TARGET FIRST
Evaluation of a modified Anti-Platelet Therapy associated with low-dose rapamycin DES Firehawk in Acute Myocardial Infarction Patients treated with complete revascularization strategy

Published: 13-04-2021
Last updated: 30-01-2025

This study has been transitioned to CTIS with ID 2024-519854-35-00 check the CTIS register for the current data. The study aims to evaluate a modified Anti-Platelet Therapy, when associated with low-dose rapamycin DES Firehawk in Acute Myocardial...

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

Summary

ID

NL-OMON54279

Source
ToetsingOnline

Brief title
Target First

Condition

- Coronary artery disorders

Synonym
Myocardial infarction

Research involving

Human

Sponsors and support

Primary sponsor: Sorin Biomedica CRM SRL
Source(s) of monetary or material Support: Sorin CRM SAS (Microport CRM)

Intervention

Keyword: Drug eluting stent, Duale antiplatelet therapy, Myocardial Infarction

Outcome measures

Primary outcome

Net Adverse Clinical and Cerebral Events (NACCE) defined as a composite of all cause death, non-fatal myocardial infarction, definite/probable stent thrombosis, stroke, or Bleeding Academic Research Consortium (BARC) type 3 or 5 bleeding at 11 months post randomization (12 months post index procedure).

Secondary outcome

BARC type 2, 3 or 5 bleeding events at 11 months post randomization (powered)

Other secondary endpoints (exploratory) are clinical endpoints at 1 month, 6 months and 12 months:

• All-cause death, non-fatal myocardial infarction, definite/probable stent thrombosis, or stroke

• BARC 3 and 5 bleeding events

• All-cause death or non-fatal myocardial infarction

• Patient-oriented composite of major adverse cardiac and cerebral events (MACCE) including all-cause death, myocardial infarction, definite/probable stent thrombosis, any stroke, any Ischemia driven repeat revascularization,, or

BARC bleeding events (type 2, 3, or 5)

• Device oriented composite endpoint of Target Lesion Failure (cardiac death, target vessel related myocardial infarction, target lesion Ischemia Driven-revascularization)

• MACE (cardiovascular death, myocardial infarction, Ischemia Driven-revascularization)

• Definite or probable stent thrombosis

• BARC 3 events

• BARC 5 events

• BARC 2 events

• Cardiovascular death

• Cardiac death

• Non cardiac death

• Myocardial infarction

• Cardiac death or non-fatal myocardial infarction

• Cardiac death, myocardial infarction, or definite/probable stent thrombosis

• Cardiovascular death, myocardial infarction, definite/probable stent thrombosis, or ischemic stroke

• Ischemic stroke

• Haemorrhagic stroke

• Ischemia-driven target lesion revascularization

• Ischemia-driven target vessel revascularization

• Cardiovascular death, myocardial infarction, or ischemic stroke

and each of the components of the primary and main secondary endpoints

Study description

Background summary

Patients with acute myocardial infarction have increased individual thrombotic risk due to several interplaying factors which led to prolonged DAPT treatment, preferably with a potent P2Y12 inhibitor. However, benefits in terms of major revascularization-related ischemic endpoints are often offset and even exceeded by increased bleeding events associated with prolonged DAPT regimens. While minor bleeding events have limited prognostic impact, major bleeding has been associated with lower survival and worse outcomes.

Advances in DES technology have improved outcomes after treatment of more complex coronary artery disease patterns, including unstable plaques. Evidence on safety of new-generation DESs in anatomic substrates with increased thrombogenicity is growing and thin-strut bioresorbable-polymer DESs have shown high safety profile. The Firehawk stent has proved to be effective and safe in the treatment of coronary artery disease in various studies. The specific feature of the Firehawk stent is to present recessed abluminal grooves facing the vessel wall and containing low-dose sirolimus bound with a bioresorbable polymer. It has been designed to reduce inflammation and hypersensitivity reactions in the coronary vessel wall, and to produce optimal anti-restenotic effects and fast vessel healing. Clinical evidence has supported the safety, efficacy and high biocompatibility profile of the Firehawk stent. Based on this, the Firehawk stent may result in shorter DAPT requirements after stenting, regardless of the underlying disease.

Evidence builds up on benefits of short DAPT followed by monotherapy with P2Y12i in ACS patients: the risk of major bleeding is reduced compared with DAPT, while the risk of MACE appears not to increase.
In patients undergoing PCI, residual coronary artery disease left untreated has been associated with significant increases in the long-term risk of death and major cardiovascular events, while complete revascularization has been associated with very low risk of repeat intervention. Complete, staged revascularization, when feasible and associated with reasonable risks, is recommended per current guidelines in the setting of (N)STEMI.

Based on these points, a modern revascularization approach in the setting of acute myocardial infarction, including complete revascularization with newer-generation highly biocompatible DES, may not require prolonged DAPT.

The TARGET FIRST Study will therefore investigate a modern approach of PCI for

patients presenting with (N)STEMI by treating them with a combination of
1) a coronary stent designed for high biocompatibility
2) a complete revascularization approach at an early timing, optimizing revascularization of the heart (no significant lesions untreated), and
3) an adapted antiplatelet therapy post stenting. The adapted antiplatelet treatment aims to cover the risk of stent related thrombotic events and systemic thrombosis while reducing ASA relating bleeding.

Study objective

This study has been transitioned to CTIS with ID 2024-519854-35-00 check the CTIS register for the current data.

The study aims to evaluate a modified Anti-Platelet Therapy, when associated with low-dose rapamycin DES Firehawk in Acute Myocardial Infarction Patients treated with complete revascularization strategy.. The modified antiplatelet therapy consists of a reduced duration of DAPT (1 month duration) followed by P2Y12 inhibitor monotherapy up to 12 months. We hypothesized that, in the setting of clinically stable, low to moderate complexity acute Myocardial Infarction patients, this modern approach combining a modified antiplatelet therapy associated with a stent with high biocompatibility feature, and complete revascularization strategy and modified antiplatelet therapy may be associated with similar outcomes, or even a significant net benefit compared with guidelines-recommended 12-month DAPT.

Study design

Prospective, international, multicentre, open-label, randomized clinical trial (post-market study). Patients will be randomized in a 1:1 ratio, leading to:
• Experimental group: AMI patients who have received single-intervention or early staged (7 days after index procedure) complete revascularization with Firehawk DES and who will receive 1 month of DAPT followed by monotherapy with a potent P2Y12 inhibitor
• Control group: AMI patients who have received single-intervention or early staged (7 days after index procedure) complete revascularization with Firehawk DES and who will receive 12 months DAPT (ASA + potent P2Y12 inhibitor)

Intervention

Subjects will be randomized (1:1) to the experimental group or the control group at the planned Month 1 visit to the hospital. Assigned treatment will start at the timepoint of randomization.

Study burden and risks

(Non)-STEMI Patients will be enrolled after successful (complete)

revascularization and before hospital discharge.

Eligible patients will be randomized (1:1) at the planned M1 (in-office) visit post enrolment to one of the following arms:
- Intervention: Potent P2Y12 inhibitor monotherapy for the following 11 months. Subjects in this group are thus treated by a complete revascularization strategy, within 7 days post index procedure and with Firehawk, followed by 1 month DAPT and 11 month monotherapy with a P2Y12i.
- Control: Dual Antiplatelet Therapy (ASA + potent P2Y12 inhibitor) for the following 11 months. Subjects in this group are thus treated by a complete revascularization strategy, within 7 days post index procedure and with Firehawk, followed by 12 months DAPT.

The P2Y12 inhibitor agent (ticagrelor, prasugrel) used for the DAPT (Aspirin + P2Y12 inhibitor) is selected by the Investigator, at the enrolment visit, based on patient*s characteristics and according to local practice and to current recommendations of the ESC guidelines. Daily doses as well as daily treatment scheme will be according to standard recommendations and European Clinical Practice Guidelines.

Subjects who are not eligible for randomization (for ex. significant ischemic or bleeding event, significant side effect, new need for OAC) will not be randomized and their study participation will be terminated.

Follow up visits are planned at 1 month, 6 months and 12 months of which the 6 month visit will be by phone.

Patients are informed that data are collected at the index PCI and at scheduled follow-ups as well as at unscheduled visits.

The investigator monitors the occurrence of Serious Adverse Events (SAEs) for each subject during the course of the study. For the purpose of this protocol, the reporting of SAEs begins directly after inclusion in the study.

The burden for the patient are the scheduled follow-up visits at 1-6-12 months post index PCI.

The potential risks and discomforts related either to the studied device or to the participation in the study, are similar to those seen with other devices commercially approved, and to those of current routine practice for the patients assigned to the control group. For the patients assigned to the treatment arm (short DAPT + cessation of aspirin), there is a potential increased risk for thrombotic/ischemic events

Complete revascularization approach and adaptation of the post PCI antiplatelet therapy based on patient profile have been investigated in multiple studies, including prescription of short DAPT (1 to 3 months) followed by P2Y12

inhibitor monotherapy to provide sustained platelet inhibition (see section 2.1). These aspects showed to be beneficial in selected patients, and are implemented in the ESC guidelines. This modern revascularization approach in the setting of acute myocardial infarction, including complete revascularization with newer-generation highly biocompatible DES, may not require prolonged post-PCI DAPT.

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

Subjects must meet all of the following criteria to be eligible for enrolment: Clinical • Subject is >= 18 years old • Subject has been hospitalised for troponin-positive Non-ST-Elevation MI, requiring early invasive treatment (PCI), or ST-Elevation MI requiring primary PCI, and this PCI occurred within the last 7 days • Subject is eligible for per-protocol antiplatelet treatments •

Subject understands and agrees with the trial requirements and procedures, and provides written informed consent before any trial-specific tests or procedures are performed • Subject is willing to comply with all protocol requirements including antiplatelet treatment strategies and follow-up visits Procedural/angiographic (related to the treatment of the (N)STEMI • Successful revascularization: - Successful delivery and deployment of the Firehawk stent(s), with final residual stenosis of <30% (visually) for all target lesions - No occurrence of significant event (such as MI, unplanned revascularisation, stent thrombosis, stroke, major vascular complication/bleeding). • All the treated lesions: - In native coronary arteries only, - In vessels with visual reference diameter >=2.25 mm and <= 4.00 mm - Implanted with the medical device - Maximum 3 lesions treated (*) - Maximum total stent length <= 80 mm. • Complete revascularization (**) performed when more than 1 significant lesion, during the index procedure or in staged procedure(s) occurring within 7 days from the index procedure. Physiologic assessment highly recommended for lesions with stenosis between 50% and 69%.

Exclusion criteria

Patients fulfilling any of the following criteria are not eligible: • Subjects with prior STEMI or prior PCI within 12 months before index admission • Prior Coronary Artery Bypass Graft (CABG) Surgery • Cardiogenic shock • Secondary PCI • Fibrinolysis • Prior stent thrombosis • Planned PCI, CABG, or surgery within 12 months after the enrolment • Need for Oral Anti-Coagulation medications (or NOAC) • Ischemic stroke or intracerebral hemorrhage (spontaneous or traumatic) within 12 months prior to index procedure • eGFR <30 mL/min/1.73 m2 or dialysis • Active bleeding at time of inclusion or high risk for major bleeding • History of bleeding diathesis or coagulopathy or subject refuse blood transfusions • Stage B or C liver cirrhosis or active cancer within 12 months prior to index procedure (or currently receiving chemotherapy or planned to receive chemotherapy) • Baseline haemoglobin <13 g/dL (12g/dL for women) or anaemia requiring transfusion in the 4 weeks prior to index procedure • Moderate or severe thrombocytopenia (<100,000/L) • Expected non-adherence to study protocol (such as current problems with substance abuse, severe impairment of cognitive skills, *) • Estimated life expectancy <=12 months • Known hypersensitivity or contraindication to any medication used in the study or any of the study stent*s components/compounds (e.g., cobalt chromium alloy, sirolimus, or structurally related compounds, polymer or individual components, P2Y12 inhibitors, or aspirin). • Subject participates in another interventional (device or drug) clinical trial within 12 months after the index procedure • Subject is a woman who is pregnant, nursing or with known intention to procreate within 12 months after the index procedure (woman of child-bearing potential who is sexually active must agree to use a reliable method of contraception from the time of screening through 12 months after the index procedure)). Investigator may require a pregnancy test to be performed within 7 days prior to the enrolment in women of child-bearing potential) Angiographic: • Any of : - In-stent restenosis or thrombosis - Chronic total occlusion - Severe calcification - True bifurcation disease (Medina class x,x,1) and side branch diameter >= 2mm (visual reference visual diameter) or bifurcation treated with 2 stents - Left main coronary artery lesion - Residual untreated dissection >= C - Implantation of a non-study stent • Extent and severity of disease is such that patient is deemed to receive

preferentially CABG within 1 year (based on current ESC guidelines)

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):	18-05-2021
Enrollment:	240
Type:	Actual

Medical products/devices used

Generic name:	FIREHAWKTM & FIREHAWK LIBERTYTM stent
Registration:	Yes - CE intended use
Product type:	Medicine
Brand name:	ACETYLSALICYLIC ACID
Generic name:	ASPIRIN
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Prasugrel
Generic name:	Effient
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Ticagrelor
Generic name:	Brilique

Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	13-04-2021
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	22-04-2021
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	26-01-2022
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	27-01-2022
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	17-02-2023
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	20-02-2023
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	15-06-2023
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
EU-CTR	CTIS2024-519854-35-00
EudraCT	EUCTR2020-005933-34-NL
CCMO	NL76265.100.21