Distal Evaluation of Functional Performance With Intravascular Sensors to Assess the Narrowing Effect: Guided Physiologic Stenting;Substudy: Characterization of Intermediate Lesions

Published: 26-04-2021
Last updated: 19-09-2024

• Demonstrate that PCI guided by iFR Co-registration is associated with superior clinical outcomes compared to PCI guided by angiography alone• To evaluate the cost-effectiveness of physiology guidance with SyncVision compared to a standard of care...

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

Summary

ID

NL-OMON54360

Source
ToetsingOnline

Brief title
DEFINE GPS;Substudy: ChIL

Condition

- Coronary artery disorders

Synonym
Coronary artery disease

Research involving
Human

Sponsors and support

Primary sponsor: Philips
Source(s) of monetary or material Support: Bedrijf

Intervention

Keyword: Guided Physiologic stenting, iFR Co-Registration, Philips SyncVision

Outcome measures

Primary outcome

Primary endpoint: Major Adverse Cardiac Events (MACE; composite of cardiac death, MI, or ischemia-driven revascularization) or hospitalization for progressive or unstable angina at 2 years

Not applicable for ChIL substudy - explanation as provided in the response letter to RTPO:
There is no endpoint. The objective of the amendment is to only collect the angiograms and invasive physiology measures that are part of a typical diagnostic assessment for equivocal coronary artery lesions that are not causing myocardial ischemia and hence do not get revascularized.
These data enable the development and validation of noninvasive tools that can estimate the hemodynamic significance associated with a range of coronary lesions.
The DEFINE GPS study is focused on comparing patient outcomes in those patients that demonstrate the need for myocardial revascularization. The angiograms and invasive physiology measures are being collected in these patients; however,

the prevalence of coronary artery disease that is indicated for

revascularization is only 30-35%; the need exists to collect data representing

the other 65-70% of the population that do not qualify for study inclusion.

Secondary outcome

Secondary endpoints (at 30 days, 1 year and 2 years if not noted otherwise):

• The primary endpoint at 30 days and 1 year

• All-cause, cardiac and non-cardiac mortality

• All MI, target vessel MI, non-target vessel MI, procedural MI, non-procedural

MI

• Ischemia-driven revascularization, including all revascularization, TVR, TLR,

non-TLR TVR, and non-TVR

• Hospitalization for progressive or unstable angina

• Stent thrombosis (definite, probable and definite/probable)

• Angina-related Quality of Life

• Healthcare resource utilization

• Cost effectiveness

Not applicable for ChIL substudy.

Study description

Background summary

Philips has developed a method to map the pressure profile of the locations and severity of blockages in diseased blood vessels. This map is created on top of

a picture created by the x-ray. Patients will either get the normal *Angiogram Alone* taken to guide their treatment, or they will get the *Angiogram with Pressure Map.*
This study is being performed to determine if the treatment that uses the Angiogram with Pressure Map results in greater relief of chest pain symptoms and reduced heart complications for two years after treatment.

Background of the ChIL substudy:
DEFINE GPS enrolls patients that qualify to have at least one vessel revascularized per criteria that are aligned with international guideline recommendations for revascularization - including those intermediate lesions demonstrating evidence of myocardial ischemia. A number of patients that are consented for study participation are excluded from enrollment due to having only angiographically present coronary stenoses in which the disease is not hemodynamically significant. This sub-study is focused on collecting additional imaging data on these intermediate vessels in patients that do not have any hemodynamically significant lesion that qualifies them for participation in DEFINE GPS.

Study objective

• Demonstrate that PCI guided by iFR Co-registration is associated with superior clinical outcomes compared to PCI guided by angiography alone
• To evaluate the cost-effectiveness of physiology guidance with SyncVision compared to a standard of care PCI strategy
• To establish the relationship between physiological guidance and improvement in associated angina and quality of life scores
• To examine the outcomes in patients in whom an optimized post-PCI iFR can versus cannot be achieved

Objective of the ChIL substudy:
• To collect baseline patient medical and demographic data along with angiographic and functional data from vessels with intermediate disease deferred from revascularization among those patients that are screen failures for including in DEFINE GPS
• To establish a body of imaging data that can be used to validate new image-based physiology applications

Study design

Multi-center, prospective, randomized controlled study employing an adaptive design study for interim sample size re-estimation

Study design of the ChIL substudy:
Multi-center, prospective, registry study among patients that consent to be randomized into the DEFINE GPS study but ultimately are not enrolled into the

study.

Intervention

The researchdoes not involve a new coronary intervention technique.

Not applicable for ChIL substudy.

Study burden and risks

Patients randomized to the physiology-guided arm will undergo multiple pressure wire measurements that the patients in the angiograph-guided arm will not. Use of any interventional device in the coronary arteries has an incidental risk associated with it. The additional use of pressure wires in the physiology-guided arm may place these patients at an incrementally higher risk associated with the extra pressure wire procedures.
The Philips IGTD pressure guide wires used in this study are cleared for commercial use by the FDA, CE marked for commercial distribution in Europe, or otherwise appropriately registered for local use. Pressure guide wires are intended for measuring pressure in the coronary vessels as described in this protocol. Nothing about their use in this protocol is considered outside of their intended use. Information related to contraindications, adverse effects, warnings, and precautions are included in the device Instructions for Use.

For ChIL substudy:
The amount of radiation exposure patients will experience will be less than those patients that qualify for the original study and require revascularization. Patients may undergo radiation exposure that is equal to or only minimally more than their baseline diagnostic coronary angiogram. The risks associated with the additional exposure is within the same level of stochastic risk as if they do not undergo any additional radiation. The high-flow pressure measurement (*FFR*) is a Class IA recommendation for assessing the significance of equivocal lesions to determine if a patient should undergo myocardial revascularization. The overall risks are minimal and the benefits are that the patient may undergo a more thorough diagnostic assessment than they normally would. Finally, the data collected through this effort may lead to tools that will minimize the need for a patient to undergo the placement of invasive pressure wires in the future.

Contacts

Public
Philips

High Tech Campus 37
Eindhoven 5656AE
NL
Scientific
Philips

High Tech Campus 37
Eindhoven 5656AE
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Adult men and women (local age of consent) who present with stable or unstable angina, or NSTEMI.
2. Undergoing cardiac catheterization with planned or possible ad hoc PCI
3. Following angiography, PCI is indicated in at least one coronary artery* on the basis of one or more of the following:
a. Presenting with NSTE-ACS (unstable angina with ECG changes or cardiac enzyme-positive NSTEMI) with an identified culprit lesion with DS >=50%;
b. One or more angiographic stenoses present with >=80% stenosis severity by visual estimation;
c. One or more angiographic stenoses present with >=50% to <80% stenosis severity by visual estimation and an abnormal non-invasive stress test in the distribution of the lesion(s) within the past 60 days;
d. One or more angiographic stenoses are present with >=50% to <80% stenosis severity by visual estimation and a spot iFR measure <=0.89.
Note: Multiple target vessels may be present. However, all must be qualified by all inclusion and exclusion criteria prior to randomization, and all qualified vessels must be treated per the randomization assignment (e.g. all with standard angiographic guidance or all with physiologic guidance). Non-culprit

vessels in patients with NSTE-ACS must qualify by one of the criteria listed in b-d above.
Staged procedures are permitted as detailed below.
4. Subject is willing to comply with all scheduled visits and tests and are able and have provided informed written consent
*May or may not be known prior to consent. If patient is consented and following angiography all inclusion criteria are not present or any exclusion criteria are present, the patient will not be randomized

For the substudy ChIL:
1. Adult men and women (local age of consent) who present with stable angina
2. Undergoing cardiac catheterization with planned or possible ad hoc PCI
3. Following angiography, at least one epicardial vessel has one or more angiographic stenoses with >=50% to <80% stenosis severity by visual estimation and a spot iFR measure > 0.89 or FFR > 0.80.
4. Subject is willing to comply with all procedure steps and has provided informed written consent

Exclusion criteria

1. STEMI within 30 days
2. PCI within the prior 12 months, or any PCI planned after the study procedure (other than planned staged procedures of randomized vessels which are allowed)
3. Prior CABG anytime
4. Silent ischemia only (i.e. no cardiac symptoms related to coronary artery disease) within the prior 4 weeks
5. Documented prior iFR pullback performed in any coronary artery including during the qualifying diagnostic angiogram
6. Any vessel with in-stent restenosis (ISR) requiring treatment
7. Cardiogenic shock defined as systolic blood pressure <90 mmHg for >20 minutes not responding to fluid resuscitation, or need for inotropic, pressor, or device-based hemodynamic support
8. Presence of unstable ventricular arrhythmias
9. Heart rate > 110, including uncontrolled atrial fibrillation (AF)
10. Decompensated congestive heart failure (NYHA Class IV or Killip Class III or IV)
11. Chronic total occlusion (CTO) of a target vessel (exception: a CTO may be present in a non-target vessel if it is supplying non-viable myocardium and there is no intent to open the CTO during the index or later procedure)
12. Coronary anatomy not amenable to pressure wire manipulation due to extreme tortuosity or complexity such that it is unlikely that a pressure wire could be passed to the distal third of the three major epicardial coronary arteries
13. Any angiographic giant thrombus (i.e., thrombus length > 3x RVD at lesion)
14. Any target vessel with < TIMI III flow

15. Any target lesion with a reference vessel diameter (RVD) less than 2.25mm except for within the side branch of a bifurcation lesion
16. Any non-target lesion with a reference vessel diameter (RVD) greater than 2.00mm that contains an >=80% stenosis and is not intended for treatment with PCI
17. Known severe aortic or mitral valve stenosis/insufficiency
18. Known non-cardiovascular comorbidity resulting in lifespan <24 months
19. Known left ventricular ejection fraction <=30%
20. Estimated creatinine clearance (MDRD formula) <30 mL/min/1.73m2 or on dialysis
21. Any cardiac or non-cardiac surgical procedure planned within 12 months after enrollment, or any procedure planned within 6 months after enrollment that would necessitate discontinuation of dual antiplatelet therapy
22. Known pregnancy or planning to become pregnant (women of child-bearing potential must have a negative pregnancy test within 1 week of enrollment)
23. Participating in another investigational drug or device study that has not reached its primary endpoint
24. Any condition such as dementia or substance abuse that may impair the patient*s ability to comply with all study procedures, including medication compliance and follow-up visits
25. Patient is a member of a vulnerable population who, in the judgment of the investigator, is unable to give Informed Consent for reasons of incapacity, immaturity, adverse personal circumstances or lack of autonomy. This may include individuals with mental disability, persons in nursing homes, children, impoverished persons, persons in emergency situations, homeless persons, nomads, refugees, and those permanently incapable of giving informed consent. Vulnerable populations also include university students, subordinate hospital and laboratory personnel, employees of the Sponsor, members of the armed forces, and persons kept in detention.

For the ChIL Substudy:
Exclusion criteria from DEFINE GPS that are relevant for the ChIL sub-study will apply and these are listed below. In addition, the ChIL sub-study has additional specific target vessel angiographic exclusions which are listed separately below.
From DEFINE GPS:
1. STEMI within 30 days
2. Prior CABG anytime
3. Cardiogenic shock defined as systolic blood pressure <90 mmHg for >20 minutes not responding to fluid resuscitation, or need for inotropic, pressor, or device-based hemodynamic support
4. Presence of unstable ventricular arrhythmias
5. Heart rate > 110, including uncontrolled atrial fibrillation (AF)
6. Chronic total occlusion (CTO) of a target vessel (exception: a CTO may be present in a non-target vessel if it is supplying non-viable myocardium and there is no intent to open the CTO during the index or later procedure)
7. Coronary anatomy not amenable to pressure wire manipulation due to extreme tortuosity or complexity such that it is unlikely that a pressure wire could be

passed to the distal third of the three major epicardial coronary arteries
8. Any angiographic giant thrombus (i.e., thrombus length > 3x RVD at lesion)
9. Any target vessel with < TIMI III flow
10. Any target lesion with a reference vessel diameter (RVD) less than 2.25mm except for within the side branch of a bifurcation lesion
11. Known severe aortic or mitral valve stenosis/insufficiency
12. Known left ventricular ejection fraction <=30%
13. Estimated creatinine clearance (MDRD formula) <30 mL/min/1.73m2 or on dialysis
14. Known pregnancy or planning to become pregnant (women of child-bearing potential must have a negative pregnancy test within 1 week of enrollment)
15. Participating in another investigational drug or device study that has not reached its primary endpoint
16. Any condition such as dementia or substance abuse that may impair the patient*s ability to fully cooperate.
17. Patient is a member of a vulnerable population who, in the judgment of the investigator, is unable to give Informed Consent for reasons of incapacity, immaturity, adverse personal circumstances or lack of autonomy. This may include individuals with mental disability, persons in nursing homes, children, impoverished persons, persons in emergency situations, homeless persons, nomads, refugees, and those permanently incapable of giving informed consent. Vulnerable populations also include university students, subordinate hospital and laboratory personnel, employees of the Sponsor, members of the armed forces, and persons kept in detention.

ChIL Sub-study Target Vessel Exclusions:
1. Target vessel angiographic imaging having radiopaque interference associated with prior cardiac implant (e.g., prior stent. artificial heart valve, pacemaker)
2. Target vessel supplied by a left main coronary artery demonstrating any disease present (isolated or non-isolated)
3. Target vessel supplied by right coronary artery demonstrating any ostial disease (located immediately at the origin of the coronary vessels from the aorta)
4. Target vessel with severe tortuosity (>=1 bends of 90° or more, or >=3 bends of 45°- 90° proximal to the diseased segment)
5. Target vessel with heavy calcification (multiple persisting opacifications of the coronary wall visible in more than one projection surrounding the complete lumen of the coronary artery at the site of the lesion.)
6. Target vessel with severe diffuse disease (more than 75% of the length of the segment having a vessel diameter of 2mm, irrespective of the presence or absence of a lesion)
7. Target vessel supplied by major collaterals
8. Target vessel has vascular abnormality precluding optimal contrast opacification (e,g, thrombus, ulceration)
9. Target vessel has an apparent muscle bridge
10. Target lesion is at a true bifurcation; i.e., Medina classification 1,0,0

or 0,1,0 or 0,0,1

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Active
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	06-07-2021
Enrollment:	521
Type:	Actual

Medical products/devices used

Generic name:	iFR Co-Registration using commercially available Philips pressure guidewires and the SyncVision co-r
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	26-04-2021
Application type:	First submission
Review commission:	RTPO, Regionale Toetsingscie Patientgebonden Onderzoek (Leeuwarden)
Approved WMO Date:	06-11-2023

Application type:	Amendment
Review commission:	RTPO, Regionale Toetsingscie Patientgebonden Onderzoek (Leeuwarden)
Approved WMO Date:	05-03-2024
Application type:	Amendment
Review commission:	RTPO, Regionale Toetsingscie Patientgebonden Onderzoek (Leeuwarden)
Approved WMO Date:	16-05-2024
Application type:	Amendment
Review commission:	RTPO, Regionale Toetsingscie Patientgebonden Onderzoek (Leeuwarden)
Approved WMO Date:	20-08-2024
Application type:	Amendment
Review commission:	RTPO, Regionale Toetsingscie Patientgebonden Onderzoek (Leeuwarden)

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	NCT04451044
CCMO	NL76491.099.21