# The REDUCE FMR Trial: Safety and Efficacy of the CARILLON Mitral Contour System in Reducing Functional Mitral Regurgitation (FMR) associated with heart failure.

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The objective of this prospective, multi-center, randomized, double-blind trial is to assess the safety and efficacy of the CARILLON Mitral Contour System in treating functional mitral regurgitation (FMR) associated with heart failure, compared to a...

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

## Summary

### ID

NL-OMON44954

**Source**
ToetsingOnline

**Brief title**
The REDUCE FMR Trial

### Condition

- Cardiac valve disorders
- Vascular therapeutic procedures

**Synonym**
The CARILLON Mitral Contour System is intented to reduce mitral regurgitation and improve heart failure symptomps

**Research involving**

Human

## Sponsors and support

**Primary sponsor:** Cardiac Dimensions PTY Ltd
**Source(s) of monetary or material Support:** Industry: sponsor= Cardiac Dimensions Pty Ltd

## Intervention

**Keyword:** Efficacy, FMR (Functional Mitral Regurgitation), Reducing, Safety

## Outcome measures

### Primary outcome

The primary efficacy endpoint is to demonstrate a statistically significant

improvement in regurgitant volume associated with the CARILLON device at twelve

(12) months, relative to the Control population.

### Secondary outcome

Safety: The following secondary safety endpoints will measure the effect of the

CARILLON Mitral Contour System on clinical safety parameters of interest,

relative to the Control population

To document the difference in the rate of major adverse events between

randomized groups, at 1 and 12-months post randomization.

Major Adverse Events are defined as a composite of the following:

- Death

- Myocardial Infarction

- Device Embolization

- Vessel Erosion, requiring percutaneous or surgical intervention

- Cardiac Perforation, requiring percutaneous or surgical intervention

- Occurrence of cardiac surgery or percutaneous coronary intervention

associated with device failure

* To assess the rate of heart failure hospitalizations (number of admissions,

and total associated days in the hospital), from the time of the index

procedure through twelve months of follow-up.

Efficacy: The following secondary efficacy endpoints will assess the effect of

the CARILLON Mitral Contour System on clinical parameters of interest, relative

to the Control population:

* To assess the change from baseline to twelve months for six-minute walk

distance

* To assess the change from baseline to twelve months in left ventricular

volumes (end diastolic and end systolic)

# Study description

**Background summary**

'Heart Failure and Functional Mitral Regurgitation':

The mitral valve is a valve between the two chambers of the left side of the heart (left atrium and left ventricle). The mitral valve opens and closes to allow blood flow between these two portions of the heart. 'Functional mitral regurgitation "occurs when the mitral valve becomes too large and not entirely closes anymore. This occurs because the left ventricle (the heart chamber which is responsible for pumping blood to the body) is increased. If the mitral valve does not close all the way anymore, a small amount of blood leaks back with each heartbeat (to the left atrium and lungs), causing the heart to pump blood and to work harder to be able to pump the same amount of blood to the rest of the body. By mitral regurgitation the heart starts to fail and patients experience symptoms such as breathlessness, fatigue (constantly tired) and / or concentration problems. This is called "heart failure".

The tool used in this medical research, the CARILLON Mitral Contour System® (CMCS), will be used for the treatment of functional mitral regurgitation. The purpose of this study is to continue the evaluation of the safety and long-term efficacy of the CMCS in people with functional mitral regurgitation due to heart failure.

**Study objective**

The objective of this prospective, multi-center, randomized, double-blind trial is to assess the safety and efficacy of the CARILLON Mitral Contour System in treating functional mitral regurgitation (FMR) associated with heart failure, compared to a randomized Control group which is medically managed according to heart failure guidelines.

**Study design**

The REDUCE FMR Trial is a prospective, multi-center, randomized, double-blind clinical trial.

Subjects will be randomized between the Treatment Group and a Control Group. Subjects will be randomized in a 3:1 ratio (Treatment : Control group).

The Treatment group will be implanted with the CARILLON device. The Control group will be medically managed according to current heart failure guidelines i,ii.

As this is a double-blinded study, both the patients (Treatment and Control groups) and the assessors of key endpoints will be blinded for 12 months.

Subjects randomized to the Control or Treatment group will have safety and efficacy assessments performed at baseline, one (1), six (6), and twelve (12) months after randomization.

Subjects randomized to the Control group may be offered the CARILLON device once they have completed the protocol defined follow-up period (Cross-Over Registry).

**Intervention**

Placement of CARILLON device.

**Study burden and risks**

The major benefit of percutaneous treatment with the CARILLON Mitral Contour System is a potential reduction in mitral regurgitation through a minimally invasive treatment method, where no current minimally invasive treatment option

exists for these subjects. The major potential benefits include:
- Clinical reduction in mitral regurgitation with a non-surgical treatment method
- Improvements in overall function including potential reduction of symptomps associated with dilated cardiomyopathy/mitral regurgitation.

Risks associated with the CARILLON Mitral Contour System include those risks associated with routine coronary angiography as well as those risks predominantly associated with the delivery and permanent placement of the CARILLON implant.
In summary, the rate of major adverse events seen in the TITAN trial (previous trial with device) was comparable to or lower than the rate of major adverse events reported and accepted with therapies that are commercially available and offered to patients with moderate heart failure. The lower rate of MAEs is consistent with the goals of a percutaneous therapy and is an important benchmark for the risk-benefit equation.

Besides the procedure the patient has to come to the hospital for screening, 1M, 6M and 12M visit, which will take in total 8-12hours. After the procedure the patient has to stay 1-2 nights in the hospital. The patient will have 5 venapuntions and 2 catherisations. Radiological exposure consists of angiograms, venograms and cinefluoroscopy with a total exposure of 10mSv throughout the whole study.
Two quality of life questionnaires at screening, 1M, 6M and 12M visit. Vital signs will be assessed at every visit.

## 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

For Main study :;1. Diagnosis of dilated ischemic or non-ischemic cardiomyopathy
2. Functional Mitral Regurgitation: - 2+ (Moderate), 3+ (Moderate/Severe), or 4+ (Severe)
3. NYHA II, III, or IV (refer to Appendix D for NYHA Classification)
4. Six Minute Walk distance of at least 150 meters and no farther than 450 meters
5. Subject meets anatomic screening criteria as determined by angiographic screening at the time of the index procedure to ensure that implant can be sized and placed in accordance with the Instructions for Use
6. Left Ventricular Ejection Fraction <= 50%
NOTE: Subjects with LVEF of 41- 50% can only be included if baseline
NYHA is class III/IV AND MR grade is 3+/4+ (moderately-severe/severe)
7. LV end diastolic dimension (LVEDD) >55mm or LVEDD/BSA >3.0cm/m2
8. Stable heart failure medication regimen for at least three (3) months (refer to Appendix G for definition of stable heart failure regimen)
9. Age >= 18 years old and <= 85 years old
10. The subject has read the informed consent, agrees to comply with the requirements, and has signed the informed consent to participate in the study
11. Female subjects of child-bearing potential must have a negative serum βHCG test;For Cross-Over registry :
1. Diagnosis of dilated ischemic or non-ischemic cardiomyopathy
2. Functional Mitral Regurgitation: - 2+ (Moderate), 3+ (Moderate/Severe), or 4+ (Severe)
3. NYHA II, III, or IV (refer to Appendix D for NYHA Classification)
4. Subject meets anatomic screening criteria as determined by angiographic screening at the time of the index procedure to ensure that implant can be sized and placed in accordance with the Instructions for Use
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7. The subject has read the informed consent, agrees to comply with the requirements, and

has signed the informed consent to participate in the study
8. Female subjects of child-bearing potential must have a negative serum βHCG test

## Exclusion criteria

Main study :
1. Hospitalization in past three (3) months due to myocardial infarction, coronary artery bypass graft surgery, and/or unstable angina
2. Hospitalization in the past 30 days for coronary angioplasty or stent placement
3. Subjects expected to require any cardiac surgery, including surgery for coronary artery disease (unprotected left main stenosis greater than or equal to 50% or, greater than or equal to 70% stenosis in at least three (3) epicardial coronary arteries in the absence of prior bypass surgery), or for pulmonic, aortic, or tricuspid valve disease within one (1) year
4. Subjects with echocardiographic documentation of non-compaction cardiomyopathy with associated hypercontractility of the cardiac structures supporting the mitral annulus
5. Subjects expected to require any percutaneous coronary intervention within 30 days of enrollment
6. Recipient of intravenous positive-inotrope infusion or intra- aortic balloon pump support within the past 30 days
7. Presence of a mechanical mitral heart valve, mitral bio-prosthetic valve or mitral annuloplasty ring
8. Pre-existing device (e.g., pacing lead) in coronary sinus (CS) / great cardiac vein (GCV), or anticipated need for cardiac resynchronization therapy (CRT) within twelve (12) months
9. Presence of a coronary artery stent under the CS / GCV in the implant target zone
10. Significant organic mitral valve pathology (e.g., moderate or severe myxomatous degeneration, with or without mitral leaflet prolapse, rheumatic disease, full or partial chordal rupture)
11. Presence of severe mitral annular calcification
12. Presence of left atrial appendage (LAA) clot. Patients with a current/ongoing (documented within the last 12 months) history of atrial fibrillation must undergo a trans-esophageal echo prior to the procedure to rule-out left atrial appendage clot to minimize the risk of thromboembolism
caused by the tissue plication
13. Cerebral vascular event within the past three (3) months
14. Presence of primary renal dysfunction or significantly compromised renal function as reflected by a serum creatinine > 2.2 mg/dL (194.5 µmol/L) OR estimated Glomerular Filtration Rate (eGFR) < 30 ml/min
15. Allergy to contrast dye that cannot be pre-medicated
16. Inability to undertake a six-minute walk test due to physical restrictions/limitations
17. Chronic severe pathology limiting survival to less than 12-months
18. Anticipated need of left ventricular assist device within twelve (12) months
19. Currently participating in an investigational study that clinically interferes
with the current study endpoints.;Cross-over registry:
1. Hospitalization in past three (3) months due to myocardial infarction, coronary artery bypass graft surgery, and/or unstable angina

2. Hospitalization in the past 30 days for coronary angioplasty or stent placement
3. Subjects with echocardiographic documentation of non-compaction cardiomyopathy with associated hypercontractility of the cardiac structures supporting the mitral annulus
4. Subjects expected to require any percutaneous coronary intervention within 30 days of enrollment
5. Recipient of intravenous positive-inotrope infusion or intra- aortic balloon pump support within the past 30 days
6. Presence of a mechanical mitral heart valve, mitral bio-prosthetic valve or mitral annuloplasty ring
7. Pre-existing device (e.g., pacing lead) in coronary sinus (CS) / great cardiac vein (GCV)
8. Presence of a coronary artery stent under the CS / GCV in the implant target zone
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with the current study endpoints.

# Study design

## Design

| | |
|---|---|
| Study phase: | 2 |
| Study type: | Interventional |
| Intervention model: | Crossover |
| Allocation: | Randomized controlled trial |
| Masking: | Double blinded (masking used) |

**Primary purpose:** Treatment

## Recruitment

NL

| | |
|---|---|
| Recruitment status: | Recruitment stopped |
| Start date (anticipated): | 07-12-2015 |
| Enrollment: | 10 |
| Type: | Actual |

### Medical products/devices used

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|---|---|
| Generic name: | CARILLON Mitral Contour System (CMCS) - Model XE2 |
| Registration: | Yes - CE intended use |

## Ethics review

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|---|---|
| Approved WMO Date: | 04-11-2015 |
| Application type: | First submission |
| Review commission: | METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht) |
| Approved WMO Date: | 30-12-2015 |
| Application type: | Amendment |
| Review commission: | METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht) |
| Approved WMO Date: | 28-12-2016 |
| Application type: | Amendment |
| Review commission: | METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht) |

## 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 | NCT02325830 |
| CCMO | NL53064.068.15 |

# Study results

Date completed: 16-07-2018

Actual enrolment: 5

**Summary results**
Trial is onging in other countries