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Carillon® Mitral Contour System® Clinical Trial Fact Sheet

Ongoing Trials

REDUCE FMR

Clinical Trial Overview: Initiated in 2015, REDUCE FMR is a prospective, blinded, randomized multi-center trial, evaluating the company's Carillon® Mitral Contour System®. Involving up to 25 leading hospitals in Europe, Australia and New Zealand, REDUCE FMR will enroll and randomize120 patients and is designed to establish Carillon as the gold standard treatment for Functional (secondary) Mitral Regurgitation (FMR) - a condition in which blood flow to the body is reduced due to an abnormally enlarged mitral valve. Patients are being enrolled and randomized into two groups: one treated with the Carillon device and the second remaining on an optimized regimen of heart failure medications, the present gold standard. This is the first blinded, randomized study in the field of FMR. European countries participating in the trial include France, Germany, the Netherlands, Poland and the United Kingdom. For more information please visit http://www.cardiacdimensions.com/PhysicianResources/current_studies.html.

Primary Study Objectives: The study will evaluate the device's ability to reduce mitral regurgitation, improve functional capacity and quality of life as well as induce reverse cardiac remodeling in a symptomatic heart failure patient population. The REDUCE FMR clinical trial follows three successful multi-center studies, featuring the Carillon device.

Study Population:

- Dilated ischemic/non-ischemic cardiomyopathy
- FMR moderate to severe (2+ – 4+)
- NYHA II to IV
- Six-minute walk distance of 150 to 450 meters
- Optimized and stable medical management

Endpoints:

- The primary endpoint to show efficacy will be reduction in regurgitant volume.
- Secondary endpoints include:
  - Major adverse event (MAE) rates at 30-days and 12 months
  - Heart Failure hospitalization rates
  - Six-minute walk distance
  - Left ventricle volumes assessed by echocardiography
  - Overall patient quality of life

Trial Timeline: Patient enrollment in the REDUCE FMR trial is currently underway.

Completed Trials

TITAN II

The TITAN II clinical trial was a follow-up to the landmark TITAN clinical trial. TITAN II was a prospective, single-arm European multi-center clinical trial initiated to further evaluate an enhanced version of the Carillon system. Patient enrollment began in 2011 and the study was completed with 12-month follow-up in 2014.

A total of 30 patients across five sites were implanted with the Carillon system and were followed for a one-year period as part of the TITAN II trial. Patients were evaluated for improvements in mitral regurgitation, functional capacity, quality of life and reverse cardiac remodeling.

Data from the TITAN II trial presented in 2014 showed significant and sustained improvements in mitral regurgitation, functional capacity, quality of life and reverse cardiac remodeling. The long-term safety and efficacy data, which were consistent with previous trials, reinforced the product enhancements that were completed in 2011. Additional results from the TITAN II trial are expected to be published in 2016.

TITAN

Initiated in 2009, the TITAN study was conducted at seven centers located in Germany, Poland, and France. The Carillon device was implanted in a total of 36 patients. The TITAN study assessed safety and efficacy at 1, 6, 12, 18, and 24 months, as well as long-term safety annually through 5 years. The primary safety endpoint showed a low rate of MAEs, with less than 2% of the study population experiencing an MAE.

The TITAN study also showed that patients experienced significant reductions in their mitral annulus dimensions. This was associated with a reduction in mitral regurgitation and improvements in other key functional parameters including NYHA (New York Heart Association) class, six-minute walk distance, and disease-specific quality of life (using the Kansas City Cardiomyopathy Questionnaire). These improvements were seen acutely as well as through the 12-month timeframe and were also associated with reverse remodeling of the left ventricle.[1]. Data from the TITAN study were published in the ***European Journal of Heart Failure*** **in August 2012.**

AMADEUS

The AMADEUS study was the first multi-center evaluation of the Carillon Mitral Contour System. The AMADEUS study was a 30-patient safety and performance study of the Carillon Mitral Contour System conducted at six centers located in Germany, Poland, and the Netherlands. The study was designed to assess the safety of the Carillon Mitral Contour System. AMADEUS enrollment was completed during the second quarter of 2007. The trial began in 2005.

The study showed a low rate of MAEs at the 30-day time point. The clinical data indicated statistically significant reductions in all quantitative echocardiographically derived parameters of mitral regurgitation, as well as clinically significant improvements of other key functional parameters including NYHA class, six-minute

[1] Siminiak, T., et al. (2012). Treatment of functional mitral regurgitation by percutaneous annuloplasty: results of the TITAN Trial. *European Journal of Heart Failure, 14*: 931–938.

walk distances, and quality of life.[2,3] Data from the AMADEUS study were published in July 2009 in *Circulation* and in August 2009 in the *American Journal of Cardiology*.

CAUTION: The Carillon Mitral Contour System has received CE Mark approval and is available for sale in the European Union.

CAUTION: The Carillon Mitral Contour System is not approved for use in the United States.

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[2] Schofer J, et al. (2009) Percutaneous mitral annuloplasty for functional mitral regurgitation: results of the Carillon Mitral Annuloplasty Device European Union Study. *Circulation*. 120: 326-333.
[3] Siminiak, T., et al. (2009) Effectiveness and Safety of Percutaneous Coronary Sinus-Based Mitral Valve Repair in Patients With Dilated Cardiomyopathy (from the AMADEUS Trial). *American Journal of Cardiology*. 104: 565-570.