Novapak Prospective Observational Clinical Trial
Statistical Analysis Plan Version 1.0
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Medtronic

Statistical Analysis Plan

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Confidentiality Statement

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1. Version History

Version	Summary of Changes	Author(s)/Title
1.0	• Not Applicable, New Document	Hui Xiong, Senior Statistician

2. List of Abbreviations and Definitions of Terms

Abbreviation	Definition
AE	Adverse Event
CE	Conformité Européene
CIP	Clinical Investigation Plan
EU MDR	European Medical Device Regulation
ISO	International Organization for Standardization
SAP	Statistical Analysis Plan

3. Introduction

Medtronic, Inc. is sponsoring the Novapak Nasal Sinus Packing and Stent Study, a prospective, observational, multi-site, non-controlled, non-randomized, case-series, investigational, clinical study. The purpose of this study is to assess the safety of the Novapak Nasal Sinus Packing and Stent device used as indicated post-operatively in patients undergoing nasal/sinus surgery. In addition, this study will observe some key measures of device effectiveness from the physician and subject perspective.

The Novapak Nasal Sinus Packing and Stent study is being conducted as a non-significant risk post-market investigational study in the US and Canada in accordance with Canadian local regulations and International Organization for Standardization (ISO) 14155:2020 in support of European Medical Device Regulation (EU MDR) regulatory submission for a Conformité Européene (CE) Mark.

The Novapak prospective observational clinical trial clinical investigation plan (CIP) provides the guidelines for this statistical analysis plan (SAP). The purpose of this SAP is to provide details for Novapak therapy-specific data analyses. Reports generated using study data may not contain all the analyses described below; however, if a report contains an objective outlined within this document, the analysis of that objective will be performed as described in this SAP. If additional analyses are required but not covered in this SAP, a separate SAP addendum may be needed.

4. Study Objectives

4.1 Primary Objective

The primary objective of this study is to assess the safety profile of the Novapak Nasal Sinus Packing and Stent device used as indicated post-operatively in patients undergoing nasal/sinus surgery.

4.2 Secondary Objectives

The secondary objectives of this study will gather data to support the effectiveness of Novapak's inherent features and claims of performance:

Adhesions – Sinus packing devices act as a space occupying stent to prevent raw tissues from contact and forming unwanted, obstructive tissue connections known as synechia or adhesions. This study will collect the number of adhesions observed by endoscopic examination as well as a grade of the adhesions based on the percentage of vertical height of the middle turbinate taken up by the adhesion. This data will be compared to historical data related to adhesions post sinus surgery.

Control of bleeding – Sinus packing devices control bleeding by absorption and pressure on the bleeding surfaces known as the tamponade effect. Chitosan a component of Novapak also has hemostatic properties. This study will collect data related to post-operative bleeding. Since bleeding can be different for each subject and based on the extent of tissue trauma; a baseline observation immediately post-surgery using the Boezaart Surgical Field Grading Scale will be collected. After the packing is applied the surgical field will be graded again. In addition, any residual bleeding will be observed and noted at the subject visits.

Aid in healing – Novapak acts as an adjunct to aid in the natural healing process by providing a moist environment for the tissues during the proliferation phase of wound healing. In addition, the chitosan component within Novapak has hemostatic properties and is antibacterial to reduce unwanted microbial action which could lead to inflammation. The physician will grade the sinuses before surgery and then at each subject visit using the Lund-Kennedy scoring system. In addition, the subjects will provide sinus health responses to the SNOT-22 questionnaire prior to surgery and again at each subject visit.

5. Investigation Plan

Prospective, observational, multi-site, non-controlled, non-randomized, case-series, with adult subjects undergoing nasal/sinus surgery and using Novapak Nasal Sinus Packing and Stent device used as indicated post-operatively with 14-day and 30-day follow-up visits. The study is expected to be conducted at up to 5 study sites located in the US and/or Canada. A minimum of 75 subjects will be enrolled in the study and one device is expected to be used per subject. Study sites that enroll faster than others will be allowed to do so in order to maintain an adequate enrollment rate; however, there is a site maximum enrollment of 60% (45 subjects) of the total enrollment. No known factors have been foreseen that may compromise the outcome of the clinical study or interpretation of the results.

6. Determination of Sample Size

As this is not a powered hypothesis-driven study, the sample size of a minimum of 75 subjects was selected that is adequate to assess the safety and treatment effectiveness of the Medtronic Novapak Nasal Sinus Packing and Stent device, not determined by statistical methods.

7. Statistical Methods

7.1 Study Subjects

7.1.1 Disposition of Subjects

Disposition of subjects will be summarized by site, product model used, follow-up visit, etc., by flow chart, table, and/or listing.

7.1.2 Clinical Investigation Plan (CIP) Deviations

If applicable, protocol deviations will be summarized by deviation type with deviation and subject counts.

7.1.3 Analysis Sets

The analysis population will include all patients that fulfill inclusion and exclusion criteria and use the Novapak Nasal Sinus Packing and Stent device in their nasal/sinus surgery.

7.2 General Methodology

Categorical variables will be summarized with frequencies and percentages.

Summaries of continuous variables will include the sample size, mean and standard deviation. Additional summaries of the number with missing data, minimum, median, maximum, or sum may be presented as appropriate.

Statistical inferences will be performed as needed. For continuous variables, t-test, ANOVA, or nonparametric Wilcoxon test will be used; for categorical variables, Chi-square test or Fisher's exact test will be used.

7.3 Center Pooling

Data from all study centers will be pooled for the analysis. Descriptive summary may be provided by study center. If substantial center heterogeneity is present, exploratory analysis may be performed to help understand the variations.

7.4 Handling of Missing, Unused, and Spurious Data and Dropouts

The analysis will be based on all observed data. No statistical techniques will be used to impute missing data for continuous or categorical outcomes. If a subject's data are missing for any reason, that subject will not be included in that portion of the analysis. The number of subjects included in each analysis will be reported so that the reader can assess the potential impact of missing data.

7.5 Adjustments for Multiple Comparisons

No adjustments for multiple comparisons will be made.

7.6 Demographic and Other Baseline Characteristics

7.6.1 Demographics

Demographics will be summarized in descriptive tables, including but not limited to:

- Age at consent (in years)
- Gender
- Race
- Ethnicity

7.6.2 Baseline Characteristics

Baseline characteristics will be summarized in descriptive tables, including but not limited to:

- Surgical history

7.6.3 Baseline Assessment

Baseline assessments will be summarized using descriptive statistics for patients with scores as follows:

- SNOT-22 score[1]
- Lund-Mackay score[2]
- Lund-Kennedy score[3]

7.7 Treatment Characteristics

Treatment characteristics will be summarized in descriptive tables, including but not limited to:

- Surgical location (left, right, or both nasal cavities)
- Model (CS3600, CS3900)

7.8 Interim Analyses

No interim analyses are planned for this study.

7.9 Evaluation of Objectives

7.9.1 Safety objective assessment

The safety objective is evaluated by:

- The number of Adverse Events that are directly attributed to the device and/or those that cannot be determined.
- The number of Adverse Events.

7.9.2 Effectiveness objective assessment

The effectiveness objective is evaluated by:

- The number of adhesions from procedure through 1-month post treatment.

- The graded percentage of vertical height of the middle turbinate taken up by the adhesion using an ordinal scale (0-3) from procedure through 1-month post treatment.
- The measure control of bleeding by comparing Boezaart Surgical Field Grading Scale scores[4] post operatively, prior to Novapak insertion and post Novapak insertion.
- The measure of healing by comparing Lund-Kennedy scores before surgery and at 2 weeks and 1-month post treatment.
- The measure of health by comparing subject scores from the SNOT-22 questionnaire before surgery and at 2 weeks and 1-month post treatment.

7.10 Changes to Planned Analysis

Not applicable.

8. Validation Requirements

Statistical programming code that affects the result of the main analysis for the primary objective shall be validated using Level I validation.

Programming code that affects the result of the main analysis for the secondary objectives shall be validated using at least Level II validation.

In addition, those main statistical analyses that are planned for publication and have not been previously validated should be validated with at least Level II validation.

Level III validation may be used for any previously validated program where only minor/administrative changes were made (e.g., change the location of the data directory). Additional measures may need to be validated as determined by statistical management.

9. References

1. SNOT-20 Copyright © 1996 by Jay F. Piccirillo, M.D., Washington University School of Medicine, St. Louis, Missouri. SNOT-22 Developed from modification of SNOT-20 by National Comparative Audit of Surgery for Nasal Polyposis and Rhinosinusitis Royal College of Surgeons of England.

2. Lund VJ, Mackay IS. Staging in Rhinosinusitis. Rhinology, 31, 183-184, 1993

3. Lund VJ, Kennedy DW. Staging for rhinosinusitis. Otolaryngol Head Neck Surg. 1997 Sep;117(3 Pt 2):S35-40. doi: 10.1016/S0194-59989770005-6. PMID: 9334786.

4. Boezaart AP, Van Der Merwe J, and Coetzee A. Comparison of sodium nitroprusside and esmolol induced controlled hypotension for functional endoscopic sinus surgery. Can J Anaesth 42:373–376,1995.