Cerebral Protection of Acute Embolic Burden During Transcatheter Aortic Valve Implantation * A Randomized Diffusion-Weighted MRI Study (CP-11134)

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To study the effect of the use of the LV 1 System with the Sentinel System, during TAVR, with respect to procedure-related cerebral embolic burden in patients assessed by DW-MRI. To limit data variability and avoid confounding effects of different...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Cardiac valve disorders
Study type	Interventional

Summary

ID

NL-OMON42354

Source
ToetsingOnline

Brief title
SENTINEL-L Study

Condition

- Cardiac valve disorders

Synonym
severe headache; dizziness; difficulty in walking; loss of balance and coordination; blurred or double vision., Stroke: inability to move one or more limbs on one side of the body; inability to understand or formulate speech; inability to see one side of the visual field; sudden

Research involving
Human

Sponsors and support

Primary sponsor: Claret Medical, Inc.
Source(s) of monetary or material Support: Funded by the sponsor (manufacturer of the study device)

Intervention

Keyword: Embolic protection device., Stroke., Trascatheter Aortic Valve Replacement.

Outcome measures

Primary outcome

Primary Endpoint:

Acute cerebral embolic burden reduction after TAVI assessed with 1.5-tesla

DW-MRI at Day 2-4 compared to baseline

Secondary outcome

Secondary Endpoints:

* MACCE @ 30 days

* Histopathology (proximal, distal, LV1 Filter)

* Neurological examinations, National Institutes of Health Stroke Scale (NIHSS)

and Modified Rankin (mRS)

* LV1 System Success

Major Adverse Cardiac and Cerebrovascular Events (MACCE) is comprised of the

following:

* All-cause mortality

* All stroke (major, minor, TIA)

* Acute Kidney Injury (Class 3)

Study description

Background summary

Stroke remains a major complication for transcatheter aortic valve replacement (TAVI) which has been reported to increase mortality 3-fold .
Diffusion-weighted magnetic resonance imaging (DW-MRI) can detect and evaluate quality, quantity and fate of cerebral embolism with subsequent acute ischemic cerebral lesions within the brain hemispheres, brain stem, and cerebellum. This technique serves as an emerging surrogate endpoint for clinical and subclinical ischemic stroke and has been used frequently to quantify thromboembolism associated with TAVI.
The Claret Medical Sentinel Cerebral Protection System was developed to protect the brain from injury caused by embolic debris. The device includes two conically shaped polyurethane filters with 140 micron holes, mounted onto nitinol self-expanding wire frames. The first filter is deployed in the brachiocephalic trunk to protect the right carotid artery; and the second filter is deployed in the left common carotid artery. The Sentinel Cerebral Protection System is safe and effective in capturing embolic debris in cardiovascular procedures. The device obtained CE mark approval in 2011. A recent randomized study (CLEAN-TAVI) demonstrated that theSentinel System is associated with a significant reduction in the number and volume of cerebral lesions as determined by Diffusion Weighted-MRI subtraction at 2 and 7 days after TAVI . In addition, the filter group showed a lower ataxia rate than the control group (9% vs 24%), indicating the potential to reduce neurologic complications. However, the Sentinel System does not protect all regions of the brain.
The LV1 System (investigational product) provides additional cerebral protection to unprotected regions of the brain. This product is similar to the Sentinel System, but is intended to be placed into in the left subclavian artery to provide protection for its branches, and in particular, the left vertebral artery (which supplies approximately 10% of the brain blood flow). This is expected to result in a further reduction in cerebral embolic burden.
To evaluate the hypothesis, that using Sentinel in combination with LV1 filter provides more complete protection of the brain, the present 3 arm controlled randomized study is designed to quantify embolic burden reduction (with Diffusion Weighted-MRI) in patients treated with the Sentinel System alone and with the Sentinel System in combination with LV1 System versus TAVI without any embolic protection.

Study objective

To study the effect of the use of the LV 1 System with the Sentinel System, during TAVR, with respect to procedure-related cerebral embolic burden in patients assessed by DW-MRI. To limit data variability and avoid confounding effects of different TAVI devices, patients enrolled will be those expected to

receive only one type of TAVI device (Boston Scientific Lotus Valve System, a next generation repositionable device).
The study population is comprised of subjects with severe native aortic valve stenosis who meet the commercially approved indications for TAVI and comply with the inclusion/exclusion criteria of the study.

Study design

Multicenter, prospective, randomized (1:1:1), open label
Treatment Arm #1: TF-TAVI with the Sentinel System and the LV1 filter
Control Arm #2: TF-TAVI without any embolic protection (primary analysis)
Control Arm #3: TF-TAVI with the Sentinel System only (secondary analysis for pilot assessment)
This study is expected to enroll a total of 72 subjects, in two phases:
- Phase 1: Total of 36 randomized (12:12:12) subjects
- Phase 2 (After interim analysis of results): Total of 36 additional randomized (12:12:12) subjects may be enrolled

Intervention

The LV1 System (investigational product) provides additional cerebral protection to unprotected regions of the brain. This product is similar to the Sentinel System, but is intended to be placed into in the left subclavian artery to provide protection for its branches, and in particular, the left vertebral artery. This is expected to result in a further reduction in embolic burden.
The LV1 System is a filter catheter, sheathed inside a commercially available 5 Fr multipurpose guidecatheter and is intended to be inserted through the left radial or left brachial artery and advanced to the junction of the left subclavian artery and the aorta where the filter is deployed. The filter is suitable for left subclavian vessels with diameters of 7 * 12mm.
During a TAVI procedure, arterial pressure is commonly monitored through a sheath placed in the left radial artery that is filled with saline and connected to an external extra-vascular blood pressure transducer. In this study, the left radial access site will be used for the LV1 System, and so in order to maintain the ability for arterial pressure to be monitored through the left radial artery, the LV1 System has been designed to allow pressure monitoring through the required multipurpose guidecatheter using the same external extra-vascular blood pressure transducer. Once the filter is deployed in the left subclavian artery, the central saline-filled lumen of the guidecatheter is used to transmit the pressure signal to the external pressure transducer connected to the side branch of the required Y-connector, in exactly the same manner as is done during TAVI procedures that do not use the LV1 System for embolic protection.

Study burden and risks

The risks and benefits associated with cerebral embolic protection devices, including their use in endovascular procedures such as TAVI , are well documented as these devices have a long history of clinical use.
The Sentinel System is CE Marked (CE 606742) and approved for marketing in the European Community. The clinical data collected for the Sentinel System demonstrate the Cerebral Protection System has a strong safety profile. The characteristics of the LV1 System are the same as the Sentinel System, with the addition of the possibility that arterial pressure may be monitored through the LV1 System.
The potential benefit of use of the LV1 System, in conjunction with the Sentinel System, is a further reduction in the acute cerebral embolic burden (i.e. cumulative number and volume of diffusion-positive brain lesions) as detected with DW-MRI given that approximately 10% of the cerebral blood supply flows through the left vertebral artery .
Recent studies have shown new lesions detected by DW-MRI in 68-91% of TAVI patients and a significant reduction in number and volume of cerebral lesions were reported where the Claret Medical Cerebral Protection System was used.
Without the Sentinel and the LV1 Systems, embolic debris could otherwise travel unimpeded via the cerebral circulation to the brain and could lead to cerebral vascular events.

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. Severe symptomatic aortic valve stenosis
2. Compatible anatomy for Sentinel and LV1 Systems:
o Sentinel System: left common carotid artery (6.5 * 10 mm) and brachiocephalic artery (9 * 15 mm) diameters
o LV1 System: left subclavian artery (7.0 * 12.0 mm) diameter
3. Subject eligible for transfemoral TAVI access with planned implantation of Boston Scientific Lotus Valve System

Exclusion criteria

1. Contraindications to TAVI per heart team
2. Current or recent cerebrovascular accident (stroke, TIA) <6 months
3. Transapical, direct aortic or subclavian TAVI access
4. Carotid stenting or endarterectomy in last 6 weeks
5. Symptomatic or asymptomatic severe occlusive carotid disease requiring concomitant Carotid Endarterectomy / stenting
6. History of atrial fibrillation (AF) including:
o Persistent AF (defined as continuous AF which is sustained beyond seven days, or lasting greater than 48 hours and less than seven days but necessitating pharmacologic or electrical cardioversion), or
o History of Paroxysmal AF during the previous 30 days. Paroxysmal AF is defined as recurrent AF (>2 episodes) that terminates spontaneously within 7 days. Episodes of AF of < 48 hours* duration that are terminated with electrical or pharmacologic cardioversion are also classified as paroxysmal AF episodes.;7. Subject with active endocarditis or other systemic infection
8. Prior aortic valve replacement
9. Concomitant procedure with TAVI such as CABG, PCI, etc.
10. Claustrophobia
11. Contraindications to MRI (subjects with any non-MRI compatible implantable temporary or permanent pacemaker or defibrillator, metal implants in field of view, metallic fragments, clips, or devices in the brain or eye before TAVR procedure). Planned implantation of non-MRI compatible pacemaker or implantable cardioverter defibrillator after TAVR
12. Allergy to intravascular contrast agents
13. Immobilization or other morbidity with life expectancy < 1 year
14. Inability to accommodate a 6F sheath (Sentinel) or 5F (LV1) into the right and left radial

or brachial arteries respectively
15. Inadequate circulation to the right or left extremity as evidenced by signs of artery occlusion (modified Allen*s test) or absence of radial/brachial pulse
16. Subjects with vascular tortuosity or anatomy that would preclude the safe introduction and placement of the Sentinel System and/or the LV1 System per anatomy screening process
17. Lack of written informed consent
18. Patients in whom anticoagulant and antiplatelet therapy is contraindicated
19. Patients with uncorrected bleeding disorders
20. Patients with compromised blood flow to the left upper extremity
21.Patient who has arterial stenosis >70% in the left subclavian artery
22.Patient whose left subclavian artery reveals significant stenosis, ectasia, dissection, or aneurysm between the aortic ostium and the left vertebral artery
23. Patient is pregnant or lactating
24. Patients requiring left axillary/subclavian access for transcatheter aortic valve implantation

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	06-02-2016
Enrollment:	24
Type:	Actual

Medical products/devices used

Generic name:	LV1 Cerebral Embolic Protection System
Registration:	No

Ethics review

Approved WMO Date:	09-12-2015
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	NL53344.078.15