Evaluation of the 5-year Safety and Performance of the Medtentia Annuloplasty Ring in Adults - Follow-up to Clinical Investigation 2010-040

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PROTOCOL No: **2010-040FU5**

PROTOCOL NAME: **Evaluation of the 5-year Safety and Performance of the Medtentia Annuloplasty Ring in Adults - Follow-up to Clinical Investigation 2010-040**

STATISTICAL ANALYSIS PLAN

Version: **1.0**

Effective Date: **27FEB2020**

Revision History

Version number	Date	Description of Modifications
1	27FEB2020	First version of the document

Distribution List

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Abbreviations

Abbreviation	Explanation
AE	*Adverse Events*
CM	*Concomitant Medications*
MedDRA	*Medical Dictionary for Regulatory Activities*
SAE	*Serious Adverse Event*
SAP	*Statistical Analysis Plan*
SAR	*Statistical Analysis Report*
TLF	*Tables, Listings, Figures*

1 GENERAL TRIAL INFORMATION

This is a statistical analysis plan (SAP) for trial MAR2010-040FU5. It is based on the final trial protocol Clinical Investigation Plan version 1.0 (08MAY2019).

1.1 Trial objectives

The primary objective of this clinical investigation is to evaluate long-term performance and safety of MAR five years after mitral valve repair surgery.

The primary safety objective is

- to evaluate the safety of the MAR in terms of longstanding complications and adverse events.

The primary performance objective is

- to evaluate the performance of the MAR 5 years post MV repair surgery.

The secondary objectives of the trial are

- to evaluate the safety of the MAR in terms of survival since the last visit of clinical investigation 2010-040,
- to obtain additional performance information.

1.2 Trial type and design

Observational, single-center, follow-up study.

2 RANDOMISATION

N/A

3 SAMPLE SIZE

The sample size will be determined by the number of qualifying subjects from the clinical investigation 2010-040 who can be located and who agree to participate in this follow-up investigation. Subjects who underwent successful MAR implantation and completed 2010-040 clinical investigation will be contacted and invited to participate in the follow-up study. Maximum of 11 subjects is anticipated to be enrolled in this follow-up clinical investigation.

4 STATISTICAL METHODS

4.1 Data sets to be analysed

The Medtentia Annuloplasty Ring population (MAR population) consists of subjects, who underwent MV repair operation with successful MAR implantation in clinical investigation 2010-040. All analysis will be performed on the MAR population.

4.2 Handling of missing values and other data conventions

Missing data will not be imputed.

4.3 Demographic and baseline characteristics

Subject disposition, demographic and other baseline data will be presented using summary statistics and data from subjects in the MAR population.

4.4 Analysis of primary objectives

9.2.1 Primary Endpoints

9.2.1.1 Safety

The occurrence, nature and frequency of significant medical events since the last visit of clinical investigation 2010-040 as defined in section 8.4 of the CIP will be listed and tabulated.

9.2.1.2 Performance

As per the CIP, the percentage of subjects with stable MR condition or any improvement in MR class as described in the ACC/AHA Guidelines 5 years after MAR implantation will be calculated with its two-sided 95% CI (if applicable). Any deviations from the planned analysis will be explained in the Statistical Analysis Report (SAR).

4.5 Analysis of secondary objectives

9.2.2 Secondary Endpoints

9.2.2.1 Safety

All-cause mortality collected retrospectively since the last visit of clinical investigation 2010-040 will be summarized in a frequency table.

The occurrence, nature and frequency of adverse device effects (ADEs) and/or device deficiencies (DDs) since the last visit of clinical investigation 2010-040 will be summarized.

Number of cardiovascular admissions occurred since the last visit of clinical investigation 2010-040 will be summarized, if applicable.

Descriptive statistics with two-sided 95% CIs, when appropriate, will be presented for all safety data for the MAR population.

4.6 Analysis of safety and tolerability

9.2.2.2 Other Safety

The number of subjects with clinically significant abnormal findings in TTE, ECG, or vital signs and type of abnormal findings will be listed and tabulated.

9.2.2.3 Performance

The MR parameters left ventricle reverse remodeling (standard measurement points) and coaptation height will be tabulated using descriptive statistics. For the same parameters, a comparison with the clinical investigation 2010-040 2-year follow-up visit will be presented by absolute change and %-change. The changes in MR parameter values may also be analyzed graphically.

The Changes in NYHA classification when compared to the clinical investigation 2010-040 2-year follow-up visit will be summarized.

The number of subjects with recurrence of MR defined as changing of MR to moderate or severe according to ACC/AHA classification determined by TTE will be tabulated.

The percentage of subjects with recurrence of MR from 2-year follow-up visit will be calculated with their two-sided 95% CI, if applicable.

Any deviations from the planned analysis will be explained in the Statistical Analysis Report (SAR).

9.2.2.4 Other

Number of subjects with re-operation or MV reintervention due MAR performance failure or malfunction will be summarized.

Quality of life scores as measured by the 15D©questionnaire will be summarized.

9.3 Reporting of Deviations

Any deviations will be collected to a deviation log by the study monitor and listed by subject in the final report.

4.7 Execution of statistical analysis

Statistical analysis will be performed by [redacted].

5 HARDWARE AND SOFTWARE

Statistical analysis, tables and subject data listings will be performed with SAS 9.4 for Windows.

6 REFERENCES

7 APPENDIX