Evaluation of XIENCE versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization

Published: 24-05-2011
Last updated: 04-05-2024

To establish the safety and efficacy of the XIENCE stents in subjects with unprotected left main coronary artery disease (either isolated to the left main trunk or associated with disease in other coronary arteries) by demonstrating that compared to…

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

Summary

ID

NL-OMON39299

Source
ToetsingOnline

Brief title
EXCEL

Condition

- Coronary artery disorders

Synonym
unprotected left main coronary artery disease

Research involving
Human

Sponsors and support

Primary sponsor: Abbott Vascular International BVBA

Source(s) of monetary or material Support: Abbott

Intervention

Keyword: coronary artery disease, pro, V, XIENCE PRIME, Xpedition

Outcome measures

Primary outcome

Primary Endpoint:

Composite measure of all-cause mortality, myocardial infarction or stroke (modified Rankin Scale >=1 and increase by >=1 from baseline) estimated via Kaplan-Meier at all randomized subjects having reached the anticipated median follow-up duration of three years (with all randomized subjects having reached a minimum of two years follow-up).

Secondary outcome

Major Secondary Endpoints:

- Composite measure of all-cause mortality, myocardial infarction and stroke (mRS >=1 and increase by >=1 from baseline) at 30 days.
- Stroke (mRS >=1 and increase by >=1 from baseline) at 30 days
- Unplanned revascularization for ischemia at an anticipated median follow-up duration of three years (with all randomized subjects having reached a minimum of two years follow-up).

Additional Powered Secondary Endpoint:

A composite of all-cause mortality, MI, stroke (mRS>=1 and increase by >=1 from baseline), or unplanned revascularization for the anticipated median follow-up of three years and with a minimum follow-up in all subjects of two years.

Other secondary endpoints:

Time points for all other secondary endpoints, unless specified otherwise, are in-hospital, 30 days, 6 months, 1, 2, 3, 4, and 5 years post-procedure. The other secondary endpoints are:

• All cause mortality

* Cardiac death

* Non-cardiac death

• All MI (periprocedural, spontaneous, Q-wave and non Q-wave) including large and small MIs

• Protocol-defined MI

• MI adjudicated per Universal MI Definition

• Stroke (all, ischemic, and hemorrhagic)

• Disability following stroke event at 90 days± 2 weeks

• Ischemia-driven revascularization

o Ischemia-driven target lesion revascularization (TLR)

o Ischemia-driven target vessel revascularization (TVR)

o Ischemia-driven non target vessel revascularization (Non-TVR)

• All revascularization (ischemia driven and non-ischemia driven)

* All target lesion revascularization (TLR)

* All target vessel revascularization (TVR)

* All non target vessel revascularization (non TVR)

• Complete revascularization at baseline procedure, anatomic and functional (see Section 19. Appendix D.)

• Stent thrombosis (ARC definition) symptomatic or asymptomatic

• Symptomatic graft stenosis or occlusion (since this requires angiographic documentation, this endpoint will be compared to symptomatic ARC definite stent thrombosis)

• Bleeding complications

o Requirement for blood product transfusion

o TIMI scale (major or minor)

o BARC scale

• Requirement for blood product transfusion

• Time from randomization to procedure; time from procedure to discharge; ICU days; time from procedure to return to work

• Major adverse events (MAE) defined as composite of the following components. MAE will be assessed in-hospital and at 30 days only.

* death

* myocardial infarction

* stroke

* Transfusion of >=2 units of blood

* TIMI major or minor bleeding

* major arrhythmia

* unplanned coronary revascularization for ischemia

* any unplanned surgery or therapeutic radiologic procedure

* renal failure

* sternal wound dehiscence

* infection requiring antibiotics for treatment

* intubation for > 48 hours

* post-pericardiotomy syndrome.

Study description

Background summary

The main blood vessels that supply blood and nutrients to your heart are called coronary (heart) arteries. The most important of these coronary arteries is the left main coronary artery. This artery sometimes becomes narrowed so that the blood flow to the heart is decreased, which can cause you to have pain in your chest and/or other symptoms. The standard treatment when this artery is blocked is coronary artery bypass graft surgery (commonly known as *CABG* or *open-heart surgery*). Recently, one or more hollow, flexible metal mesh tubes, called stents, have been placed inside the left main coronary artery to keep it open. This can improve blood flow to the heart without major surgery. Some stents are coated with a drug (*drug-coated stents*) while others are not (*uncoated stents*). Studies in recent years show that drug-coated stents may be better at decreasing the heart arteries re-narrowing compared to the uncoated stents.
This Trial will use the drug-coated stents named:
1. the XIENCE PRIME
2. the XIENCE V
3. the XIENCE Xpedition
4. the XIENCE Pro

These stents are made by the Trial Sponsor and described in detail below. The XIENCE stents are designed to treat blockages in your heart arteries.
The Purpose of the Trial is to see if the XIENCE stents are a safe and effective treatment for the narrowing of your left main heart artery when compared to CABG surgery.

Study objective

To establish the safety and efficacy of the XIENCE stents in subjects with unprotected left main coronary artery disease (either isolated to the left main trunk or associated with disease in other coronary arteries) by demonstrating that compared to coronary artery bypass graft surgery, treatment of the left main stenosis ± other significant coronary lesions with the XIENCE stents will result in non-inferior or superior rates of the composite measure of all-cause mortality, myocardial infarction or stroke at an anticipated median follow-up duration of three years.

Study design

Randomized Clinical Trial (RCT)

Prospective, unblinded, randomized multicenter trial of approximately 2600 subjects enrolled at up to 165 U.S. and international centers.
Following diagnostic angiography demonstrating significant left main disease and consensus of the local Heart Team that the subject meets the study entry criteria, subjects will be consented and randomized 1:1 to:
a) PCI using the XIENCE stents (N=1300), or
b) CABG (N=1300).

Follow-up for all randomized subjects will continue for five years with an option for additional follow-up to 10 years.

Universal Registry
An additional group of approximately 1000 consecutive subjects with angiographically significant left main disease treated by participating qualified investigators during the course of this study who are either not eligible for randomization or for other reasons are not randomized will be consented for the Universal Registry, and followed through the time of initial treatment per standard of care with either PCI, CABG or medical therapy.

Approximately 100 consecutive subjects from the Universal Registry with a >=50% and <70% visually estimated angiographic diameter stenosis who otherwise meet all enrollment criteria, but without significant ischemia by noninvasive testing consistent with significant left main disease, and in whom IVUS shows a MLA >6.0 mm2 and/or a FFR >0.80, will be analyzed separately as intermediate lesion subjects, and followed through the time of initial treatment per standard of care with either PCI, CABG or medical therapy.

Intervention

Group I: PCI using the XIENCE stents (N=1300)

Group II: Coronary artery bypass grafting (CABG) (N=1300)

Study burden and risks

see section E9

Contacts

Public
Abbott Vascular International BVBA

Park Lane, Culliganlaan 2B
Diegem 1831
BE
Scientific
Abbott Vascular International BVBA

Park Lane, Culliganlaan 2B
Diegem 1831
BE

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

• Unprotected left main coronary artery (ULMCA) disease with angiographic diameter stenosis (DS) >=70% (visually estimated) requiring revascularization as assessed by both a participating
interventional cardiologist and cardiac surgeon (local Heart Team), or;• ULMCA disease with angiographic DS >=50% but <70% (visually estimated) requiring revascularization as assessed by both a participating interventional cardiologist and cardiac surgeon (local Heart Team), with one or more of the following present:
- Non-invasive evidence of ischemia referable to a hemodynamically significant left main lesion (large area of ischemia in both the LAD and LCX territories, or in either the LAD or LCX territory in the absence of other obstructive coronary artery disease to explain the LAD or LCX defect), or stress-induced hypotension, or stress-induced fall in LVEF, or stress-induced transient ischemic dilatation of the left ventricle, or stress-induced thallium/technetium lung uptake, and/or
- IVUS MLA <=6.0 mm2, and/or
- FFR <=0.80
OR
Left Main Equivalent Disease: Left main Medina classification 0,1,1 bifurcation disease (diameter stenosis of both the true ostial LAD and LCX [within 5mm of the left main distal

bifurcation]) >= 50%, in the absence of significant angiographic stenosis in the left main coronary artery, may also be enrolled if one of the following conditions are present:
- Both the ostial LAD and ostial LCX stenoses are >= 70% stenotic by visual estimation, or
- If one or both of the ostial LAD and ostial LCX stenoses are >=50% and <70% stenotic by visual estimation, then this lesion(s) is demonstrated to be significant either by
a) non-invasive evidence of ischemia in its myocardial distribution; and/or
b) FFR <=0.80; and/or
c) IVUS MLA <=4.0 mm2 (FFR is preferred).
Note: if both the ostial LAD and ostial LCX stenoses are >=50% and <70% stenotic by visual estimation, then both lesions must be significant by these criteria for the patient to be eligible for enrollment.;• Clinical and anatomic eligibility for both PCI and CABG as agreed to by the local Heart Team
- Interventionalist determines PCI appropriateness and eligibility
- Surgeon determines surgical appropriateness and eligibility;• Silent ischemia, stable angina, unstable angina or recent MI
- If recent MI, CK-MB must have returned to normal prior to randomization;• Ability to sign informed consent and comply with all study procedures including follow-up for at least three years;• The subject must be >= 18 years of age

Exclusion criteria

• Prior PCI of the left main trunk at any time prior to randomization;• Prior PCI of any other (non-left main) coronary artery lesions within one year prior to randomization;• Prior CABG at any time prior to randomization;• Need for any concomitant cardiac surgery other than CABG (e.g. valve surgery, aortic repair, etc.), or intent that if the subject randomizes to surgery, any cardiac surgical procedure other than isolated CABG will be performed;• CK-MB greater than the local laboratory upper limit of normal, or recent MI with CK-MB levels still elevated
Note: Subject with a recent MI in whom the troponin levels are still elevated but falling and in whom the CK-MB is within normal range may be enrolled, with the CK-MB levels used to assess periprocedural MI.;• Subjects unable to tolerate, obtain or comply with dual antiplatelet therapy for at least one year;• Subjects requiring or who may require additional surgery (cardiac or non cardiac) within one year;• The presence of any clinical condition(s) which leads the participating interventional cardiologist to believe that clinical equipoise is not present (i.e. the subject should not be treated by PCI, but rather should be managed with CABG or medical therapy (reasons will be documented in the Heart Team worksheet));• The presence of any clinical condition(s) which leads the participating cardiac surgeon to believe that clinical equipoise is not present (i.e. the subject should not be treated by CABG, but rather should be managed with PCI or medical therapy (reasons will be documented in the Heart
Team worksheet));• Pregnancy or intention to become pregnant (female subjects of child bearing potential must have a negative pregnancy test within 7 days of the index procedure);• Non cardiac co-morbidities with life expectancy less than 3 years;• Other investigational drug or device studies that have not reached their primary endpoint
;Angiographic exclusion criteria (the subject is not eligible for randomization
if any of the following are present):

• Left main diameter stenosis <50% (visually assessed);• SYNTAX score >=33, as determined by the consensus of at least one participating interventional cardiologist and one surgeon of the local Heart Team;• Visually estimated left main reference vessel diameter <2.25 mm or >4.5 mm (post dilatation up to 4.5mm is allowed);• The presence of specific coronary lesion characteristics or other cardiac condition(s) which leads the participating interventional cardiologist to believe that clinical equipoise is not present (i.e. the subject should not be treated by PCI, but rather should be managed with CABG or medical therapy - reasons will be documented);• The presence of specific coronary lesion characteristics or other cardiac condition(s) which leads the participating cardiac surgeon to believe that clinical equipoise is not present (i.e. the subject should not be treated by CABG, but rather should be managed with PCI or medical therapy - reasons will be documented)

Study design

Design

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):	28-06-2011
Enrollment:	160
Type:	Actual

Medical products/devices used

Generic name:	XIENCE PRIME;XIENCE V EECSS;XIENCE Xpedition;XIENCE Pro
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	24-05-2011
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	29-03-2012
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	29-07-2013
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	23-01-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	04-12-2014
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	NL33242.078.10