The DESyne BDS Plus RCT: A Randomized Clinical Trial to Assess the Elixir DESyne BDS Plus Drug Eluting Coronary Stent System for the Treatment of de novo Native Coronary Artery Lesions

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To evaluate the safety, effectiveness and performance of the DESyne BDS Plus DECSS (Test) as compared to the CE Mark approved DESyne X2 Novolimus Eluting Coronary Stent System (DESyne X2 NECSS; DESyne X2) (Control) in the treatment of de novo native...

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

Summary

ID

NL-OMON55926

Source
ToetsingOnline

Brief title
DESyne BDS Plus RCT

Condition

- Coronary artery disorders

Synonym
coronary artery disease, narrowing of the coronary artery

Research involving
Human

Sponsors and support

Primary sponsor: Elixir Medical Corporation
Source(s) of monetary or material Support: Elixir Medical Corporation

Intervention

Keyword: Drug Eluting Stent, Percutaneous Coronary Intervention

Outcome measures

Primary outcome

Primary Endpoint

The primary endpoint is target lesion failure (TLF) at 3 days or through hospital discharge, whichever comes first. Target lesion failure (TLF) is defined as a per-subject hierarchical count of cardiovascular death, target vessel MI, and clinically-indicated target lesion revascularization.

Secondary outcome

Primary Endpoint

The primary endpoint is target lesion failure (TLF) at 3 days or through hospital discharge, whichever comes first. Target lesion failure (TLF) is defined as a per-subject hierarchical count of cardiovascular death, target vessel MI, and clinically-indicated target lesion revascularization.

Acute Success Endpoints

o Device Success: Successful delivery of the designated device and a final residual stenosis < 30% by QCA

o Procedure Success: Successful delivery of the designated device and a final residual stenosis < 30% by QCA without TLF through hospital discharge.

Note: The final assessment of the residual stenosis is performed by the independent QCA core laboratory in this study for this endpoint calculation. The visual estimate performed by the physician is not used in the calculation. The visual assessment by the physician as a final result is recommended in the protocol to be <10% and no greater than 15%.

Additional clinical endpoints will be assessed at each follow-up point: 3 days or hospital discharge (whichever comes first), 1, 6, 12, 24 and 36 months and include:

• Target Lesion Failure (TLF) is a per-subject hierarchical count of cardiovascular death, target vessel MI, and clinically-indicated target lesion revascularization (per ARC-2)

• Death (per ARC-2)

o Cardiovascular and Non-cardiovascular

• MI (per ARC-2)

o Q-wave and non-Q-wave

o Target vessel and non-target vessel

• Target Lesion Revascularization (TLR) (per ARC-2)

o Clinically indicated and non-clinically indicated

• Target Vessel Revascularization (TVR) (per ARC-2)

o Clinically indicated and non-clinically indicated

• Target Vessel Failure (TVF) is a per-subject hierarchical count of cardiovascular death, target vessel MI, and clinically-indicated target vessel revascularization (per ARC-2)

• Device Thrombosis (ARC-2 definite and probable)

A The powered secondary endpoint of Late Lumen Loss (LLL) by QCA at 6 months will be evaluated in the Imaging Subset to test for non-inferiority of DESyne BDS Plus to DESyne X2.

Angiographic imaging will be undertaken to assess the vessel, lesion, and stent pre-procedure, during the procedure (peri-procedure), and post-procedure for all patients, and again at 6-month follow-up in the subset of approximately 60 patients (30 in each arm), in the selected imaging centers for the following parameters:

• Acute recoil

• MLD

• % DS

Additional parameters may be assessed

OCT imaging assessment of the lesion and stent will be undertaken both at post-procedure and again at 6-month follow-up in approximately 60 patients (30 in each arm) included in the 6-month angiography subset in the selected imaging centers for the following parameters

• Assessment of lumen, and device diameters, areas and volumes

• Strut coverage

• Assessment of thrombus

• Descriptive analysis lesion and stent morphology

Additional parameters may be assessed.

Study description

Background summary

The primary method used today to treat coronary artery stenosis is the use of coronary stents coated with anti-proliferative drugs which allow localized delivery of the drug to the specific lesion site. Studies evaluating drug eluting stent systems loaded with anti-proliferative agents such as sirolimus, have shown success of these devices in reducing the amount of neointimal hyperplasia following stent implantation and reducing the need of repeat revascularization procedures in patients.
The DESyne BDS Plus Drug Eluting Coronary Stent System (DESyne BDS Plus DECSS) represents a modification of the DESyne BD Novolimus Eluting Coronary Stent System, and the DynamX Sirolimus Eluting Coronary Bioadaptor System, which have been evaluated in clinical studies as well as the DESyne BDS Sirolimus Eluting Coronary Stent System. All are CE-Mark approved. Similar to the above listed products, the DESyne BDS Plus is fabricated from the same CoCr alloy material. The stent has a bioresorbable polymer drug coating, containing the same Sirolimus drug and polymer coating as used on the DESyne BDS System, and the DynamX Sirolimus System. In addition to sirolimus, the DESyne BDS Plus also has the factor Xa inhibitor Rivaroxaban and the direct thrombin inhibitor Argatroban in the coating matrix. These drugs are intended to potentially reduce the surface area thrombus during and/or following percutaneous coronary intervention (PCI).

Study objective

To evaluate the safety, effectiveness and performance of the DESyne BDS Plus DECSS (Test) as compared to the CE Mark approved DESyne X2 Novolimus Eluting Coronary Stent System (DESyne X2 NECSS; DESyne X2) (Control) in the treatment of de novo native coronary artery lesions.

Study design

The DESyne BDS Plus Randomized Clinical Study is a prospective, multi-center, single blind, randomized clinical study. Randomization (1:1; DESyne BDS Plus : DESyne X2) of up to 200 patients (100 in each arm) requiring treatment of up to two de novo coronary artery lesions <= 34 mm in length in vessels >= 2.25 mm and <= 3.5 mm in diameter will be conducted. The study will be conducted in two parts, with randomization of the first 100 subjects (Cohort 1) followed by the randomization of an additional 100 subjects (Cohort 2).
Up to two target lesions, located in separate epicardial vessels (RCA, LCX or LAD), which meet the inclusion/exclusion criteria, may be treated with the assigned study device. Alternatively, one target lesion may be treated with the assigned study device after successful, uncomplicated treatment with any

commercially-available DES of a non-target lesion, located in a separate epicardial vessel. Acceptable example: RCA non-target lesion and LAD target lesion. Not Acceptable example: LAD non-target lesion and 1st diagonal target lesion.
All patients will undergo pre, peri and post-procedure angiography.
In an imaging subset of approximately 60 subjects (30 per arm), Angiography and OCT will be performed at index procedure, and again at 6 month follow-up.
The PK sub-study will enroll up to 10 non-randomized subjects treated only with the DESyne BDS Plus device, with a maximum of 3 DESyne BDS stents implanted. The PK sub-study is being conducted to assess the blood pharmacokinetics of the three drugs (Sirolimus, Rivaroxaban, Argatroban) eluted from the DESyne BDS Plus after implantation. PK measurements will be conducted by obtaining plasma blood samples at pre-treatment, and post-treatment at 10 minutes, 30 minutes, 1, 2, 4, 6, 12, 24, 72 hours, and 7 days. In addition, all PK subjects will undergo clinical assessments/follow-up at 3 days or hospital discharge (whichever comes first), 1, 6, 12, 24 and 36 months. The PK sub-study subjects are not considered part of the primary analysis population.

Intervention

Percutaneous coronary intervention with stent implantation

Study burden and risks

Potential Risks
The use of stenting for the treatment of narrowing of the coronary arteries has been shown to be an effective treatment with acceptable risks. These risks are not specific to either the DESyne BDS Plus Stent or the control DESyne X2 Stent and are similar to risks associated with any stent implantation procedure. There is extensive clinical experience with coronary catheterization procedures (procedure to examine the coronary artery with thin tube), balloon angioplasty, and stenting. However, even with the successful implantation of the stent, there is a still a chance of the treated area re-narrowing. A new-narrowing of the coronary artery may cause the return of your chest pain. If a new narrowing occurs, it may require further treatment, including bypass surgery (During a bypass operation, a bypass using a vein or artery is created, which serves as a bridge for a closed blood vessel) , additional angioplasty or stent placement. The risks associated with angiography have been explained to you by your doctor.

The drug used on the stent is in such a low dose there is little potential to cause side effects. However, if you experience any signs of an allergic reaction such as rash, itching or swelling, inform your physician immediately. Always advise your doctor of any medication you are taking so they may assess potential drug interactions. Eating/drinking grapefruit may potentially interfere with Sirolimus or Novolimus.

Previous stent studies have shown a 1 to 2 % chance of a blood clot forming within the stent. As with any balloon or stent procedure, if clotting of the stent does occur, it may lead to repeat catheterization, angioplasty, myocardial infarction (heart attack), urgent bypass surgery, or death. Any additional risks associated with the stent such as insufficient vessel support or malaposition (the stent is not against the vessel wall) have been carefully examined and are similar to that of any commercially available drug eluting stent.

Other risks are bleeding into the stomach, bleeding at the puncture site used for your procedure (thigh or arm), stroke and reduced white blood cell count.

Finally, this treatment may involve some additional risks to you, the nature of which is unknown or may involve unforeseeable risks to you or your embryo or fetus if you become pregnant.

Potential Benefits
The use of stents, including the control stent, has been shown to reduce the incidence of new narrowing in the artery. The additional potential benefit of the DESyne BDS Plus Stent is that the drugs applied to the stent may potentially reduce blood clots on the surface of the stent for a period after implantation. Also, the information obtained from this study may provide future potential benefits to others

Cons/burdens of study participation:

There may be some discomfort from the procedures during the study. For example: taking a blood sample can be a little painful and bruising may result.

Taking part in the study will cost the patient extra time especially if included in the imaging substudy. The subject will need to come to the hospital for imaging follow-up, if included in the sub-study which will require extra time and travel expense, an additional angiographic examination including extra contrast media for the angiogram and OCT as well as extra radiation, and the potential for bruising at the access site (femoral or radial).

Contacts

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Scientific
Selecteer

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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 must be at least 18 years of age
2. Patient is able to understand the risks, benefits and treatment alternatives of receiving the DESyne BDS Plus DECSS or the DESyne X2 NECSS and provide written informed consent or oral consent (in urgent PCI) as allowed per hospital standard and as approved by the local Ethics Committee, prior to any clinical study-related procedure
3. Indication for a percutaneous intervention with stent implantation in native epicardial arteries including patients with stable coronary artery disease and acute coronary syndromes including NSTEMI and STEMI.
• If patient is presenting with STEMI, enrollment should take place only if sufficient research staff is available and the center is trained to perform PCI in an acute setting
4. Patient must be an acceptable candidate for coronary artery bypass graft (CABG) surgery
5. Patient agrees to undergo all clinical study required follow up visits, angiograms, and imaging testing (as applicable)
6. Patient agrees not to participate in any other clinical research study for a period of one year following the index procedure (long term follow-up or observational studies are permitted)

Angiographic Inclusion Criteria
7. Target lesion(s) must be de novo coronary artery lesion(s) and must be located in a separate* vessel from other target or non-target lesions.
• If a non-target lesion is present, it must have been treated successfully and without complication** prior to proceeding with treatment of the target lesion
8. Target lesion(s) must have a reference vessel diameter (RVD) of >= 2.25 and <= 3.5 mm by visual estimation
9. Target lesion(s) must measure <= 34 mm in length, and able to be covered by a single device with 2 mm of healthy vessel on either side of planned implantation site
10. Target lesion(s) must be in a major artery or branch with a visually estimated stenosis of >= 50% and <100%. When two target lesions are treated, they must be located in separate major epicardial vessels
*The definition of epicardial vessels is the LAD, LCx and RCA, and is inclusive of their branches. For example, the patient must not have lesions requiring treatment in both the LAD and a diagonal branch.
**Assessment of successful treatment of the non-target lesion will be per physician*s decision, however, acute complications and/or adverse events associated with the non-target lesion should be considered unsuccessful. Examples of unsuccessful treatment include but are not limited to: inability to deploy stent, major dissection requiring multiple stent placement, stent embolization, ST, prolonged chest pain, persistent ECG changes, etc.
Additional Inclusion Criteria for PK study:
11. Patients participating in PK study may be treated with only the DESyne BDS Plus during Index Procedure.

Exclusion criteria

1. Acute myocardial infarction with Killip Class III and IV
2. Acute myocardial infarction requiring resuscitation
3. Acute myocardial infarction requiring IABP or ventilation support
4. Patient had fibrinolysis prior to PCI
5. Patient has current unstable ventricular arrhythmias
6. Patient has a known left ventricular ejection fraction (LVEF) < 30%
7. Patient has received a heart transplant or any other organ transplant or is on a waiting list for an organ transplant
8. Patient is receiving or scheduled to receive chemotherapy for malignancy within 30 days prior to or after the procedure
9. Patient is receiving immunosuppression therapy, other than steroids or has known immunosuppressive or autoimmune disease (e.g., human immunodeficiency virus, systemic lupus erythematosus, etc.)
10. Patient has a known hypersensitivity or contraindication to aspirin, both heparin and bivalirudin, clopidogrel, prasugrel or ticagrelor, Novolimus, Sirolimus, Rivaroxaban, Argatroban, CoCr alloys, PLLA polymers or contrast sensitivity that cannot be adequately pre-medicated

11. Elective surgery is planned within the first 6 months after the procedure that will require discontinuing either aspirin or clopidogrel or other P2Y12 inhibitors
12. Patient has severe renal dysfunction (CKD IV or V, eGFR <30) or is on dialysis
13. Patient has had a cerebrovascular accident (CVA) or transient ischemic neurological attack (TIA) within the past six months
14. Patient has had a significant GI or urinary bleed within the past six months
15. Women of childbearing potential (unless they have a negative pregnancy test within 7 days of index procedure), or women who are pregnant or nursing
16. Patient has other medical conditions or known history of substance abuse (alcohol, cocaine, heroin, etc.) that may cause non-compliance with the clinical study plan, confound the data interpretation, or be associated with a limited life expectancy (i.e., less than one year)
17. Patient is already participating in another clinical study which has not reached the primary endpoint (long-term follow-up or observational studies are permitted)

Angiographic Exclusion Criteria
18. Patient with vessel rupture and/or visible pericardial effusion
19. Target lesion aorto-ostial location or within 5mm of the origin of the vessel (LAD, LCX, RCA)
20. Target lesion is severely calcified and/or requires use of rotational atherectomy or cutting balloon, the use of scoring is allowed
21. Target Lesion located in the Left Main artery
22. Target Lesion located within an arterial or saphenous vein graft or distal to a diseased arterial or saphenous vein graft
23. Target Lesion involves a bifurcation >2.5 mm, or which requires a planned 2 or more stent technique
24. Previous placement of a stent within 10 mm of a target lesion
25. Another clinically-significant lesion (> 50%) is located in the same major epicardial vessel as a target lesion
26. Target vessel was previously treated with any type of PCI < 6 months prior to index procedure
27. Unsuccessful or complicated PCI in a non-target vessel < 48 hours prior to index procedure
28. Target vessel has a planned staged PCI <= 6 months after the index procedure
Additional Exclusion Criteria for PK study:
29. Target vessel was previously treated with any type of PCI < 6 months prior to index procedure
30. Patient with planned staged PCI within 90 days after study procedure
31. Patients who have a non-target lesion treated during the study procedure

Study design

Design

Study phase:	3
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):	13-09-2022
Enrollment:	30
Type:	Actual

Medical products/devices used

Generic name:	DESyne X2 Novolimus Eluting Coronary Stent System
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	03-06-2022
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO Date:	27-07-2022
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO Date:	31-10-2023
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	NCT05033964
CCMO	NL80228.000.22