= 2.25 mm and <= 4.00 mm;
3. Target lesion(s) length must be <= 34 mm in length (the intention should be to cover the whole lesion with one (1) stent of adequate length);
4. Target lesion(s) must have visually estimated stenosis >= 50% and < 100% with Thrombolysis in Myocardial Infarction (TIMI) flow > 1. For lesions with visually estimated stenosis >= 50% and <= 70%, additional confirmation by ACC/AHA guideline compliant physiologic assessment is required;
5. Coronary anatomy is likely to allow delivery of a study device(s) to the target lesion(s).

## Exclusion criteria

1. Subject has clinical symptoms or ECG changes consistent with acute STEMI; Subject may

be included if primary PCI for STEMI was successfully completed and subject is clinically and hemodynamically stable with cardiac enzymes documented to be decreasing >= 72 hours prior to the study procedure;
2. Subject has cardiogenic shock, hemodynamic instability requiring inotropic or mechanical circulatory support, intractable ventricular arrhythmia, or ongoing intractable angina;
3.- Subject has received an organ transplant or is on a waiting list for an organ transplant;
4. Subject is receiving or scheduled to receive chemotherapy 30 days before or after the index procedure;
5. Subject requires a planned PCI (including staged procedures) or CABG after the index procedure; CABG or surgical or catheter-based valvular intervention within 12 months of) the index procedure;
6. Subject was previously treated at any time with intravascular brachytherapy;
7. Subject has a known allergy to contrast (that cannot be adequately premedicated) and/or the study stent systems or protocol-required concomitant medications (e.g. platinum, platinum-chromium alloy, stainless steel, sirolimus, everolimus or structurally related compounds, polymer or individual components, all P2Y12 inhibitors, or aspirin);
• Subject has one of the following (as assessed prior to the index procedure):
a. Other serious medical illness (e.g. cancer, congestive heart failure) with estimated life expectancy of <=24 months;
b. Current problems with substance abuse (e.g. alcohol, cocaine, heroin, etc.);
c. Planned procedure that may cause non-compliance with the protocol or confound data interpretation;
9. Subject is receiving chronic (>=72 hours) anticoagulation therapy (e.g. heparin, coumadin) for indications other than acute coronary syndrome (ACS);
10. Subject has a platelet count < 100,000 cells/mm3 or > 700,000 cells/mm3;
11. Subject has a white blood cell (WBC) count < 3,000 cells/mm3;
12. Subject has documented significant liver disease including laboratory evidence of hepatitis;
13. Subject is on dialysis or has a baseline serum creatinine level > 2.0 mg/dL (177µmol/L);
14. Subject has a history of bleeding diathesis or coagulopathy or will refuse blood transfusions;
15. Subject has a history of a CVA or a TIA within the past 6 months;
16. Subject has an active peptic ulcer or active GI bleeding;
17. Subject has severe symptomatic heart failure (i.e. NYHA class IV);
18. Subject intends to participate in another investigational drug or device clinical study within 12 months after the index procedure
19. Subject has a known intention to procreate within 12 months after the index procedure (a woman of child bearing potential who is sexually active must agree to use a reliable method of contraception from the time of screening through 12 months after the index procedure);
20. Subject is pregnant or nursing (subject must have a negative pregnancy test within 14 days prior to the index procedure if a woman of childbearing potential);
21. Subject is participating in another investigational drug or device study;
22. Planned use of cutting balloon, atherectomy or atherectomy orbital, laser or other) any other form of treatment of the target lesion(s) during the index procedure other than plain balloon angioplasty and the randomized stent.;Angiographic Exclusion Criteria (visual estimate):
1. Subject has a planned treatment of >= 3 lesions;

2. Subject has a planned treatment of >= 2 major epicardial vessels;
3. Subject has a planned treatment of a single lesion with >= 1 stent;
4. Subject has 2 target lesions in the same vessel that are separated by <= 15 mm ;
5. Subject*s target lesion(s) is located in the left main coronary artery;
6. The subject*s target lesion(s) is located within 3 mm of the origin of the (LAD or LCX) coronary arteries ;
7. Subject*s target lesion(s) is located within a saphenous vein graft (SVG) or arterial graft;
8. Subject*s target lesion(s) will be accessed via SVG or arterial graft;
9. Subject has a target lesion(s) with TIMI flow of 0 (total occlusion) or TIMI flow 1 prior to guide wire crossing;
10. Subject*s target lesion(s) treated during the index procedure that involves a complex bifurcation (e.g. bifurcation lesion requiring treatment with more than one (1) stent); see Complex Bifurcation definition in the Definition section of this protocol.)
11. Subject*s target lesion is located within 10 mm of a previously implanted stent or involves in-stent restenosis.
12. Subject has unprotected left main coronary artery disease (> 50% diameter stenosis);
13. Subject has been treated with any type of PCI (i.e. balloon angioplasty, stent, cutting balloon or atherectomy) within 24 hours of the index procedure
14. Subject has thrombus or possible thrombus, present in the target vessel (by visual estimate).

# Study design

## Design

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| 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): | 22-02-2018 |
| Enrollment: | 550 |
| Type: | Actual |

### Medical products/devices used

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|---|---|
| Generic name: | coronary drug-eluting stent |
| Registration: | Yes - CE intended use |

## Ethics review

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| Approved WMO Date: | 16-01-2018 |
| Application type: | First submission |
| Review commission: | MEC-U: Medical Research Ethics Committees United (Nieuwegein) |
| Approved WMO Date: | 07-02-2018 |
| Application type: | Amendment |
| Review commission: | MEC-U: Medical Research Ethics Committees United (Nieuwegein) |
| Approved WMO Date: | 11-09-2018 |
| Application type: | Amendment |
| Review commission: | MEC-U: Medical Research Ethics Committees United (Nieuwegein) |
| Approved WMO Date: | 13-12-2018 |
| Application type: | Amendment |
| Review commission: | MEC-U: Medical Research Ethics Committees United (Nieuwegein) |
| Approved WMO Date: | 01-02-2019 |
| Application type: | Amendment |
| Review commission: | MEC-U: Medical Research Ethics Committees United (Nieuwegein) |
| Approved WMO Date: | 26-03-2019 |
| 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 | NCT03190473 |
| CCMO | NL62683.100.17 |