Aortic Replacement using Individualised Regenerative Allografts: Bridging the Therapeutic Gap

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

Summary

ID

NL-OMON43320

Source
ToetsingOnline

Brief title
ARISE

Condition

- Cardiac valve disorders

Synonym
Aortic Valve Disease

Research involving
Human

Sponsors and support

Primary sponsor: corlife oHG
Source(s) of monetary or material Support: EU Commission

Intervention

Keyword: Aortic Valve/Surgery, Bioprosthesis, Tissue Scaffolds

Outcome measures

Primary outcome

Primary safety endpoints:

1. Cardiovascular Adverse Reactions, e.g. all-cause mortality, major stroke, life-threatening (or disabling) bleeding, acute kidney injury-stage 3 (including renal replacement therapy), peri-procedural myocardial infarction, major vascular complication, repeat procedure for valve-related dysfunction (surgical or interventional therapy).
2. Serious Adverse Reactions, e.g. infections, immunological reactions, etc.

Primary efficacy endpoint:

Freedom from valve dysfunction leading to re-intervention or explantation at end of the study.

Secondary outcome

Secondary safety endpoints:

1. Blood parameters as additional safety data to support presence/absence of adverse reactions.
2. Time to reoperation, explantation and/or death.

Secondary efficacy endpoints (i.e. at end of the study in comparison to at implantation):

1. Diameters of the ARISE AV.

2. Transvalvular gradients.

3. Valve competence assessed by noninvasive imaging tools such as

echocardiography or cardiac magnetic resonance imaging.

Study description

Background summary

Both acquired and congenital heart disease can require heart valve replacement. Currently available heart valve substitutes are, however, not ideal as they require life-long anticoagulation, with the risk of bleeding when manufactured from non-organic material, or they degenerate when derived from animals (xenografts) or human tissue donors (homografts), leading to the need for frequent reoperation, especially in children and young adults. An ideal heart valve substitute is durable, does not require life-long anticoagulation and would have the potential to grow even when implanted in pediatric patients.

Over the last decade, tissue engineering (TE) has become a promising strategy to obtain more durable bioprosthetic valves. Allogenic matrices, established by TE methods, have successfully been tested in large animal models and show excellent hemodynamic results and mechanical integrity. Clinical applications, with and without pre-seeding of autologous stem cells have been performed in pediatric and adult patients. In recent years, implantation of non-seeded decellularized homografts became clinical practice for pulmonary valve replacement as spontaneous recellularization was observed by different research groups.

The use of a decellularized homograft for the more frequently affected aortic valve is a logical and imperative next step for this regenerative approach, but one which harbors specific physiological challanges. Haverich.and colleagues, after successful long term testing in large animal models, have used decellularized allogenic heart valve matrices for aortic valve replacement on the basis of compassionate use in 43 carefully selected patients with auspicious initial clinical results in retrospective assessment.

Study objective

The purpose of this investigation is to evaluate decellularized homograft for aortic valve replacement (ARISE AV) rates in comparison to current valve substitutes within a large prospective multicentre surveillance at 6 leading European Centres for Cardiothoracic Surgery regarding re-operation and re-intervention, hemodynamic performance, growth potential and long-term

durability.

Study design

This is a prospective, non-randomized, single-arm, multicentre surveillance study to be conducted in Europe. After ARISE AV implantation, patients will be followed and assessed at discharge, 3-, 6-, 12- and, if applicable, 24- months, thereafter.

Study burden and risks

Not applicable.

Contacts

Public
corlife oHG

Feodor-Lynen-Straße 23
Hannover D-30625
DE
Scientific
corlife oHG

Feodor-Lynen-Straße 23
Hannover D-30625
DE

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)

Children (2-11 years)
Elderly (65 years and older)

Inclusion criteria

1. Indication for aortic valve replacement according to current medical guidelines in valvular heart disease.
2. Informed consent of legal guardians or patients, assent of patients.

Exclusion criteria

1. The patient has not provided surveillance informed consent.
2. The patient shall not suffer from
a. generalized connective tissue disorders (e.g. Marfan syndrome), or
b. active rheumatic disorders, or
c. severe asymmetric calcification of the valve ring.
3. The coronary arteries of the patient shall not be in abnormal position or heavily calcified.
4. Patients shall not show hypersensitivity against sodium dodecyl sulphate (SDS), sodium desoxycholate (SDC), human collagen (or other elastic fibers) or Benzonase®.

Study design

Design

Study type:	Observational non invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	02-10-2017
Enrollment:	25
Type:	Actual

Ethics review

Approved WMO Date:	02-02-2017
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden)

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	NCT02527629
CCMO	NL59027.058.16