# Aortic Replacement using Individualised Regenerative Allografts: Bridging the Therapeutic Gap

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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…

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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

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## 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

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|---|---|
| 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

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|---|---|
| Approved WMO Date: | 02-02-2017 |
| Application type: | First submission |
| Review commission: | METC Leiden-Den Haag-Delft (Leiden) |
| | metc-ldd@lumc.nl |

# 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 |