BOLT LITHOTRIPSY RESTORE TRIAL FOR CAD

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The objective of this clinical study is to assess the safety and effectiveness of the Apollo Intravascular Lithotripsy (IVL) System for lithotripsy-enhanced balloon dilatation of calcified, stenotic de novo coronary lesions prior to stenting.The...

Ethical review	Approved WMO
Status	Will not start
Health condition type	Coronary artery disorders
Study type	Interventional

Summary

ID

NL-OMON51450

Source
ToetsingOnline

Brief title
RESTORE CAD

Condition

- Coronary artery disorders
- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Synonym
coronary artery stenose, shockwave and balloon theraphy

Research involving
Human

Sponsors and support

Primary sponsor: Bolt Medical, Inc.
Source(s) of monetary or material Support: Het bedrijf Bolt Medical;Inc.;de sponsor van de studie;financierd het onderzoek.

Intervention

Keyword: angioplasty, artery, coronary, Intravascular, Lithotripsy

Outcome measures

Primary outcome

Safety:

The primary safety endpoint is freedom from major adverse cardiac events (MACE) within 30 days following the index procedure. MACE is defined as the occurrence of cardiac death, MI or TVR.

• Myocardial Infarction (MI) is defined as CK-MB level > 3 times the upper limit of lab normal (ULN) value with or without new pathologic Q wave 12 to 24 hours post procedure or at discharge (periprocedural MI) and by the Fourth Universal Definition of Myocardial Infarction beyond discharge (spontaneous MI)

• Target Vessel Revascularization (TVR) is defined as revascularization at the target vessel (including the target lesion) after completion of the index procedure.

Effectiveness:

The primary effectiveness endpoint is the rate of procedural success defined as successful stent delivery with a residual stenosis <50% (angiographic core laboratory assessed) and freedom from in-hospital MACE.

Secondary outcome

The secondary endpoints are:

1. Device crossing success defined as the ability to deliver the IVL catheter across the target lesion and delivery of lithotripsy without serious

angiographic complications immediately after IVL.

2. Angiographic success defined as stent delivery with < 50% residual stenosis and without serious angiographic complications.

3. Procedural success defined as stent delivery with a residual stenosis <= 30% (core laboratory assessed) and without in-hospital MACE.

4. Angiographic success defined as stent delivery with <=30% residual stenosis and without serious angiographic complications.

5. Serious angiographic complications defined as severe dissection (Type D to F), perforation, abrupt closure, and persistent slow flow or persistent no reflow.

6. MACE within 6 months.

7. Target lesion failure (TLF) defined as cardiac death, target vessel MI (Q wave and non-Q wave), or ischemia-driven target lesion revascularization (ID-TLR) by percutaneous or surgical methods at 30 days and 6 months.

8. At each time period: All deaths, cardiac deaths, MIs, TV-MIs, procedural and nonprocedural MIs, ID-TVRs, ID-TLRs, non-ID-TLRs, non-ID-TVRs, all revascularizations (ID and non-ID), and stent thrombosis (Academic Research Consortium (ARC) definite, probable, definite or probable).

9. Sensitivity analyses will be reported for MI using the Fourth Universal Definition of MI and the Society for Cardiovascular Angiography and Interventions (SCAI) definitions at 30 days and 6 months.

Study description

Background summary

Coronary artery disease (CAD) is caused by atherosclerosis within the coronary arteries which results in arterial narrowing and restricted blood flow to the heart. This can lead to symptoms of angina and decreased heart function. CAD is the most common form of heart disease and the leading cause of death in the United States (Braun, 2018). Although the mortality for this condition has gradually declined in western countries, it still causes about one-third of all deaths in people older than 35 years (Nichols 2014).

Patients with symptomatic CAD typically fall into one of two subtypes, those with stable ischemic heart disease (SIHD) and those with acute coronary syndromes (ACS). SIHD results from slow growing plaques that over time narrow the coronary artery until ischemia and symptoms develop. Non-invasive testing such as stress tests or cardiac CT scans are helpful in diagnosing this condition. Anti-anginal medications are the initial treatment of choice for these patients, however those with ongoing symptoms can derive significant benefit from revascularization (Bangalore, 2020). Patients with ACS have unstable atherosclerotic plaques that fissure or rupture and acutely or partially obstruct a coronary artery. These patient*s symptoms usually do not resolve with medications alone and require urgent revascularization.

Current Treatments options are:
- Pharmacotherapy: Antiplatelets (e.g., aspirin, P2Y12 inhibitors), antianginals (e.g., beta-blockers, nitrates, calcium channel blockers), lipid control (e.g., statins, non-statin LDL lowering treatments, non-LDL therapies), glycemic control.
- Coronary Bypass grafting (CABG): Currently indicated for patients with complex 3-vessel coronary artery disease involving the proximal left anterior descending artery (LAD) and/or left main coronary artery (LM). Depending on the complexity of disease, when compared to percutaneous coronary intervention in the SYNTAX trial, CABG is associated with a decrease need for repeat revascularization and similar to improved periprocedural morbidity and mortality, at the expense of a longer initial hospitalization. For patients who are not surgical candidates due to multiple comorbid conditions, PCI and medical therapy remain the only therapeutic options.
- Transcatheter Coronary interventions:
• Percutaneous transluminal anioplasty (PTA): first performed in 1977, it was one of the first treatment options for CAD and is associated with low complication rates. Isolated balloon angioplasty is no longer the treatment of choice as it is plagued by high rate of failure resulting from restenosis and vascular recoil.
• Cutting and scoring balloons special balloons that contain microsurgical blades bonded to its* surface with the intention of scoring/cutting into atherosclerotic plaque.
• Drug-coated balloons (DCB) delivers antiproliferative drugs to local arterial

tissue and reduces risk of restenosis (Picard, 2017).
• Atherectomy - a minimally invasive endovascular surgery technique to remove or debulk atherosclerotic plaque from diseased arteries.
• Lithotripsy (IVL): lithotripsy has been around since the early 1980s, and used to break down stones in the kidney, gallbladder, or ureter with sound waves. Since then, the procedure has been adapted for intravascular calcium modification using sonic pressure waves to modify intimal and medial calcium.
• Cryoplasty: uses nitrous oxide to optimize the dilation effects of standard angioplasty by delivering cryothermal energy to the atherosclerotic plaque.
• Stents: routine implantation of stents has improved the clinical course after balloon angioplasty and is now standard in the treatment of stenosis of native coronary arteries and venous bypass vessels (Ruß, 2009).

The study involves the evaluation of a new medical device (Apollo IVL system) which uses a combination of Lithotripsy (IVL) with a low pressure balloon to break the plague and widen the affected artery.

Study objective

The objective of this clinical study is to assess the safety and effectiveness of the Apollo Intravascular Lithotripsy (IVL) System for lithotripsy-enhanced balloon dilatation of calcified, stenotic de novo coronary lesions prior to stenting.
The data is used for obtaining market access.

Study design

The RESTORE CAD study is a pre-market prospective, non- randomized, multicenter study to obtain data for support of market access.

The follow-up period is 6 months.

The tests performed within the study are standard of care, limiting the risk of participating in the study for the patients.

A total of 60 subjects is planned, exclusive of roll-in subjects for primary analysis. In addition to the primary analysis sample size, up to a maximum of twenty (20) roll-in subjects will be allowed.

Intervention

The study procedure consists of standard percutaneous coronary interventional (PCI) techniques, including access site preparation, introduction of the catheter portion of the device, inflation and deflation of the balloon, withdrawal of the catheter, stent implantation, and access site closure.

PCI is performed via either femoral or radial access with a minimum 6F guiding catheter. The IVL catheter is passed across the lesion over a standard 0.014* guidewire. If the IVL catheter will not cross the lesion, adjunctive tools (buddy wire, balloon predilatation, or guide catheter extension) can be used at operator discretion before reinsertion of the IVL catheter. Atherectomy or cutting/scoring balloons is not permitted.

Once the balloon is placed in the target lesion area, the balloon is inflated to 4 ATM and a treatment cycle is activated by pressing and holding the treatment activation button, leading to delivery of pulsatile acoustic (shockwaves) for up to the defined number of pulses per treatment cycle.

A different diameter IVL balloon may be used if significant vessel tapering occurs in the target lesion.

The number of IVL catheters used is dependent on lesion length, vessel diameter of the treated segments, and total number of pulses required to effectively treat the target lesion.

Study burden and risks

Potential risks associated with the Apollo Intravascular Lithotripsy System can be associated with device use, general anesthesia, catheterization and diagnostic imaging for subjects with CAD.

The potential risks and discomforts associated specifically with treating CAD with the Apollo IVL System are expected to be similar to the risks associated with the use of other commercially available, standard of care devices.

Potential risks/adverse events associated with the Apollo IVL system, general anesthesia, catheterization and diagnostic imaging for subjects with CAD ,as reported in the published literature, are outlined below.
Risks/adverse events may be local or systemic in nature and vary from minor reactions to major reactions that may be life-threatening or result in death.

Documented risks associated with standard catheter-based cardiac interventions/procedures are reported in the published literature and include, but are not limited to, the following:
• Abrupt vessel closure
• Allergic reaction to contrast medium, anticoagulant and/or antithrombotic therapy
• Aneurysm
• Arrhythmia
• Arteriovenous fistula
• Bleeding complications
• Cardiac tamponade or pericardial effusion
• Cardiopulmonary arrest

• Cerebrovascular accident (CVA)
• Coronary artery/vessel occlusion, perforation, rupture or dissection
• Coronary artery spasm
• Death
• Emboli (air, tissue, thrombus or atherosclerotic emboli)
• Emergency or non-emergency coronary artery bypass surgery
• Emergency or non-emergency percutaneous coronary intervention
• Entry site complications
• Fracture of the guide wire or failure/malfunction of any component of the device that may or may not lead to device embolism, dissection, serious injury or surgical intervention
• Hematoma at the vascular access site(s)
• Hemorrhage
• Hypertension/ Hypotension
• Infection/sepsis/fever
• Myocardial Infarction
• Myocardial Ischemia or unstable angina
• Pain
• Peripheral Ischemia
• Pseudoaneurysm
• Renal failure/insufficiency
• Restenosis of the treated coronary artery leading to revascularization
• Shock/pulmonary edema
• Slow flow, no reflow, or abrupt closure of coronary artery
• Stroke
• Thrombus
• Vessel closure, abrupt
• Vessel injury requiring surgical repair
• Vessel dissection, perforation, rupture, or spasm

In addition, patients may be exposed to other risks associated with coronary interventional procedures, including risks from conscious sedation and local anesthetic, the radiographic contrast agents used during angiography, the drugs given to manage the subject during the procedure, and the radiation exposure from fluoroscopy.

Risks identified as related to the device and its use:
• Allergic/immunologic reaction to the catheter material(s) or coating
• Device malfunction, failure, or balloon loss of pressure leading to device embolism, dissection, serious injury or surgical intervention
• Atrial or ventricular extrasystole
• Atrial or ventricular capture

Potential Benefits:
Potential benefits to the subjects participating in this study may include but are not limited to: no surgical incision - faster recovery, less pain, reduced

hospital stay, and reduced complications.

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. Age of subject is >=18.
2. Subjects with native coronary artery disease (including stable or unstable angina, or silent
ischemia) suitable for PCI
3. For patients with unstable ischemic heart disease, biomarkers (troponin or CK-MB) must be less
than or equal to the upper limit of lab normal within 12 hours prior to the procedure (note: if
both labs are drawn, both must be normal).

4. For patients with stable ischemic heart disease, biomarkers may be drawn prior to the index
procedure or at the time of the procedure from the side port of the sheath.
o If drawn prior to the procedure, biomarkers (troponin or CK-MB) must be less than or equal
to the upper limit of lab normal within 12 hours of the procedure (note: if both labs are
drawn, both must be normal).
o If biomarkers are drawn at the time of the procedure from the side port of the sheath prior to
any intervention, results do not need to be analyzed prior to enrollment (note: CK-MB is
required if drawn from the sheath).
5. Left ventricular ejection fraction (LVEF) >25% within 6 months (note: in the case of multiple
assessments of LVEF, the measurement closest to enrollment will be used for this criterion; may
be assessed at time of index procedure)
6. Subject or legally authorized representative, signs a written Informed Consent form to
participate in the study, prior to any study-mandated procedures
7. Lesions in non-target vessels requiring PCI may be treated either:
o >30 days prior to the study procedure if the procedure was unsuccessful or complicated; or
o >24 hours prior to the study procedure if the procedure was successful and without
complications (defined as a final lesion angiographic diameter stenosis <30% and TIMI 3
flow (visually assessed) for all non-target lesions and vessels without perforation, cardiac
arrest or need for defibrillation or cardioversion or hypotension/heart failure requiring
mechanical or intravenous hemodynamic support or intubation, and with no post-procedure
biomarker elevation >normal); or
o >30 days after the study procedure

Angiographic Inclusion Criteria
1. The target lesion must be a de novo coronary lesion that has not been previously treated with any
interventional procedure
2. Single de novo target lesion stenosis of protected LMCA, or LAD, RCA or LCX (or of their
branches) with:
o Stenosis of >70% and o Stenosis >50% and <70% (visually assessed) with evidence of ischemia via
positive stress

test, or fractional flow reserve value < 0.80, or iFR <0.90 or IVUS or OCT minimum lumen
area < 4.0 mm2
3. The target vessel reference diameter must be > 2.5 mm and < 4.0 mm
4. The lesion length must not exceed 40 mm
5. The target vessel must have TIMI flow 3 at baseline (visually assessed; may be assessed after
pre-dilatation)
6. Evidence of calcification at the lesion site by, a) angiography, with fluoroscopic radio-opacities
noted without cardiac motion prior to contrast injection involving both sides of the arterial wall
in at least one location and total length of calcium of at least 15 mm and extending partially into
the target lesion, OR by b) IVUS or OCT, with presence of > 270 degrees of calcium on at least
1 cross section
7. Ability to pass a 0.014* guide wire across the lesion

Exclusion criteria

1. Any comorbidity or condition which may reduce compliance with the protocol, including follow-up visits
2. Subject is a member of a vulnerable population as defined in 21 CFR 56.111, including
individuals with mental disability, persons in nursing homes, children, impoverished persons,
persons in emergency situations, homeless persons, nomads, refugees, and those incapable of
giving informed consent. Vulnerable populations also may include members of a group with a hierarchical structure such as university students, subordinate hospital and laboratory personnel,
employees of the Sponsor, members of the armed forces, and persons kept in detention
3. Subject is participating in another research study involving an investigational agent
(pharmaceutical, biologic, or medical device) that has not reached the primary endpoint
4. Subject is pregnant or nursing (a negative pregnancy test is required for women of child-bearing
potential within 7 days prior to enrollment)
5. Unable to tolerate dual antiplatelet therapy (i.e., aspirin, and either clopidogrel, prasugrel, or
ticagrelor) for at least 6 months (for patients not on oral anticoagulation)
6. Subject has an allergy to imaging contrast media which cannot be adequately

pre-medicated
7. Subject experienced an acute MI (STEMI or non-STEMI) within 30 days prior to index
procedure, defined as a clinical syndrome consistent with an acute coronary syndrome with
troponin or CK-MB greater than 1 times the local laboratory*s upper limit of normal
8. New York Heart Association (NYHA) class III or IV heart failure at time of index procedure
9. Renal failure with serum creatinine >2.5 mg/dL, GFR <40 or chronic dialysis
10. History of a stroke or transient ischemic attack (TIA) within 6 months, or any prior intracranial
hemorrhage or permanent neurologic deficit
11. Active peptic ulcer or upper gastrointestinal (GI) bleeding within 6 months
12. Untreated pre-procedural hemoglobin <10 g/dL or intention to refuse blood transfusions if one
should become necessary
13. Coagulopathy, including but not limited to platelet count <100,000 or international normalized
ratio (INR) >1.7 (INR is only required in subjects who have taken warfarin within 2 weeks of
enrollment)
14. Subject has a hypercoagulable disorder such as polycythemia vera, platelet count >750,000 or
other disorders
15. Uncontrolled diabetes defined as a HbA1c > l0%
16. Subject has an active systemic infection on the day of the index procedure with either fever,
leukocytosis or requiring intravenous antibiotics
17. Subjects in cardiogenic shock
18. Uncontrolled severe hypertension (systolic BP >180 mm Hg or diastolic BP >110 mm Hg)
19. Subjects with a life expectancy of less than 1 year
20. Non-coronary interventional or surgical structural heart procedures (e.g., TAVR, MitraClip,
LAA or PFO occlusion, etc.) within 30 days prior to the index procedure
21. Planned non-coronary interventional or surgical structural heart procedures (e.g., TAVR,
MitraClip, LAA or PFO occlusion, etc.) within 30 days after the index procedure
22. Subject refusing or not a candidate for emergency coronary artery bypass grafting (CABG)
surgery
23. Planned use of atherectomy, scoring or cutting balloon, Shockwave lithotripsy device or any
investigational device other than the study device
24. High SYNTAX Score (> 33) if assessed as standard of care, unless the local heart team has met

and recommends PCI is the most appropriate treatment for the patient
25. Unprotected left main diameter stenosis >30%
26. Target vessel is excessively tortuous defined as the presence of two or more bends >90º or three
or more bends >75º
27. Definite or possible thrombus (by angiography or intravascular imaging) in the target vessel
28. Evidence of aneurysm in target vessel within 10 mm of the target lesion
29. Target lesion is an ostial location (LAD, LCX, or RCA, within 5 mm of ostium) or an
unprotected left main lesion
30. Target lesion is a bifurcation involving a side branch of 2.5mm or more with ostial diameter
stenosis >=50%, and intention to treat the side branch with balloon and/or stent
31. Second lesion with >50% stenosis in the same target vessel as the target lesion including its side
branches
32. Target lesion is located in a native vessel that can only be reached by going through a saphenous
vein or arterial bypass graft
33. Previous stent within the target vessel implanted within the last year
34. Previous stent within 10 mm of the target lesion regardless of the timing of its implantation
35. Angiographic evidence of a dissection in the target vessel at baseline or after guidewire passage

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	10
Type:	Anticipated

Medical products/devices used

Generic name:	The Apollo Intravascular Lithotripsy (Apollo IVL) System
Registration:	No

Ethics review

Approved WMO Date:	09-02-2023
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (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
CCMO	NL81513.000.22