Prospective, Single-arm Pivotal Study for the Treatment of Subjects with Severe Symptomatic Calcific Aortic Valve Stenosis Using Valvosoft® Non-Invasive Ultrasound Therapy (NIUT)

Published: 20-05-2022
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The objective of the study is to evaluate the safety and performance of a new Non-Invasive Ultrasound Therapy (NIUT) with Valvosoft® in the treatment of CAS.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Cardiac valve disorders
Study type	Observational invasive

Summary

ID

NL-OMON53861

Source
ToetsingOnline

Brief title
Valvosoft Pivotal Study

Condition

- Cardiac valve disorders

Synonym
Calcified Heart valve

Research involving
Human

Sponsors and support

Primary sponsor: CARDIAWAVE SA
Source(s) of monetary or material Support: industrie

Intervention

Keyword: Calcific Aortic Valve Stenosis, Non-Invasive Ultrasound Therapy, Performance, Safety

Outcome measures

Primary outcome

Safety: Rate of MACE <20% (NIM 5%) at 30-days post-procedure Performance:

Improvement in clinical status assessed by means of a decrease in NHYA

functional class at 30 days post procedure

Secondary outcome

Safety: 1. Rate of MACE peri-procedural and at 3-, 6- and 12-months

post-procedure; 2. All-cause mortality at 30 days, 3-, 6- and 12-months

post-procedure; 3. Rate of stroke (disabling and non-disabling; ischemic and

hemorrhagic) at 30-days, 3-, 6- and 12-months post-procedure; 4. Rate of all

adverse events up to 12 months. Performance: 1. Change of 10% in of aortic

stenosis by means of aortic valve area (AVA) (assessed by the independent

echocardiographic Central Core Laboratory) at 30 days compared to baseline 2.

Change in severity of aortic stenosis by means of aortic valve area (AVA)

(assessed by the independent echocardiographic Central Core Laboratory) at 6-

and 12-months compared to baseline; 3. Change in severity of aortic stenosis by

means of transvalvular pressure gradient (mean & peak) and other hemodynamic

parameters (EF, Vmax, LVOT-Cardiac Output, LVOT Cardiac Index, LVOT Mean & Peak

Gradient, LVOT Peak Velocity, LVOT Stroke Volume indexed) at 30-days, 6- and

12-months compared to baseline (assessed by the independent echocardiographic Central Core Laboratory). Clinical assessment: 1. Change in clinical status assessed by means of a decrease in NYHA functional class from baseline to 3-, 6- and 12-months; 2. Frequency of presyncope/syncope and angina at 30-days, 3-, 6- and 12-months; 3. Improvement of quality of life by means of EQ-5D and KCCQ from baseline to 30-days, 6-, and 12-months; 4. Change in 6-minutes* walk test from baseline to 30-days, 6- and 12-months.

Study description

Background summary

Calcific Aortic Stenosis (CAS) affects 2 13% of the population aged 65 and over. It has become a major public health concern because of the ageing western population (by 2030 one person in three will be over the age of 65 in Europe). The mean survival rate is 2 3 years for patients diagnosed with severe symptomatic CAS: about 1.3 million patients in Europe are affected at present. The only medical response to CAS is currently invasive: Surgical Aortic Valve Replacement (SAVR) and Transcatheter Aortic Valve Replacement (TAVR). The morbidity associated with both procedures remains high: 2 5% of patients die during surgery or after 30 days, 17% die within 1 year, 35% within 3 years. These surgeries also cause numerous complications (strokes, infections and infarctions). The cost to the community is ultimately extremely high: e.g., more than 100,000$ per patient in the United States. In Europe and in the US, direct and indirect costs associated with aortic valve disease were over 50 billion$ in 2012.
Moreover, not all patients are eligible for open-heart surgery or TAVR or they refuse surgery (about 10 to 15% of patients).
CARDIAWAVE has developed a new non-invasive, real-time image-guided, therapeutic approach to treat patients suffering from Calcific Aortic Stenosis. CARDIAWAVE*s Valvosoft device is a new Non-Invasive Ultrasound Therapy (NIIUT) based on a disruptive technology involving delivering an extremely precise and focused ultrasound beam to perform a reparative effect on the aortic valve leaflets, softening the valve*s tissues, restoring leaflet mobility, and therefore improving the overall clinical status related to the aortic valve stenosis.

Study objective

The objective of the study is to evaluate the safety and performance of a new Non-Invasive Ultrasound Therapy (NIUT) with Valvosoft® in the treatment of CAS.

Study design

Prospective, Multicenter, Single-arm, Pivotal Study.

Study burden and risks

The potential risks and benefits of participating in the present clinical investigation are explicitly described in the Patient Information Sheet and are to be explained to each subject and/or his/her legal representative prior to participating in the study.
The risks of the procedure encompass those related to sedation medication and those specific to the treatment, including:
• Allergic reaction to the material of Valvosoft Applicator (silicone).
• Aortic valve damage (hematoma, infiltration, perforation).
• Aortic valve regurgitation.
• Aortic valve thrombosis.
• Arrhythmia.
• Conduction disturbance.
• Death.
• Embolism: gas, (calcific) valve material.
• Heart failure.
• Hemolysis.
• Myocardial infarction.
• Pain.
• Sensitive surrounding structures/tissues damage (e.g. aorta, atrioventricular node, lungs, myocardium,
valves).
• Skin lesion, bruise or ribs fracture.
• Stroke.
• Injuries to User.
There may be other potential AEs that are unforeseen at this time. The occurrence of the above listed potential AEs may lead to discontinuation of the procedure or study withdrawal and/or need for an alternative treatment (SAVR, TAVR, balloon angioplasty).
Since Valvosoft is an investigational device, risks are not entirely known, but are not believed to be more serious than those related to above mentioned therapies.
Any known risks for participation in this study have been minimized during the development process of Valvosoft and will be minimized through center selection and training, implementation of a DSMB, User training program and proctoring as well as in the conduct and management of the study including a careful selection of patients, compliance with the Protocol and investigational device IFU.

The sponsor, Medical Expert, and coordinating Investigator have determined that this clinical investigation is justified because the potential benefits outweigh the potential risks.

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

A subject must meet following criteria to be enrolled in the investigation:
1. Subject suffering from severe symptomatic calcific aortic valve stenosis; and
2. Subject is not recommended by the local Heart Team for immediate TAVR/SAVR;
or
3. Subject who refuses TAVR/SAVR, documented by local Heart Team; and
4. Age >=18 years; and
5. Subject willing to provide a written informed consent prior to participating

in the study; and
6. Subject who can comply with the study follow-up or other study requirements; and
7. Subject is eligible for the Valvosoft procedure according to Clinical Review Committee (CRC)

Exclusion criteria

A subject must not meet any of the following criteria to be enrolled in the investigation: 1. Subject with severe aortic regurgitation; or 2. Subject with unstable arrhythmia not controlled by medical treatment; or 3. Subjects with implanted mechanical valve in any position or bio-prosthetic valve in aortic position; or 4. Subject has a chest deformity not allowing optimal placement of the applicator and visualization of the aortic valve; or 5. Cardiogenic shock or other hemodynamic instability; or 6. Left Ventricular Ejection Fraction <=30%; or 7. Subject with mean AVAI <0,24 $cm^2/m2$; or 8. History of heart transplant; or 9. Subject requiring other cardiac surgery procedures (bypass graft surgery, mitral valve procedure, tricuspid valve procedure) within one month after Valvosoft procedure; or 10. Cardiac imaging evidence of vegetation, or 11. Acute myocardial infarction (MI) within one month prior to enrolment; or 12. Valve depth not suitable for NIUT (depth >125mm with respect to the Valvosoft imaging probe). 13. Stroke or transient ischemic attack (TIA) <=1 month prior to enrollment; or 14. Subject who is pregnant, or plan to become pregnant during the 12*months study follow*up period; or 15. Subject who is participating in another research study for which the primary endpoint has not been reached; or 16. Balloon aortic valvuloplasty (BAV) <=3 months prior to enrollment; or 17. Current endocarditis; or 18. Leukopenia (WBC <4000 cell/µL), anemia (Hgb <8 g/dL), thrombocytopenia (platelet count <15.000 cell/µL), or history of coagulopathy or hypercoagulable state; or 19. Life expectancy <12 months due to non-cardiac co-morbid conditions; or 20. Other medical, psychological, or social condition which, in the opinion of the investigator, precludes the subject from study participation. 21. Subjects who do not have Social Security and who are under legal restraint 22. Subjects who cannot read or write or are mentally not or partially capable of giving informed consent.

Study design

Design

Study type: Observational invasive
Masking: Open (masking not used)

Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	21-11-2022
Enrollment:	20
Type:	Actual

Medical products/devices used

Generic name:	Valvosoft
Registration:	No

Ethics review

Approved WMO Date:	20-05-2022
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:	19-10-2022
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	22-03-2023
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO Date:	11-07-2023
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	24-01-2024
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	NCT05235568
CCMO	NL80372.000.22