Evaluation with OFDI of strut coverage of Terumo new Drug Eluting Stent TCD-10023 with biodegradable polymer at 1, 2 and 3 months.

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The primary purpose of the study is Optical Frequency Domain Imaging (OFDI) investigation of strut coverage of the sirolimus-eluting stent with biodegradable polymer at 1, 2 and 3 months after stent implantation This study is the pilot study to...

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

Summary

ID

NL-OMON38569

Source
ToetsingOnline

Brief title
DISCOVERY 1-TO-3 STUDY

Condition

- Coronary artery disorders

Synonym
Coronary artery disease and arterial stent strut coverage - narrowings of coronary arteries and tissue growth (enodthelium) inside the stent

Research involving
Human

Sponsors and support

Primary sponsor: Terumo
Source(s) of monetary or material Support: Funding by industry: Terumo Europe nv

Intervention

Keyword: - Drug Eluting Stent (DES), - OFDI, - Strut coverage

Outcome measures

Primary outcome

The primary endpoint is OFDI assessed percent stent strut coverage at 3 months

post procedure.

Hypothesis: <20% uncovered struts at 3 months post procedure

NOTE: the Primary endpoint will be assessed for all single stent lesions.

Secondary outcome

1. Number (%) of stent strut coverage at 1 and 2 months

2. Number (%) of stented lesions which have >10 % uncovered stent struts at 1,

2 or 3 months

3. Number (%) of stented lesions which have >20% uncovered struts at 1, 2 or 3

months

4. Percentage of acquired malapposed struts at 1, 2 and 3 months

5. Amount of in-stent intimal hyperplasia (mm3) at 1, 2 and 3 months

6. Amount of in-segment intimal hyperplasia (mm3) at 1, 2 an d 3 months

7. Neo-intimal thickness (µm) at 3 months

8. In-stent late-lumen loss at 3 months by QCA

9. In-segment late lumen loss at 3 months by QCA

10. Target Lesion Revascularization (TLR) at 1, 3, and 12 months post-procedure;

11. Target Vessel Revascularization (TVR) at 1, 3 and 12 months post-procedure;

12. Target Lesion Failure (TLF), composite endpoint of Cardiac Death, target vessel related Myocardial infarction (MI) and Clinically Indicated TLR at 1, 3 and 12 months post-procedure;

13. Major Cardiac Adverse Events (MACE) defined as cardiac death, MI (Q wave and non-Q wave), emergent coronary artery bypass surgery, or target vessel revascularization (TVR) at 1, 3 and 12 months post-procedure.

14. Stent thrombosis at 1, 3 and 12 months post-procedure;

NOTE: all secondary endpoints will be assessed for single stent lesions and overlapping stent lesions.

Study description

Background summary

Stent thrombosis is a rare, but serious event as it is linked to myocardial infarction, sudden death and heart failure. It occurs in 0.7-1.0% of the PCI procedures within 1 year and has an annual incidence rate of 0.1 to 0.7% thereafter, depending on the type of stent is used. Therefore, prevention of stent thrombosis in the early (<30 days after PCI), late (>30 < 360 days) and very late (>360 days) phase is of important clinical relevance.

Currently dual antiplatelet therapy (DAPT) is given for at least of 9-12 months after coronary drug-eluting stent implantation in order to lower the risk for early and late stent thrombosis, though this merely based on non-randomised observations and expert opinion. Furthermore, DAPT therapy is not a 100% protective therapy, as stent thrombosis still occurs under DAPT regimen. And whether extended DAPT beyond one year after DES implantation is beneficial remains to be determined, but is very likely to be associated with a higher bleeding risk for the patient.

Stent related factors to stent thrombosis are the amount of uncovered stent struts and the extend of malapposed stent struts to the vessel wall. Both are highly related to the type of stent used, in which the polymer (in combination with the drug) causes incomplete healing of the vessel wall, chronic

inflammation or hypersensitivity reaction and eventually incomplete re-endothelialization or incomplete coverage and embedment of the stent in the vessel wall. Usage of more biocompatible durable polymers or biodegradable polymers have the potential to overcome the above mentioned triggers for stent related factors of stent thrombosis. This has recently been proven in comparative stent studies, like COMPARE I, SPIRIT IV and LEADERS, in which the more biocompatible or biodegradable polymer coated drug-eluting stents had a significantly lower amount of stent thrombosis compared to the first generation drug-eluting stents or were at least equivalent to the proven biocompatible durable fluoropolymer of the thin-strut Cobalt-Chromium everolimus-eluting stent (COMPARE II, RESOLUTE AC).

OCT or OFDI are new intravascular imaging modalities with a much higher resolution compared to intravascular ultrasound (IVUS). These new techniques have been used to investigate the amount of coverage and the amount of malaposition of the stent struts.
Though there are no universal accepted criteria for the relationship between stent coverage or malapposition and stent thrombosis, recent studies with the newer generation drug-eluting stents have shown that stent coverage is >90% and malapposition is < 3 % of the total investigated stent struts by OCT at 6 to 13 months post implantation.

Purpose of this pilot study is to investigate the absolute stent coverage at 1, 2 and 3 months after stent implantation of a new thin strut Cobalt-Chromium sirolimus-eluting stent with an abluminal biodegradable polymer, which resolves in 3 month time. After 3 months, when the polymer is dissolved and the drug is released, an inert bare metal stent resides. This will pave the way for a large scale randomized trial, showing that a 3 month DAPT regimen will be as safe as 6 to 9 months DAPT and potentially will result in less bleedings.

OFDI Analysis
In the last decade the powerful imaging technique - optical frequency domain imaging - has gained popularity and is frequently used to study pattern of vessel healing after DES implantation and also to assess potential underlying mechanisms for adverse events, particularly those causing stent thrombosis. It has been hypothesized that delayed healing and insufficient strut coverage are predisposing factors for stent thrombosis development.
In a systematic review of strut coverage of different DES, assessed by optical coherence tomography at 6 months, the first generation sirolimus eluting Cypher stent and paclitaxel eluting Taxus stent showed respectively 10.86% and 5.49% of uncovered struts. At 9 months Cypher stent had 8.12% uncovered struts while Xience everolimus eluting stent had 3.12%, similar to TCD-10023 stent at 6 months (3.8%). The overall frequency of malapposed struts in TCD-10023 stent was 1.66% at 6 months being among the lowest reported.1 The result obtained in RESOLUTE all-comer trials assessing DES coated with zotarolimus (Endeavor Resolute) and everolimus (Xience) eluting stents, showed coverage rate of 92.6% and 94.2% respectively.2 This study tested strut coverage at 13 months

post-stent implantation in two stents having similar design to TCD-10023 stent, except that both have permanent polymers indicating that TCD-10023 has strong tendency towards good strut coverage as even at 6-months percentage of covered struts was higher.

Guagliumi et al. studied the impact of stent alloys on human vascular response to everolimus by comparing two DES with different platforms (cobalt chromium - Xience DES and platinum chromium-Promus Element), with similar coating and drug formulation. They found that at 6 months both stents had similar behaviour towards the vessel wall with low rate of strut malapposition (1.51% in platinum chromium and 1.80% in cobalt-chromium). Those findings are also very similar to 1.66% in TCD-10023 DES. At the same time the percentage of uncovered struts was higher than in TCD-10023 (8.5% and 5.9% in platinum-and cobalt-chromium respectively).

All those findings indicate excellent results of the TCD-10023 stent, which considering the design concept will allow us to investigate the safety profile within 3 months after implantation and potentially to investigate shorter DAPT regimens and therefore less bleeding risk after stent implantation without compromising safety.

Study objective

The primary purpose of the study is Optical Frequency Domain Imaging (OFDI) investigation of strut coverage of the sirolimus-eluting stent with biodegradable polymer at 1, 2 and 3 months after stent implantation
This study is the pilot study to assess feasibility of shorter DAPT after PCI with this new stent.

Study design

Prospective, single arm, multicenter, open label study with adaptive design.
All patients will undergo angiographic follow-up at 3 months, OFDI imaging after baseline and at 1, 2 and 3 months, and clinical follow-up out to 1 year.

Intervention

All eligible patients will be treated with the study stent: sirolimus eluting coronary stent TCD-10023 with biodegredable polymer. No comparator arm.

Study burden and risks

Nature and extend of the burden:
Before and after stent implantation a blood test (approximately 15 ml for analysis of cardiac enzymes) and ECG will be performed according to the standard procedure of the hospital. An OFDI-evaluation of the treated lesions

will be performed after stent implantation. Dual antiplatelet therapy (DAPT) will be prescribed for a period of at least 6 months according to hospital routine practice. The patients will be asked to visit the hospital at 3 months for an evaluation of patient's general well-being and a routine physical examination, and for angiographic and OFDI evaluation of all treated lesions. At 12 months patients will receive phone call from the research personnel to ask about their general well-being and health condition.

Possible risks associated with participation:
The potential risks of the stent implantation in this study are not different from the potential risks associated with the standard procedure of stent placement and they may include the following:
* Major bleeding from the groin site depends on whether blood thinning drugs are used (4 in 100 patients)
* Death (less than 7 in 1,000 patients)
* Emergency bypass surgery (15 in 10,000 patients)
* Heart attack (4 in 1,000 patients)
* Stroke (2 in 1000 patients) risk may vary depending on whether blood thinning drugs are used.
* There is also no guarantee that the stent will keep the vessel open and reduce subsequent re-narrowing of the artery

Although very unlikely, there may be unforeseeable risks that are not known at this time. The results of the stent placement can not be guaranteed 100%. If the procedure is not successful, repeat intervention(s) and/or coronary by-pass surgery may be necessary.

Any coronary angiogram involves the use of radiation as part of the special X-Ray procedure. The dose of radiation received from one coronary angiogram is equivalent to two years natural background radiation.
The risks for the angiogram are:
* Death (1 in 10,000 patients)
* Emergency angioplasty +/- stent (1 in 1,000 patients)
* Emergency bypass surgery (1 in 10,000 patients)
* Heart Attack (5 in 10,000 patients)
* Stroke (7 in 10,000 patients)
* Bleeding (4 in 100 patients)

The risks related to the use of the OFDI catheter are not different to those of a balloon dilatation and/or stenting procedure alone. It is important to inform you however that extra catheters will be introduced into your coronary arteries. This implies a small risk of harming the vessel; patients may feel some chest pain (caused by cramp of the coronary artery). Damage to or movement of the stent are possible. Upon occurrence of these complaints these can quickly be relieved by using medication. Exceptionally implantation of another stent or bypass surgery may be necessary.

Benefits associated with participation:
Patients will not have any immediate benefit from participating in this clinical investigation except that the treating physician will follow up on the patients' medical condition on a regular base so every sign of illness can be detected in time. The results of this study will be used for scientific purposes which will result in increased knowledge on the best treatment procedures and medications for the medical conditions patients are suffering.

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. Patient is at least 18 years old;
2. Patients is a suitable candidate for PCI;
3. Patient has multi-vessel disease with >=2 de-novo lesions in native coronary arteries

suitable for treatment with TCD-10023 DES;
4. Target lesions are suitable for OFDI examination;
5. Patient requires staged procedure between 3-5 weeks after baseline procedure, according to investigator*s judgement;
6. Target vessel reference diameter is between 2.5 - 4.0 mm (visual assessment);
7. Patient has provided written informed consent;
8. Patient is affiliated to social security or equivalent system (France only).

Exclusion criteria

1. Patient has known allergy to sirolimus, cobalt, chromium, nickel, or contrast agent (that cannot be adequately premedicated);
2. Patient is not a suitable candidate for use of DAPT because of active or recent bleedings or for use of vitamin K antagonist, like warfarin, dabigatran, rivaroxaban or acenocoumarol;
3. Patient is presenting with STEMI at baseline procedure;
4. Patient has Killip class > 1 at admission;
5. Patient is in cardiogenic shock;
6. Patient is a female of childbearing potential;
7. Patient has life expectancy of less then 1 year;
8. Patient is expected to undergo major surgery within 3 months;
9. Patient has Left Main disease >= 50%;
10. Target lesion at bifurcation requiring 2 stents technique;
11. Target lesions are severely calcified;
12. Target lesion is aorta-ostially located (within 3 mm of vessel origin);
13. Patient has renal failure defined as estimated Glomerular Filtration Rate (eGFR) <50 mL/min/1.73m^2;
14. Target lesions require preparation other than balloon pre-dilatation;
15. Patient is currently participating in an investigational drug or device study 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 become commercially available since then, are not considered investigational trials;
16. In the Investigator*s opinion patient has (a) co-morbid condition(s) that could limit the patient*s ability to participate in the study, compliance with follow-up requirements or impact the scientific integrity of the study;
17. Patient is under judicial protection (France only).

Study design

Design

Study phase: 3

Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-12-2013
Enrollment:	36
Type:	Anticipated

Medical products/devices used

Generic name:	coronary drug eluting stent
Registration:	No

Ethics review

Approved WMO Date:	19-12-2013
Application type:	First submission
Review commission:	TWOR: Toetsingscommissie Wetenschappelijk Onderzoek Rotterdam e.o. (Rotterdam)
Approved WMO Date:	07-05-2014
Application type:	Amendment
Review commission:	TWOR: Toetsingscommissie Wetenschappelijk Onderzoek Rotterdam e.o. (Rotterdam)
Approved WMO Date:	03-09-2014
Application type:	Amendment
Review commission:	TWOR: Toetsingscommissie Wetenschappelijk Onderzoek Rotterdam e.o. (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
ClinicalTrials.gov	NCT01844843
CCMO	NL44520.101.13