Randomized Comparison of Abluminus DES+ Sirolimus-Eluting Stents versus Everolimus-Eluting Stents in Coronary Artery Disease Patients with Diabetes Mellitus Global (ABILITY Diabetes Global)

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To compare in diabetic patients eligible for percutaneous coronary intervention (PCI) with minimal exclusion criteria, the efficacy and safety of Abluminus/Abluminus DES+ sirolimus-eluting stents (SES) versus XIENCE Everolimus-Eluting Stents (EES)....

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

Summary

ID

NL-OMON54418

Source
ToetsingOnline

Brief title
ABILITY Diabetes Global

Condition

- Coronary artery disorders
- Glucose metabolism disorders (incl diabetes mellitus)
- Autoimmune disorders

Synonym
coronary artery disease

Research involving

Human

Sponsors and support

Primary sponsor: Concept Medical Inc.
Source(s) of monetary or material Support: Industry: Concept Medical

Intervention

Keyword: Acute coronary syndrome, Diabetes Mellitus, Multivessel Coronary artery disease, PCI

Outcome measures

Primary outcome

- Primary:

o Ischemia-driven Target Lesion Revascularization (idTLR) at 1-year Follow-Up

(powered for non-inferiority and sequentially superiority).

o Target lesion failure (TLF - composite of cardiovascular death, target vessel

myocardial infarction [MI], or ischemia driven target lesion

revascularization) at 1-year FU, powered for non-inferiority

Secondary outcome

-- Secondary:

1) Safety composite endpoint of the occurrence of cardiovascular death and

target-vessel myocardial infarction (MI) at 1 year (non-inferiority).

2) In case the co-primary TLR endpoint (TLR for non-inferiority) will be

demonstrated at 1 year, then the occurrence of idTLR at 2-year FU will

be evaluated (efficacy endpoint - superiority).

3) In case the co-primary TLF endpoint (TLF for non-inferiority) will be demonstrated at 1 year, then the occurrence of the composite of cardiovascular death, target vessel MI and idTLR (TLF) at 1-year FU will be evaluated (safety endpoint - superiority).

4) Bleeding BARC 2 or greater

- Others:

* Composite of cardiovascular death, target vessel MI and idTLR (TLF) at 2 years.

* Occurrence of cardiovascular death and target-vessel myocardial infarction (MI) at 2 years.

* All-cause mortality up to 2 years from procedure.

* Stroke up to 2 years from procedure.

* Stent thrombosis (defined for grade and timing according to the Academic Research Consortium2).

* Technical success.

* Clinical procedural success.

* Occurrence of idTLR at 2-year FU.

* Target vessel revascularization (TVR) up to 2 years.

Study description

Background summary

Diabetes mellitus (DM) is a growing global public health problem. Some 415 million people worldwide or one in eleven adults are estimated to have DM. If the current trend in diabetes prevalence continues, by 2040 some 642 million people, or one adult in ten, will have diabetes.

Patients with DM are more affected by coronary artery disease and when treated by coronary angioplasty with stent implantation they remain at higher risk for in-stent restenosis and adverse cardiovascular events even in the drug-eluting stent (DES) era.

The presence of DM (particularly insulin-treated DM) has been a consistent, independent predictor of in-stent restenosis in most stent trials and registries. First-generation drug-eluting stents (DESs) reduced the need for repeat revascularization with a similar safety profile when compared with bare-metal stents.
Data from several direct randomized comparisons, registries, and meta-analyses of sirolimus-eluting stents (SES) and paclitaxel-eluting stents (PES) in diabetics have been reported. In all of these studies have been significantly underpowered to define whether there are true differences in clinical safety or efficacy between SES and PES in diabetic patients.
Furthermore, PCI, using the second-generation everolimus-eluting stent (EES), has been shown to result in better long-term outcomes than when first-generation DES are used in all-comer populations.
Although sirolimus and everolimus-eluting stents have been suggested to be less efficacious than PES in diabetic patients, the data have been conflicting.
The benefits of EES compared to PES in reducing clinical and angiographic restenosis were present in most subgroups in the SPIRIT trials (although underpowered for subgroup analysis). However, among 337 patients with diabetes randomized in SPIRIT II and SPIRIT III trials, EES compared to PES resulted in non-significant differences in the 1-year proportions of TLR (despite a significant reduction in late loss), whereas both late loss and TLR were markedly reduced with EES in 886 patients without diabetes. Similarly, in the SPIRIT IV randomized trial, EES compared with PES provided similar clinical outcomes in diabetic patients with no difference in terms of TLF between the two groups.

In this study, the included patients will present diabetes mellitus and are scheduled to undergo a coronary angioplasty for one or more narrowing(s) in the coronary arteries. Once included, the patients will receive either Abluminus/Abluminus DES+ sirolimus-eluting stents (SES) or Everolimus-Eluting Stents (EES) and will be followed for two years.
The purpose of the study is to compare in diabetic patients the efficacy and

safety of these two drug-eluting stents used for coronary artery narrowing treatment.

Study objective

To compare in diabetic patients eligible for percutaneous coronary intervention (PCI) with minimal exclusion criteria, the efficacy and safety of Abluminus/Abluminus DES+ sirolimus-eluting stents (SES) versus XIENCE Everolimus-Eluting Stents (EES). At least 40% of patients are expected to be affected by multivessel coronary artery disease and 30% with the acute coronary syndrome.

Study design

Prospective, multicenter, multinational, randomized, open label, 2-arm parallel groups

Intervention

The included patients will undergo a Percutaneous coronary intervention (PCI) with either Abluminus/Abluminus DES+ sirolimus-eluting stents (SES) or Everolimus-Eluting Stents (EES).

Study burden and risks

Implantation of one of the study devices as it has been specially designed for diabetic patients may result in improved cardiovascular function and improved further quality of life in patients (Lower chance of restenosis in the long term, lower chance of hospitalisation due to cardiac disease in the long term, lower chance of chest pain). These benefits can however not been guaranteed.

Generally, all patients will receive a higher degree of telephone and clinical follow-up than he/she would outside of the
study environment and have a dedicated clinical study team following his/her progress.

It is hoped that through this study, information gained on the safety and efficacy of the devices used will help in the
management of future patients with similar conditions

Potential adverse events which may be associated with the implantation of a coronary stent in a native coronary artery include those risks associated with percutaneous transluminal coronary angioplasty as well as additional risks related to the use of the stent.

As with any treatment of narrowing of one or more coronary artery lesions, the

major complications are:
•Death: less than 1%
•Stroke: 0.5%
•Heart Attack: 2-5%
•Bleeding (major and minor): 2-5%
•The risk of a blockage of the stent(s), called stent thrombosis and the potential risk of heart attack or death due to
this blockage is less than 5% within 1 year after implantation.
The doctors performing angioplasties use X-rays to direct the stent to the correct position. No additional radiation will
be used in the study and patients' exposure to the radiation will be part of the normal care and should carry no extra
risks. High doses of x-ray have the potential to cause skin damage, however, we do not anticipate this angioplasty
will exceed the accepted threshold.

Contacts

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US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age

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

Inclusion criteria

Inclusion criteria: Clinical Inclusion Criteria 1. Patient understands the trial requirements and the treatment procedures and provides written informed consent; 2. Age >= 18 years (>= 19 years of age for South Korea and >= 21 years of age for Singapore); 3. Diabetic patients: either: a. Patient with a previous documented diagnosis of diabetes mellitus (Type 1 or Type 2) and currently undergoing pharmacological treatment (oral hypoglycemic agents or insulin) b. Newly diagnosed diabetes: either: i. Fasting plasma glucose (FPG) >=126 mg/dL (7.0 mmol/L). Fasting is defined as no caloric intake for >=8 hours or ii. Two-hour plasma glucose >=200 mg/dL (11.1 mmol/L) following a 75g oral glucose tolerance test or iii. HbA1c level >= 7% (53 mmol/mol) Patients who are newly diagnosed are included even if they are not on pharmacological treatment (oral hypoglycemic agents or insulin) 4. Symptomatic coronary artery disease including chronic stable angina, silent ischemia, and non-ST-segment elevation acute coronary syndrome (NSTE-ACS) 5. Patient is eligible for percutaneous coronary intervention (PCI); Previous PCI (with balloon angioplasty or stenting) is allowed if performed >12 months before index procedure; 6. Patient is willing and able to comply with all protocol-required follow-up evaluations. Angiographic Inclusion Criteria (visual estimate) 7.Presence of >=1 de novo coronary artery stenosis >50% in a native coronary artery which can be treated with a stent ranging in diameter from 2.25 to 4.0 mm and can be covered with 1 or multiple stents; and 8. No limitation to the number of treated lesions, number of vessels, or lesion length if the patient is judged eligible for PCI by the treating physician according to the local standard of care.

Exclusion criteria

Exclusion criteria: Clinical Exclusion Criteria: 1. Patient lacking capacity (i.e. patient suffering from dementia and others) to provide informed consent 2. Patients in cardiogenic shock as defined in appendix A; 3. Patient has known allergy to the study stent system or protocol-required concomitant medications (e.g. aspirin, clopidogrel, prasugrel, ticagrelor, heparin, stainless steel, cobalt, chromium, sirolimus, everolimus, radiographic contrast material) that cannot be adequately pre-medicated; 4. Planned surgery (cardiac and non-cardiac) within 6 months after the index procedure unless the dual-antiplatelet therapy (DAPT) can be maintained throughout the peri-surgical period; 5.Patients undergoing primary percutaneous coronary intervention for ST-segment elevation myocardial infarction (STEMI) 6. Patient is pregnant, nursing, or is a woman of child-bearing potential who is not surgically sterile, < 2 years postmenopausal, or does not consistently use effective

methods of contraception; 7. Patient has any other serious medical illness (e.g., cancer, end-stage congestive heart failure) that may reduce life expectancy to less than 12 months; 8. Acute or chronic renal dysfunction (serum creatinine >3.0 mg/dl); 9. Currently participating in another investigational drug or device study. Angiographic Exclusion Criteria: 10. In-stent restenotic lesions; 11. Lesions involving venous or arterial bypass grafts.

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:	Recruiting
Start date (anticipated):	14-01-2021
Enrollment:	451
Type:	Actual

Medical products/devices used

Generic name:	Abluminus/Abluminus DES+ Sirolimus-Eluting Stent System
Registration:	Yes - CE intended use

Ethics review

Approved WMO

Date:	23-10-2020
Application type:	First submission

Review commission:	METC Amsterdam UMC
Approved WMO Date:	03-11-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-12-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-12-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-01-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	31-03-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-03-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-08-2023
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389

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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	NCT04236609
CCMO	NL72858.018.20