Direct Implantation of Rapamycin-Eluting Stents with Bio-Erodible Drug Carrier Technology Utilizing the Second Generation Svelte Drug-Eluting Coronary Stent Integrated Delivery System (IDS).

Published: 26-03-2013
Last updated: 26-04-2024

The study objective is to assess the safety and efficacy of the Svelte Drug-Eluting Coronary Stent Integrated Delivery System (IDS) compared to the Resolute IntegrityTM Drug-Eluting Stent in patients with single, de novo coronary artery lesions.

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

Summary

ID

NL-OMON39917

Source
ToetsingOnline

Brief title
DIRECT II

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;Inc.

Intervention

Keyword: Direct stenting, Drug-eluting coronary stent, Randomized trial, Sirolimus

Outcome measures

Primary outcome

The primary safety endpoint is angiographic Target Vessel Failure (TVF) at

6-months post-procedure; the primary efficacy endpoint is angiographic in-stent

Late lumen Loss (LL) at 6-months post-procedure.

Secondary outcome

Safety:

•Clinically-driven Target Lesion Revascularization (TLR) at 1 and 6-months and

yearly through 5-years post-procedure;

•Composite of cardiac death, MI attributed to the target vessel and clinically

driven TLR at 1 and 6-months post-procedure and yearly up to 5-years;

•Composite of all-cause mortality, any MI and any revascularization, TVR or

revascularization of non-target vessels at 5-years post-procedure;

•Stent thrombosis at 1 and 6-months and yearly for 5-years post-procedure;

•Acute success rates:

-Device Success: Attainment of < 30% final residual stenosis of the

target lesion;

-Direct Stenting Success: Attainment of < 30% final residual stenosis of

the target lesion without pre-dilatation;

-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 MACE.

Efficacy:

•In-stent and in-segment angiographic binary restenosis at 6-months

post-procedure;

•In-stent and in-segment Minimum Lumen Diameter (MLD) at 6-months

post-procedure;

•In-segment Late lumen Loss (LL) at 6-months post-procedure;

•Neointimal hyperplasia (% lumen volume) at 6-months post-procedure measured by

optical coherence tomography (OCT) in patients treated with the Svelte

Drug-Eluting Coronary Stent Integrated Delivery System (IDS); and

•Strut coverage (% of struts malapposed, protruding non-covered, protruding

covered, non-protruding covered) at 6-months post-procedure measured by OCT in

patients treated with the Svelte Drug-Eluting Coronary Stent Integrated

Delivery System (IDS).

Study description

Background summary

Coronary artery stenting has evolved substantially since the first use of stents as an adjunct to balloon angioplasty in the early 1990s. The performance of coronary stents has improved considerably, with stenting now the primary mode of revascularization in percutaneous coronary interventions (PCI).

Percutaneous transluminal coronary angioplasty (PTCA) has been widely used to treat patients with symptomatic coronary artery disease (CAD). The major limitations of PTCA (abrupt closure, PTCA-induced intimal dissection and

restenosis) have been addressed through the development of coronary stents. Steady improvements in stent design and adjunctive medical therapies over the preceding two decades have resulted in marked improvement in the safety and efficacy of PCIs. Estimates for in-hospital adverse events (death, myocardial infarction, stent thrombosis) are less than 1% in a recent U.S. multicenter registry.

Conventional PCI practice usually includes pre-dilatation of the target lesion prior to stent placement. This convention is dictated, in part, by the characteristics of first generation stents, which were higher profile, stiff devices which could not reliably be delivered to lesions. Additionally, these stents were hand-crimped onto balloon catheters, resulting in tenuous securement of the stents to their delivery systems. These features made pre-dilatation of the target lesion virtually mandatory to allow stent delivery. However current generation stents and stent delivery systems increasingly allow for stent placement without pre-dilatation, a strategy known as *direct stenting*.

Direct stenting is currently employed in approximately 30-40% of PCI procedures and has been compared to conventional stenting (using pre-dilatation) in numerous observational studies and randomized trials using bare metal stents. In select lesions (lower degrees of lesion calcification with minimal vessel tortuosity), high rates of technical and procedural success have been observed. Additionally, significant reductions in procedure time, radiation exposure, contrast administration, and cost have been realized with comparable 6 - 12-month clinical outcomes.

While PCI with stenting for CAD is associated with high rates of clinical success and low procedural morbidity, the risks of radiation exposure, contrast use and access site bleeding, as well as overall procedure costs in general, are not negligible. Clinical risks are incrementally higher in patients with advanced age multi-vessel disease requiring staged procedures, chronic kidney disease and peripheral arterial disease making minimization of these risks of paramount importance.

A direct stenting strategy offers the possibility to further reduce the risk of adverse
events in high-risk PCI patients, decreasing contrast requirements and radiation dose to the operator and patient while providing the added benefit of reducing procedural time and cost.
The Svelte Medical Systems Drug-Eluting Coronary Stent Integrated Delivery System (IDS) is a balloon-expandable, thin-strut cobalt-chromium (CoCr) coronary stent eluting sirolimus from a fully bio-erodible drug carrier mounted on a low-profile, fixed-wire balloon catheter. The system has a 0.014* lesion entry profile, is compatible with 5 French (minimum ID .056*) or larger guiding catheters and is indicated for direct stenting.

Fixed-wire systems were introduced in the early days of PCI to provide lower profile options in the event of abrupt vessel closure and treatment of more complex lesions. As stents evolved throughout the 1990s, conventional PTCA balloons became mostly relegated to pre-and post-dilate lesions, which drove the market toward the use of guidewire-based devices. The need to re-cross lesions for further treatment (i.e. for post-dilatation or secondary stenting) additionally limited use of the fixed-wire platform. Reports of wire fractures and difficulties with balloon deflation further dampened enthusiasm for these early fixed-wire systems. These early limitations of fixed-wire technology, along with the development of lower profile guidewire-based systems, resulted in the abandonment of the fixed-wire balloon catheter. However in an era where more challenging lesions are being treated and even greater value is being placed on the clinical and procedural benefits associated with direct stenting, the Svelte IDS represents an important advance in the improvement of PCI. Advanced fixed-wire and balloon technologies coupled with a low-profile, highly flexible stent, make the Svelte IDS the first material improvement in stent delivery technology in more than a decade.

The current study is proposed in order to collect information about the safety and performance of the Svelte IDS in the treatment of stenotic lesions in de novo native coronary arteries. A large body of published data now exists to demonstrate the superiority of drug-eluting stents (DES), and especially sirolimus-eluting stents, over bare metal stents. However, in spite of the clinical efficacy of DES, there are ongoing concerns regarding the long-term biocompatibility of durable polymers, including polymers used on currently commercialized DES. It is believed that these polymers may, in the long term, incite inflammation, which could lead to late *catch-up* (restenosis) or late stent thrombosis. Due to the concern with durable polymers, there is renewed interest in developing DES with bio-erodible, non-inflammatory coatings.

The pharmacokinetics of the Svelte IDS have been carefully designed to mimic drug release of the Cypher (Cordis/ Johnson & Johnson) and Xience (Abbott) DES. The Svelte drug carrier is designed to erode in 9-12 months, leaving behind only a thin-strutted cobalt chromium stent. The potential exists to reduce lingering or late inflammation that may be caused by commercially available durable polymers. This clinical trial is designed to assess the safety and longer-term efficacy of the Svelte IDS, as described in greater detail below.

The Svelte IDS represents a new, very low profile, highly deliverable coronary stent platform allowing for direct stenting in the majority of coronary artery lesions. In addition to the well-known benefits of direct stenting procedural efficiencies realized with the Svelte IDS may provide substantial cost savings as well as reductions in procedure time, radiation exposure (for patient and operator), and bleeding complications. Use of the sirolimus-eluting version of the Svelte IDS may further provide substantial reductions in long-term restenosis and target lesion revascularization compared to the bare-metal stent

version of the system. The highly biocompatible and fully bio-erodible Svelte drug carrier may also improve long-term safety and offer the potential to reduce the need for long-term dual anti-platelet therapy. The safety and efficacy of the Svelte IDS with bioerodible drug carrier will be assessed in this study.

Study objective

The study objective is to assess the safety and efficacy of the Svelte Drug-Eluting Coronary Stent Integrated Delivery System (IDS) compared to the Resolute IntegrityTM Drug-Eluting Stent in patients with single, de novo coronary artery lesions.

Study design

A prospective, randomized, active-control, multi-center clinical trial comparing the safety and efficacy of the Svelte Drug-Eluting Coronary Stent Integrated Delivery System (IDS) to that of the commercially available Resolute IntegrityTM Drug-Eluting Stent. One hundred fifty-nine (159) patients (2:1 randomization Svelte IDS: Resolute IntegrityTM to establish non-inferiority in the primary efficacy endpoint of in-stent late lumen loss) will be treated in up to twenty (20) centers in Europe and Brazil, with clinical and angiographic follow-up at 6-months to assess the primary endpoints of angiographic Target Vessel Failure (TVF) and Late Lumen Loss (LL), as well as secondary safety and efficacy endpoints. Additional clinical follow-up will take place at 1-month and annually through 5-years.

Intervention

Angiography and coronary angioplasty.

Study burden and risks

Svelte has conducted risk analysis for the Svelte Drug-Eluting Coronary Stent Integrated Delivery System (IDS) 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 bare-metal version of the Svelte IDS has obtained the CE Mark and is commercially available in select accounts in Brazil and Europe, utilizing either a radial and femoral approach.

2.1 Potential or Anticipated Adverse Events
Adverse events may be associated with the use of a coronary stent in native coronary arteries:

• Abrupt vessel closure
• Access site pain, hematoma or hemorrhage
• Acute myocardial infarction
• Allergic reaction to anticoagulants or antiplatelet therapy, contrast medium, or stent material
• Aneurysm, pseudoaneurysm, or arteriovenous fistula (AVF)
• Angina
• Arrhythmias, including VF and VT
• Cardiac tamponade
• Cardiogenic shock
• Death
• Emboli, distal (air, tissue or thrombotic emboli)
• Emergency surgery, coronary artery bypass or peripheral vascular
• Hemorrhage, requiring transfusion
• Hypotension/hypertension
• Infection, local and/or systemic
• Ischemia, myocardial
• Peripheral ischemia/peripheral nerve injury
• Pulmonary edema
• Renal failure
• Respiratory failure
• Restenosis of stented segment
• Vessel Spasm
• Stent embolization, misplacement, migration
• Stent thrombosis/occlusion (acute and subacute)
• Stroke/cerebrovascular accident/transient ischemic attack (TIA)
• Total occlusion of coronary artery
• Vessel trauma, dissection, perforation, rupture or injury, including coronary

Sirolimus, when prescribed as an oral medication, may interact with the drugs/foods listed below. Medications that are strong inhibitors of CYP3A4 might reduce Sirolimus metabolism in vivo. Hence, co-administration of strong inhibitors of CYP3A4 may increase the blood concentrations of Sirolimus.
• Antibiotics (ciprofloxacin, ofloxacin)
• Glucocorticoids
• HMGCoA reductase inhibitors (simvastatin, lovastatin)
• Cisapride (theoretical potential interaction)
• Sildenafil (Viagra®) (theoretical potential interaction)
• Antihistaminics (terfenadine, astemizole)

Contacts

Public
Svelte Medical Systems, Inc.

Central Avenue 675
New Providence NJ 07974
US
Scientific
Svelte Medical Systems, Inc.

Central Avenue 675
New Providence NJ 07974
US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1.Patient is >=18 years old;
2.Patient is eligible for percutaneous coronary intervention (PCI);
3.Patient is an acceptable candidate for emergent coronary artery bypass graft (CABG) surgery;
4.Patient has clinical evidence of ischemic heart disease, stable or unstable angina, silent ischemia, or a positive functional study;
5.Female subjects of childbearing potential must have a negative pregnancy test within 7-days before the trial procedure;
6.Patient or subject*s legal representative has been informed of the nature of the trial and agrees to its provisions and has provided written informed consent as approved by the Hospital Research Ethics Committee (HREC) of the respective investigational site; and
7.Patient agrees to comply with specified follow-up evaluations and to return to the same investigational site where the procedure was performed.
8.Patient has either a single target lesion, or two lesions (target and non-target) located in separate coronary arteries;
9.If a non-target lesion is treated, it must be treated first and only with commercially available PTCA balloons and/or stents. Post PCI of the non-target vessel, all of the following conditions must be met:

a.Residual diameter stenosis < 30%;
b.Absence of any angiographic complications;
c.Absence of ischemic symptoms; and
d.Absence of significant new arrhythmia or ECG monitoring changes suggestive of ischemia.
10.Reference vessel >= 2.5 mm and <= 3.5 mm in diameter by visual estimate;
11.Target lesion < 20 mm in length by visual estimate (the intention is to cover the entire lesion with one stent of adequate length); and
12.Target lesion stenosis >= 50% and < 100% by visual estimate.

Exclusion criteria

1.Patient is currently enrolled in another investigational device or drug trial that has not completed the primary endpoint or that clinically interferes with the current study endpoints Note: Trials requiring extended follow-up for products that were investigational, but have since become commercially available, are not considered investigational trials;
2.The patient requires a staged procedure of the target vessel within 6-months or a staged procedure of a non-target vessel within 30-days post-procedure;
3.The target lesion requires treatment with a device other than PTCA prior to stent placement (such as, but not limited to, directional coronary atherectomy, excimer laser, rotational atherectomy, etc.);
4.Any DES deployment anywhere in the target vessel within the past 9-months;
5.Any BMS deployment anywhere in the target vessel within the past 6-months;
6.Any previous stent placement within 10 mm (proximal or distal) of the target lesion;
7.Myocardial infarction within 72-hours of the index procedure, with the exception of:
a.Patients who have had a STEMI and PCI to the culprit lesion may be included if they have a suitable lesion in another vessel, and have been clinically and hemodynamically stable for 72-hours;
b.Patients who have had a non-STEMI may be included if their troponin levels are within the laboratory normal range within 24-hours pre-procedure.
8.Co-morbid condition(s) that could limit the patient*s ability to participate in the trial or to comply with follow-up requirements, or impact the scientific integrity of the trial;
9.Concurrent medical condition with a life expectancy of less than 12-months;
10.Documented left ventricular ejection fraction (LVEF) <= 30%;
11.Unstable angina pectoris from an extra-cardiac cause (Braunwald Class A I-III);
12.Known allergies to the following: Acetylsalicylic acid (ASA), Clopidogrel bisulfate, Ticlopidine, Prasugrel, Rapamycin, Zotarolimus, PEAIII AcBz, Heparin/ Bivalirudin, or contrast agent (that cannot be adequately premedicated);
13.Platelet count < 100,000 cells/mm3 or > 700,000 cells/mm3 or a WBC < 3.000 cells/mm3 or hemoglobin < 100g/l;
14.Acute or chronic renal dysfunction (serum creatinine > 170µmol/L);
15.History of a stroke or transient ischemic attack (TIA) within the prior 6-months;
16.Active peptic ulcer or upper gastrointestinal (GI) bleeding within the prior 6-months;
17.History of bleeding diathesis or coagulopathy or will refuse blood transfusions; and
18.Patients requiring ongoing anticoagulation with warfarin or dabigatran.
19.Total occlusion (TIMI 0 or 1);

20.Target vessel has angiographic evidence of thrombus
21.Target vessel is excessively tortuous or has heavy calcification;
22.Significant (> 50%) stenosis proximal or distal to the target lesion that might require revascularization or impede run off;
23.Target lesion is located in or supplied by an arterial or venous bypass graft;
24.Ostial target lesion (within 5.0 mm of vessel origin) or any location within the left main coronary artery;
25.Target lesion involves a side branch > 2.0 mm in diameter; and
26.Unprotected Left Main coronary disease (stenosis > 50%).

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	25-05-2013
Enrollment:	50
Type:	Actual

Medical products/devices used

Generic name:	coronary drug-eluting stent
Registration:	No

Ethics review

Approved WMO

Date:	26-03-2013
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	09-01-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	NL42184.078.12