Compare Absorb
ABSORB bioresorbable scaffold vs. Xience metallic stent for prevention of restenosis following percutaneous coronary intervention in patients at high risk of restenosis. ;Annex study of in-stent restenosis
COMPARE ABSORB ISR study: A single-arm, annex study of patients with in-DES restenotic lesions requiring PCI and treated with Absorb BVS

Published: 31-08-2015
Last updated: 17-01-2025

The purpose of the current investigation is therefore to prove the short-term equivalence and long-term benefit of the ABSORB scaffold over a Xience in patients at high risk of restenosis or with complex lesion(s).Diabetic substudyTo assess the...

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

Summary

ID

NL-OMON54699

Source
ToetsingOnline

Brief title
Compare Absorb, Compare Absorb ISR

Condition

- Coronary artery disorders

Synonym
Ischemic heart disease - risk for restenosis

Research involving
Human

Sponsors and support

Primary sponsor: Maasstadziekenhuis
Source(s) of monetary or material Support: unrestricted grant van Abbott

Intervention

Keyword: bioresorbable, PCI, restenosis, stent

Outcome measures

Primary outcome

The primary endpoints of the study are target lesion failure (TLF) as defined as a composite of cardiac death, myocardial infarction (MI) in target vessel territory and clinically indicated target lesion revascularization. The details of the definitions are described in the Appendix II. Briefly, SCAI consensus definition is used to adjudicate peri-procedural MI occurring within 48 hours after index procedure, while the 3rd universal definition is used for spontaneous MI.

Diabetic substudy

Superiority of ABSORB BVS vs. XIENCE in terms of total plaque regression at 62 months, Defined as; percentage change in total atheroma volume (TAV) (computed

as: (TAV (follow-up) * TAV (post-procedure) / TAV (post-procedure)) x 100.

Total atheroma volume is calculated as the sum of the differences between EEM and lumen areas across all evaluable slices: total atheroma volume = (EEMCSA*LUMENCSA), where EEMCSA =external elastic membrane cross-sectional area and LUMENCSA=luminal cross-sectional area. - Core-lab based

Smart Follow-up

Cumulative rate of angina pectoris at one year (excluding episode within 7 days after index procedure).

Compare Absorb ISR: Annex study of in-stent restenosis

Angiographic net gain at 1 year

Secondary outcome

Main study:

• Components of primary endpoints

• Target vessel failure and its components

• All revascularization

• Peri-procedural MI (per SCAI definition) and spontaneous MI (per the 3rd universal definition)

• Definite or probable stent/scaffold thrombosis (per ARC)

• Cumulative recurrent or worsening angina at 12 months, excluding the angina episodes that occurred during index hospitalization or in the 7 days post index

procedure, whichever came first (refer to appendix III)

• Health care cost related to diagnostic workup of presumed coronary ischemia and therapies in the first 12 months, excluding the cost during index hospitalization or in the 7 days post index procedure (whichever came first)

• Angina status at 1, 6 and 12 months per Seattle angina questionnaire

• Quality of life at 1, 6 and 12 months as assessed by EQ5D

• For STEMI patients, TIMI flow, myocardial blush and ST-segment resolution on ECG

• Health care costs related to target vessel failure up to 5 years

• All-cause mortality

Diabetic substudy

Angiographic Endpoints

• In-stent/in scaffold LLL at 62 months defined as MLD post-nitrate at 62 months follow-up minus MLD post procedure post nitrate at index and IVUS endpoints are intended postnitrate, unless otherwise specified) procedure by QCA - Core-lab based

• In stent/in-scaffold and in-segment proximal and distal Angiographic Binary Restenosis (ABR) rate at follow up (62 months, according to randomization) by QCA (segment defined as from 5 mm proximal to 5 mm distal to stent/scaffold edges; binary stenosis defined as diameter stenosis of 50% or more at follow up).

• In-scaffold/In-stent, in-segment, proximal and distal % diameter stenosis (DS) post-nitrate pre-implantation, post-procedure and at 62 months (according to randomization) by QCA

• In-stent/in-scaffold acute lumen gain defined as Minimum Lumen Diameter (MLD) post nitrate at index procedure minus baseline MLD post nitrate by QCA

• In-scaffold/in-stent net gain, defined as MLD post-nitrate at follow-up minus MLD post-nitrate pre-implantation at 62 months (according to randomization) by QCA.

IVUS Endpoints

• Total Plaque change between pre-procedure and at 62 months

• Mean/Minimum Lumen diameter/area/volume

• Mean/Minimal Scaffold/Stent diameter/area/volume

• Mean/ Minimal Vessel diameter/area/volume pre-procedure, postprocedure and (if analyzable) at 62 months follow-up (according to randomization)

• Percentage of patients with late gain

• Acute incomplete apposition (post-implantation), persisting incomplete apposition, late acquired incomplete apposition and resolved incomplete apposition (if analyzable) at 62 months

• Mean/maximum neo-intimal hyperplasia area (mm2) at 62 months (if analyzable)

Clinical/procedural endpoints

Clinical and procedural endpoints will be according to COMPARE ABSORB main study.

Smart Follow-up

Secondary endpoints:

% angina free based on angina frequency domain of SAQ

Adherence to Follow-up

A composite of death and MI

5 domains of SAQ

Health care cost related to diagnostic workup of presumed coronary ischemia and therapies

Primary endpoint based on SMART FUP vs. on hospital visits are also compared in the same patients with SMART FUP

Annex study of in-stent restenosis Compare Absorb ISR

• Device success (lesion based analysis)

• Procedural success (subject based analysis)

• Primary and secondary endpoints of the main Compare Absorb trial

• Angiographic endpoints

o Descriptive analysis at index post-procedure and at 1 year +/- 28 days follow-up

o In-scaffold, In-segment late loss (LL), proximal and distal LL

o In-scaffold, in-segment, proximal and distal Minimum Luminal Diameter (MLD)

o In-segment, proximal and distal % Diameter Stenosis (DS)

o In-scaffold, in-segment Angiographic Binary Restenosis (ABR) rate

o In-scaffold/in-stent net gain (being the change in MLD between 1 year versus

pre-implantation)

o Conformability assessed by change in curvature and angulation between pre-,

post-procedure and follow-up

Study description

Background summary

In patients with a simple lesion, the ABSORB first-in-man trials showed a clinical safety up to 5 years with potential late benefits such as lumen enlargement, plaque reduction and restoration of vasomotion. These phenomena start to appear >=1-2 years after implantation of bioresorbable scaffold in due course of bio-resorption. Based on the clinical safety demonstrated in the ABSORB A and B studies, the fully bio-resorbable everolimus-eluting scaffold had acquired a CE-mark in Europe and became commercially available.

Until now extensive dissemination of revascularization with a bioresorbable scaffold has occurred without randomized comparison with a metallic drug-eluting stent. The ABSORB II randomized trial comparing a metallic everolimus-eluting stents with drug-eluting bioresorbable scaffolds was initiated in Europe in 2011. Currently the 3 randomized trials are ongoing to acquire regulatory approval in China, Japan and USA. In these randomized trials, however, the patients with complex lesion(s) are excluded.

The performance and long-term safety/efficacy of bio-resorbable scaffolds in complex lesions still remain unclear. Unlike a metallic stent, the polymeric device is inherently limited in an expansion range and therefore pre-procedural sizing is mandatory to avoid overexpansion of the device, which might result in acute mechanical dis-integrity. Similarly, implantation of the device in lesions with a large side-branch is currently not recommended to prevent mechanical disintegrity caused by complex bifurcation scaffolding such as crush, T-scaffolding, or culottes techniques.

The purpose of the current investigation is therefore to prove the short-term equivalence and long-term benefit of the ABSORB scaffold over a Xience in patients at high risk of restenosis or with complex lesion(s).

Diabetic substudy
The ABSORB bioresorbable vascular scaffold system (ABSORB BVS), combining the

drug elution with the reabsorption of the scaffold, may preserve the natural function of the coronary artery (motility and positive remodeling) as well as the chance of bypass grafting in case of failure of percutaneous treatment.

Smart Follow-up
In the ABSORB II trial, it was observed that the patients receiving the BVS had significantly less angina episodes during the first year than the patients implanted with Xience stents (16.4% versus 25.6%), however the there was no difference in the SAQ scores between the 2 groups. The hypothesis is that, as the Seattle questionnaire only reflects on the preceding 4 weeks and is performed only 2 or 3 times during the follow up, a more longitudinal (frequent) follow up performed via a connected platform will detect more episodes of angina, increase the adherence of the pts than traditional FU (questionnaire at FU visits and Seattle questionnaire) between normal FU pts and the SMART FU pts.

Compare Aborb ISR: Annex study of in-stent restonsis
Restenosis after implantation of a drug eluting stent (DES) is a rare event and its mechanisms are specific and multi-factorial thereby hindering direct extrapolation of the results obtained in bare-metal stent restenosis. Its optimal treatment remains to be determined. Small studies and registries have suggested that the use of limus eluting stent for DES restenosis may be associated with better angiographic results and a lower rate of recurrent target lesion revascularization (TLR) compared to plain balloon angioplasty and, even more recently, to drug-eluting balloon. The absence of additional layer of metallic struts, when using bioresorbable scaffold, could have a positive impact in terms of clinical outcome in combination with a non-inferior angiographic result.

Study objective

The purpose of the current investigation is therefore to prove the short-term equivalence and long-term benefit of the ABSORB scaffold over a Xience in patients at high risk of restenosis or with complex lesion(s).

Diabetic substudy
To assess the performance of Absorb BVS family scaffold compared to Xience everolimus eluting stents family in diabetic patients with complex coronary artery disease, in terms of regression of the total plaque (percentage change in total atheroma volume) at 62 months.

Smart Follow-up
To evaluate the efficacy, performance and cost effectiveness of a web bassed,

connected self-evaluation of angina using companion dedicated tablet (SMART FUP®) during the first year of follow-up (Smart follow-up group) in the COMPARE ABSORB trial.

Compare Aborb ISR: Annex study of in-stent restonsis
To evaluate the safety, efficacy and performance of Absorb scaffold in the treatment of subjects with ischemic heart disease caused by in-DES restenotic coronary artery lesions

Study design

The Compare ABSORB trial is a randomized (1:1; ABSORB family scaffold versus XIENCE family stent), active control, single-blind, non-inferiority, European multi-center clinical trial. Two thousand and one hundred subjects will be enrolled at up to 42 European sites.

Clinical follow-up at 30 days, 180 days, 1, 2, 3, 4, 5, 6 and 7 years days post-procedure. Hospital visits are planned at 1 month (* 7 days), 6 months (* 14 days) and 1 year (* 30 days). An assessment of the anginal status, cardiovascular drug use and any Serious Adverse Events is recorded during clinical follow-up visits. Phone contacts are scheduled at 2 year (* 30 days), 3 year (* 30 days) and 4 years (* 30 days), 5, 6 and 7 years.
Quality of Life questionnaire (EQ5D) and Seattle Angina Questionnaire (SAQ) at 30, 180 and 360 days post-procedure and at the time of any recurrent event
Questionnaire on perception of patients about the type of device implanted is performed at 30, 180 and 360 days post-procedure.
Chest symptoms potentially related to angina is assessed using a dedicated structured questionnaire (Appendix III) at 1, 6 and 12 months and at intermittent events.
Cost effectiveness of two treatment arms related to chest pain or angina is assessed at one year using unit costs in 5 countries.

Diabetic substudy
Prospective, randomized, active control, single blinded, multi-center clinical investigation using ABSORB BVS compared to XIENCE.*The two groups of randomized patients will undergo angiographic and IVUS follow up at 62 months after the index procedure. Main analyses by intention to treat.

Smart Follow-up
Prospective, multi-center study as an ancillary of the Compare Absorb randomized controlled trial.

Compare Absorb ISR: Annex study of in-stent restenosis

Prospective, multi-centre, open label, single arm study as an annex registry of the Compare Absorb randomized controlled trial

Intervention

All patients will undergo coronary angiography and PCI on clinical indication. Based on their randomization outcome they will get a Absorb bioresorbable Scaffold or a Xience stent implanted.

Diabetic substudy
Baseline:
IVUS: to be performed pre-procedure and post-procedure

Invasive follow-up:
Angiography: All subjects at 62 months follow-up
IVUS: to be performed after angiography. All subjects at 62 months follow-up

Compare Absorb ISR: Annex study of in-stent restenosis
Repeat angiography will be performed one year after index procedure

Study burden and risks

All patients will undergo coronary angiography and PCI on clinical indication. Based on their randomization outcome they will get a Absorb bioresorbable Scaffold or a Xience stent implanted.
In addition patients will be asked to come to the clinic for follow up visits at 1, 6 and 12 months. Often these visits can be combined with their out-clinic visit planned for their normal clinical follow-up.
At 2, 3, 4, 5, 6, 7 year patients will be contacted by phone with some questions about their current health status.

Diabetic substudy
Patients will get an IVUS during the index PCI and in addition they will have to be hospitalized for 1 day after 5 years for an controle angio and IVUS.

Smart Follow-up
The patients included in the substudy will receive a box including a companion dedicated tablet, with a connected activity tracker bracelet, a connected wireless blood pressure cuff and a connected wireless scale, they will be asked to report every week on their angina status and answer to dedicated questions via the "Smart Follow-Up" online Platform.

Compare Absorb ISR: Annex study of in-stent restenosis

Repeat angiography will be performed one year after index procedure

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

Patients (18-80 years old) with at least one of the following:
i) High-risk characteristics for restenosis
• Medically treated Diabetes and/or multivessel disease of which more than one de-novo target lesion to be treated with the study scaffold/stent
ii) Complex target lesion
Single de-novo target lesion satisfying at least one of the following:
• Lesion length >28 mm
• Small vessels: Target lesion reference vessel diameter between 2.5-2.75 mm
• Lesion with pre-existing total occlusion (pre-procedural TIMI = 0)

Pre-existing occlusion is supposed to be present before procedure and does not include the culprit lesion in the setting of acute myocardial infarction.
• Bifurcation with single stent strategy
Patients with in-stent restenosis (ISR) of a drug-eluting stent are admitted to a separate annex study protocol: Compare Absorb ISR, Inclusion criteria Diabetic substudy
• Diabetes Mellitus
• All other general inclusion criteria according to Compare Absorb main study eligibility criteria., inclusion / exclusion criteria Smart Follow up substudy
- As same as the the Compare Absorb main study, Inclusion criteria in-stent restenosis annex study Compare Absorb ISR
• Patients who are excluded from the main Compare Absorb randomised study, due to the presence of in-DES restenosis
• Patients aged 18-80 years
• high risk of restenosis due to the presence of up to two in-DES restenosis lesions in one or two different epicardial vessels that could be treated with Absorb scaffold(s)

Exclusion criteria

•Age <18 years or >75 years
•Renal insufficiency (GFR/MDRD <45 ml/min)
•Known comorbidities which make patients unable to complete 5-year follow-up
•Known non-adherence to DAPT
•Patients on oral anticoagulation
•Cardiogenic Shock (Killip >2)
•LVEF <30%
* Patients at high bleeding risk who are not suitable for long-term DAPT
* Pregnant woman
•Following lesion characteristics:
• --Target lesion reference vessel diameter (RVD) < 2.5 and > 4 mm
• --STEMI with RVD of >3.5mm of the culprit target lesion
• --Target lesion with in-stent/scaffold thrombosis
• --Graft lesions as target lesions
• --Aorto-ostial lesion(s)
• --Left main lesion
• --Severe tortuosity of target vessel
• --In-scaffold/in-stent restenosis
• --Bifurcation target lesion with intended 2 stent/scaffold strategy,
Exclusion criteria Diabetic sub-study are the same as for the main study,
Exclusion criteria in-stent restenosis annex study Compare Absorb ISR
• Similar to the main Compare Absorb study except for the exclusion for in-stent restenosis
Additional lesion exclusion criteria:
• Bare metal stent restenosis requiring intervention in the target vessel(s)

• Initial DES size of < 2.5 mm, or in the absence of information on previous DES size, target vessel diameter < 2.5 mm
• Previous 2 stent technique in the target lesion if it is a bifurcation lesion
• Recurrent in-DES restenosis in the target vessel
• More than one layer of metallic DES/BMS at the target lesion site
Non-target lesion and target lesion in the same epicardial coronary artery (right coronary artery, left circumflex artery or left anterior descending artery)

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:	Completed
Start date (anticipated):	28-09-2015
Enrollment:	460
Type:	Actual

Medical products/devices used

Generic name:	ABSORB bioresorbable vascular scaffold
Registration:	Yes - CE intended use

Ethics review

Approved WMO

Date:	31-08-2015

Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	12-10-2015
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	18-12-2018
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	03-05-2023
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	20-09-2024
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	NCT02486068
CCMO	NL54100.101.15