STENTYS Coronary Stent System Clinical Trial in Patients with Acute Myocardial Infarction

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To evaluate the safety and effectiveness of the STENTYS Coronary Stent System in the treatment of de novo stenotic lesions in coronary arteries in subjects undergoing primary revascularization due to Acute ST Segment Elevation Myocardial Infarction...

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

Summary

ID

NL-OMON38520

Source
ToetsingOnline

Brief title
APPOSITION V

Condition

- Coronary artery disorders

Synonym
Heart-attack, Myocardial Infarction

Research involving
Human

Sponsors and support

Primary sponsor: STENTYS
Source(s) of monetary or material Support: sponsor

Intervention

Keyword: Acute Myocardial Infarction, Coronary stent, Self expanding stent, STENTYS

Outcome measures

Primary outcome

Target vessel failure (TVF), defined as cardiac death, target vessel recurrent myocardial infarction (MI) [Q or Non Q-Wave], or clinically driven target vessel revascularization (TVR) by percutaneous or surgical methods at 365 days post-procedure. We hypothesize that STENTYS Coronary Stent System will be non-inferior to Multi-Link Vision* coronary stent system.

Secondary outcome

SECONDARY POWERED ENDPOINT:

Acute stent malapposition (ASM) diagnosed by IVUS at the time of the index stent implantation. We hypothesize that STENTYS Coronary Stent System will be superior to Multi-Link Vision* coronary stent system.

SECONDARY ENDPOINTS:

1. Rate of ST segment resolution defined as percentage of subjects with >70% resolution of ST elevation in the most affected ECG lead within 90 minutes of completion of the stent procedure.

2. Rate of final TIMI myocardial perfusion grade 3 as determined by the angiographic core laboratory.

3. Major Adverse Cardiac Events (MACE): defined as cardiac death, recurrent MI (Q wave and non-Q wave), emergent bypass surgery (CABG), or clinically driven target lesion revascularization (TLR) by percutaneous or surgical methods at 30

days, 6, 9, and 12 months, and annually through 3 years follow-up.

4. Composite endpoint of cardiac death and recurrent MI at 30 days, 6, 9, and 12 months , and annually through 3 years follow-up.

5. TVF at 30 days, 6, and 9 months, and annually through 3 years follow-up.

6. Target lesion failure (TLF) at 30 days, 6, 9 and 12 months, and annually through 3 years follow-up.

7. Rates for each component of the MACE, TLF and TVF composite endpoints (cardiac death, MI, CABG, TVR, and TLR) reported at 30 days, 6, 9, and 12 months, and annually through 3 years follow-up.

8. Strut disconnections

9. Acute Success Rates:

a. Device Success: Attainment of < 30% final residual stenosis of the target lesion using only the assigned stent.

b. Lesion Success: Attainment of < 30% final residual stenosis of the target lesion using any percutaneous method.

c. Procedure Success: TIMI grade 3 and no in-hospital MACE.

10. Bleeding or vascular complications at discharge.

11. Stent thrombosis (ST) at 30 days, 6, 9 and 12 months, and annually through 3 years follow-up.

a. Definite ST

b. Definite/probable ST

c. All ST

12. Rate of procedural myocardial blush score of 3.

13. Late IVUS/Angiographic Endpoints (on the first 105 evaluable of 150

eligible subjects consecutively enrolled at IVUS-designated centers with a follow-up angiographic procedure conducted at 12-13 months, accounting for a 30% drop-out rate, and assuring at least 70 evaluable Stentys treated subjects) at 12-13 months, and after clinical TVF endpoint assessment (2:1 STENTYS:Multi-Link Vision*).

a. In-segment percent diameter stenosis (%DS) (within the 5 mm margins proximal and distal to stent)

b. In-stent percent diameter stenosis (%DS)

c. In-segment late loss

d. In-stent late loss

e. In-segment binary restenosis (stenosis of > 50% of the reference vessel diameter)

f. In-stent binary restenosis

g. In-stent minimum lumen diameter (MLD)

h. Late stent malapposition by IVUS on a per-strut, per-cross sectional area, and per-stent basis

i. Tissue prolapse

j. Neointimal hyperplasia area at minimum lumen area (MLA) site

k. Neointimal hyperplastic (NIH) volume

l. Percent NIH volume obstruction

m. Rates of positive and negative remodeling.

14. Optical Coherence Tomography (OCT) Sub-study Endpoints (on 60 patients from the IVUS cohort consecutively enrolled at selected sites with OCT capability)

a. Acute stent malapposition per strut, per cross sectional area and per

stent level

b. Late stent malapposition at 12-13 months

Study description

Background summary

Bare Metal Stents in Acute Myocardial Infarction
Coronary artery disease continues to be the most common cause of morbidity and mortality in the occidental world. Originally, coronary angioplasty alone had been successfully used to treat the symptoms of this condition but was associated with a high rate of restenosis (30% to 50%), necessitating repeat revascularization procedures1. Treatment of coronary atherosclerotic disease has been significantly advanced by interventional cardiology, and in particular the advent of coronary arterial stents. In comparison to angioplasty alone, stents have reduced the incidence of angiographic as well as clinical restenosis, the recurrence of angina, the need for coronary arterial bypass graft (CABG) surgery, the need for repeat revascularization and the occurrence of major adverse cardiac events (MACE)2-4.
According to data from NHANES 2005*2008 (NCHS; unpublished NHLBI tabulation), the overall prevalence for MI is 3.1% in US adults over 20 years of age. MI prevalence is 4.3% for men and 2.2% for women. Among non-Hispanic whites, MI prevalence is 4.3% for men and 2.1% for women. Among non-Hispanic blacks, MI prevalence is 4.3% for men and 2.2% for women. Among Mexican Americans, MI prevalence is 3.0% for men and 1.1% for women5. On the basis of pooled data from the FHS, ARIC, and CHS studies of the NHLBI, within 1 and 5 year after a first MI, 19% and 36% of men, and 26% and 47% of women aged > 45, will die. Differences also exist between subjects from different ethnical backgrounds: at over 65 years of age, 25% of white men, 30% of white women, 25% of black men, and 30% of black women will die within a year after a first MI. These differences exist for 5 year outcomes as well (21% of white men and women, 33% of black men, and 26% of black women)5
Acute myocardial infarction (AMI) is usually the consequence of thrombotic occlusion of a major epicardial coronary artery. Mechanical reperfusion with percutaneous coronary intervention (PCI) can reduce myocardial damage, reinfarction, heart failure, and death. In a meta-analysis of RCTs comparing BMS to balloon angioplasty in subjects with acute myocardial infarction, stenting was associated with reduced rates of reocclusion (6.7% vs. 10.1%, OR 0.62, 95% CI 0.40 to 0.96, p = 0.03) and angiographic restenosis (23.9% vs. 39.3%, OR 0.45, 95% CI 0.34 to 0.59, p<0.001), as well as a reduction in target vessel revascularization (TVR; 12.2% vs. 19.2%, OR 0.50, 95% CI 0.37 to 0.69, p<0.001)5.
Currently, the Multi-Link stent is the only bare-metal stent licensed in the US

for treating subjects with acute MI.
Despite the apparent successes, problems remain due to failure to achieve optimal stent apposition and normal myocardial reperfusion. Early stent malapposition may be due to incomplete expansion or undersizing of balloon-expandable stents. Several studies have emphasized the importance of early malapposition in the setting of ST elevation MI, in which substantial thrombotic burden and the presence of diffuse vasoconstriction may be contributory. The incidence of incomplete stent deployment and undersizing is between 20% and 30% when assessed by angiography and even higher when IVUS is used for assessment6,7. It was recently demonstrated that identification of stent undersizing by visual estimate is a strong predictor of stent thrombosis6; this was usually caused by severe calcification, high thrombotic burden with subsequent vasoconstriction or incorrect judgment of the true coronary vessel size by the performing operator 6-10. An intravascular ultrasound sub study of the HORIZONS-AMI trial enrolled 241 subjects with 263 native coronary lesions (201 PES, 62 BMS) with baseline imaging.
Post-intervention acute stent malapposition (ASM) occurred in 40.3% BMS-treated lesions11. In a recent analysis, early stent thrombosis found in autopsies of subjects who suffered acute coronary disease and were implanted with either BMS or DES in the 30 days prior to their death, were significantly associated with stent malapposition12.
The STENTYS Coronary Stent System includes a self-expanding bare metal (nitinol) stent on a rapid exchange (RX) delivery system. In view of the theoretical implications of malapposition, the self-expanding property may offer a potential benefit.
The APPOSITION II study compared the STENTYS Coronary Stent System with a balloon-expandable stent in AMI, with the primary endpoint of malapposition at 3 days per OCT. The study demonstrated that subjects treated with balloon-expandable stents had three times higher percentage of malapposed struts immediately after the procedure. At 3 days, 0.58% of struts were malapposed in the STENTYS Coronary Stent System group under OCT vs. 5.46% in the balloon-expandable group, representing a 10-fold reduction. On a per-patient basis, 13.9% in the self-expanding stent group vs. 37.1% in the balloon-expandable group had malapposed stents (defined as *5% malapposed struts) immediately after the procedure; at 3 days, none of the subjects in the self-expanding stent group vs. 28% in the balloon-expandable group had malapposed stents ($p < 0.001$).
Improvement in acute apposition may also translate into lower rate of 30-day major adverse cardiac events (MACE). In HORIZONS-AMI, MACE occurred in 5.5% of subjects13. In the APPOSITION III post market registry (N=1002), evaluating the long term clinical benefit of the STENTYS stent for AMI with ST-elevations (STEMI) in a real-life setting, 30-day MACE was 3.5%. (G. Amoroso, Euro PCR, May 18, 2012)
In the current study we aim to assess the safety and effectiveness of the STENTYS Coronary Stent System compared with the Multi-Link Stent with respect to the primary endpoint of target vessel failure and a powered secondary

endpoint of acute apposition.

Study objective

To evaluate the safety and effectiveness of the STENTYS Coronary Stent System in the treatment of de novo stenotic lesions in coronary arteries in subjects undergoing primary revascularization due to Acute ST Segment Elevation Myocardial Infarction (STEMI) as compared to the Multi-Link bare metal coronary stent platform (Abbott Vascular, Inc.).

Study design

This study is designed as a prospective, multicenter, randomized controlled trial to assess the effectiveness and safety of STENTYS Coronary Stent System in the treatment of de novo stenotic lesions in coronary arteries in subjects undergoing primary revascularization due to AMI as compared with Multi-Link Coronary Stent Platform (Abbott Vascular).

Subjects undergoing primary revascularization for acute myocardial infarction (AMI) will undergo PCI with the STENTYS Coronary Stent System in the treatment group and the Multi-Link stent in the control group, randomized in 2:1 ratio.
Enrollment will include 880 subjects (586 in the STENTYS group and 294 in the control group) at up to 60 sites worldwide (a minimum of 50% North American subjects will be planned).
A maximum of 50 subjects will be enrolled at any one site.
A 10% drop-out rate of subjects is assumed, resulting in 792 evaluable subjects (528:264).

Subjects will be randomized to undergo PCI with the STENTYS Coronary Stent System or Multi-Link stent using a centralized randomization process and stratified by site. Random-block size randomization will be used.

The secondary powered endpoint (ASM) will be assessed by IVUS at the time of the index stent implantation, in the first 212 (141:71) consecutively enrolled subjects (the IVUS cohort).

Late angiographic and IVUS endpoints will be assessed in the 105 subjects out of IVUS cohort, at 12-13 months after the index procedure, and after assessment of the clinical TVF endpoint (2:1 STENTYS:Multi-Link).
Early and late OCT endpoints will be assessed in a sub-study of 60 subjects from the IVUS cohort, consecutively enrolled at selected sites with OCT capability.

Adjudication of study endpoints will be determined by an independent clinical events committee (CEC). The CEC will rule on all deaths throughout the study and will adjudicate the occurrence of clinical study endpoints and reports of

device failures in accordance with the definitions pre-specified within this protocol. CEC members will be blinded to treatment group.

Review of safety data and risks to subjects will be monitored by an independent data safety monitoring board (DSMB) at pre-specified enrollment milestones. The DSMB is charged with assuring patient safety during the course of the study and may, among other things, recommend that the study should be stopped if the data demonstrates that subjects are at an unacceptable risk of harm due to their study participation. The DSMB may determine that additional meetings and data review are necessary and will notify the sponsor, STENTYS Inc., if additional meetings are requested by DSMB members.

Intervention

Stent Placement Procedure

An angiogram (x-ray film of the heart) will be performed. The angiogram procedure will start with a needle puncture in either your groin, or wrist, after the area is numbed with a local anesthetic. A thin and flexible wire and catheter (a long thin hollow tube) will be used to inject contrast dye (a liquid that makes your heart vessels visible on x-ray) into your arteries, and then a device similar to an x-ray machine will be used to locate the narrowing in your artery. You may feel a warm sensation from the dye, but this feeling will usually go away after a few minutes.
Your artery must be sufficiently open to proceed with the intervention. Therefore, if a blood clot is present, a thrombectomy catheter may be used to remove the clot from the obstructed artery (thrombus aspiration). A small flexible catheter will then be passed through your arteries to the narrowed region in the heart. If required, your doctor will use a small balloon to make the artery a bit larger prior to implanting the stent. The stent is then implanted by withdrawing a sheath that covers the stent (if you have a STENTYS stent implanted) so that the stent expands, or by inflating a balloon and pressing the stent against the artery wall (if you have a Multi-Link Vision stent implanted). After the stent is implanted, your doctor may choose to inflate a balloon within the stent to help the stent fully expand (post-dilation). The exact procedure will be performed according to your doctor*s usual practice. At the end of the procedure, the catheter will be removed, leaving just the stent in place. Another angiogram will be performed.

At the end of the procedure, the catheters and wires are removed and you will lie flat for a period of time determined by your doctor. After the procedure, you will be monitored in the hospital until hospital discharge. Additional ECGs and routine blood tests will be performed during your stay at the hospital. You will be required to take the same medications usually given to all patients that receive a stent. These medications are aspirin (which will be for the rest of your life) and/or clopidogrel, prasugrel, or ticlopidine for at least 12

months.

You may also be asked to sign a separate informed consent for the PCI procedure.

If you are one of the first 212 subjects enrolled into the study, you will undergo intravascular ultrasound (IVUS) right after your stent has been implanted. If you are amongst the 120 subjects enrolled at an IVUS-designated site, you will be asked to have another angiogram and intravascular ultrasound (IVUS) within one month of your 12 month visit. Of these 120 patients undergoing angiography and IVUS, 60 patients will undergo OCT (Optical Coherence Tomography Imaging) which is an additional medical imaging procedure to determine how well a stent has healed. With IVUS and OCT, a tiny catheter is inserted into a coronary vessel, which allows your physician to see images inside the coronary arteries. The primary benefits of IVUS and OCT are that these methods provide added detail of the inside of the artery, the diameter (width) of the artery, information about the plaque in the walls of the artery, and how the stent is positioned against the wall of the artery

Study burden and risks

RISKS AND DISCOMFORTS

Risks Associated with cardiovascular stent implantation in coronary arteries

There are risks associated with the placement and use of stents. Some of the potential complications include:
* Death
* Abrupt coronary vessel closure or spasm (involuntary contraction)
* Allergic/anaphylactoid reaction to procedural medications (anticoagulant, antithrombotic, etc.) or contrast medium
* Allergic reaction to stent components (nickel)
* Aneurysm (widening of a blood vessel), pseudoaneurysm (widening that looks like an aneurysm), or arteriovenous fistula (abnormal passage)
* Arrhythmia (the heart may beat irregularly or stop beating completely)
* Atrial fibrillation (one of the chambers of the heart may beat irregularly)
* Balloon rupture
* Bleeding
* Cardiac tamponade (compression of the heart caused by blood or fluid accumulation in the space between the myocardium [the muscle of the heart] and the pericardium [the outer covering sac of the heart])
* Cardiogenic shock (the heart is unable to pump enough blood for the needs of the body)
* Cerebral vascular accident (damage to the blood vessels of the brain caused by a clot or bursting of a blood vessel)
* Dissection (tear in the layers of the walls) of the coronary arteries or the aorta
* Embolism (air, tissue, device or thrombus)

* Hematoma (mass of blood in the tissues) at the access site
* Hypotension (low blood pressure)/hypertension (high blood pressure)
* Insertion site infection (an infection of the hole in leg artery where the device was inserted into your body)
* Ischemia/infarction of tissue/organ (loss of blood flow to tissues or organs)
* Kidney damage
* Limb ischemia (loss of blood flow to the leg)
* Device failure or malfunction (failure to place to the stent or to place stent at the intended site)
* Myocardial infarction (heart attack)
* Perforation (a hole or injury to the heart or blood vessels)
* Renal failure (the kidneys cease to work correctly)
* Restenosis (returned to narrowing) of the stented artery
* Sepsis (massive infection throughout the body)
* Total occlusion (blockage) of the coronary artery
* Transfusion (receiving blood to replace lost blood)
* Unstable angina (unexpected chest pain not related to physical activity)
* Vasospasm (blood vessel spasms which lead to narrowing of the blood vessels)
* Transient ischemic attack (temporary loss of blood to parts of your brain that does not cause permanent damage)
* Vascular injury (injury to the blood vessels)

Obtaining blood can cause pain, bleeding, bruising, or swelling at the site of the needle stick. Fainting sometimes occurs and infection rarely occurs.

IVUS and OCT may be associated with added risk, including injury to the artery or blood clot formation. The added risk is less than 1%.

Important Information for Women If you are female, this procedure and/or treatments may involve unforeseeable risks to the embryo or fetus should you be pregnant at the time of treatment. If you are female, you will not be enrolled in the study if you are pregnant or might become pregnant. If you are of child bearing potential you must have a negative pregnancy test at the time of baseline procedures.

POSSIBLE BENEFITS IF YOU JOIN THIS STUDY

It is possible that there may be no direct benefit to you as a consequence of participating in this study and receiving this device, but the device may be able to help heart function and might stabilize your condition during and/or after the heart procedure.

Contacts

Public
STENTYS

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Clinical:
1. Subject * 18 years old.
2. Subject experiencing clinical symptoms consistent with AMI of >30 min. in duration.
3. ST elevation *1 mm in *2 contiguous leads or new left bundle branch block, or true posterior MI with ST depression of *1 mm in *2 contiguous anterior leads.
4. Symptom duration is <12 hours prior to signing informed consent.
5. Subject should be in catheterization laboratory and procedure started within 2 hours of consent.
6. Patient provides written informed consent.
7. Patient agrees to all required follow-up procedures and visits.;Angiography:
1. Based on coronary anatomy, PCI is indicated for the culprit lesion with anticipated use of stenting.

2. The vessel diameter is either known or expected to be 2.5-4.0 mm, without excessive tortuosity or diffuse distal disease.
3. Lesion length *12mm and * 23mm

Exclusion criteria

Clinical:
1. 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.
2. A previous coronary interventional procedure of any kind within 30 days prior to the procedure.
3. Female patients of childbearing potential known to be pregnant.
4. Patients undergoing cardiopulmonary resuscitation.
5. Cardiogenic shock (SBP <80 mmHg for >30 minutes, or requiring IV pressors or emergency IABP for hypotension).
6. The subject requires multi-vessel PCI at time of index procedure or any staged procedure of the target vessel within 9 months or any non-target vessel within 30 days post-procedure.
7. 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.). Thrombus aspiration may be used per operator discretion.
8. Attempted thrombolysis.
9. Co-morbid condition(s) that could limit the subject*s ability to participate in the trial or to comply with follow-up requirements, or impact the scientific integrity of the trial.
10. Concurrent medical condition with a life expectancy of less than 12 months.
11. Known left ventricular ejection fraction (LVEF) < 25% at the most recent evaluation (prior to the index hospitalization).
12. History of cerebrovascular accident or transient ischemic attack in the last 6 months.
13. Active peptic ulcer or active gastrointestinal (GI) bleeding.
14. History of bleeding diathesis or coagulopathy or inability to accept blood transfusions.
15. Known hypersensitivity or contraindication to aspirin, heparin or bivalirudin, clopidogrel or ticlopidine, cobalt, nickel, or sensitivity to contrast media, which cannot be adequately pre-medicated.
16. Known serum creatinine level > 2.5 mg/dl, eGFR <30, or hemodialysis dependent.
;Angiography:
1. Unprotected left main coronary artery disease (obstruction greater than 60% in the left main coronary artery that is not protected by at least one non-obstructed bypass graft to the left anterior descending (LAD) or left circumflex (LCX) artery or a branch thereof).
2. Multi-vessel intervention required during the index 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):	15-05-2013
Enrollment:	120
Type:	Actual

Medical products/devices used

Generic name:	Self-expandable stent
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	26-04-2013
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-11-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-07-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	NCT01732341
CCMO	NL43594.018.13