Statistical Analysis Plan (SAP)

A Prospective, Multi-Center Study of the ECHELON Endopath™ Staple Line Reinforcement Device in Gastric and Lung Resection Procedures

Protocol Number: ESC-2018-03

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A Prospective, Multi-Center Study of the ECHELON Endopath™ Staple Line Reinforcement Device in Gastric and Lung Resection Procedures

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Revision History

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Table of Contents

1 Introduction

This is the Statistical Analysis Plan (SAP) for the final analysis of data collected under Protocol ESC-2018-03. This SAP describes in detail the statistical methodology and statistical analyses for this protocol.

1.1 Study Objectives

The primary objective of this study is to prospectively evaluate safety in a post-market setting following use of ECHELON ENDOPATH™ Staple Line Reinforcement (ECHELON SLR) in gastric and lung resection procedures per its Instruction For Use (IFU). The secondary objective will be to capture usability data of the device.

1.2 Study Design

This is a prospective, single-arm, multi-center clinical study designed to evaluate the intra-operative performance of the staple line reinforcement device in gastric and lung resection procedures in a post-market setting. Investigators are to perform the procedure using the device in compliance with their standard surgical approach and the ECHELON ENDOPATH™ Staple Line Reinforcement Device IFU.

Each site will utilize consecutive screening and enrollment in an effort to generate a random and representative patient population sample. Subjects will be consented and screened anytime during a period of 8 weeks prior to the date of surgery. Subjects will be considered treated when at least one ECHELON SLR has been placed during the procedure. Procedures will be performed per each institution's standard-of-care (SOC). All treated subjects will be followed post-operatively through discharge and again at 28, 70, and 135 days (± 14 days) post-surgery. From the surgery date to study exit the duration will be approximately 19 weeks. Follow-up by phone for subjects is allowed when an on-site visit is not planned.

A minimum of 243 and a maximum of 431 eligible subjects are planned to be enrolled in up to 16 sites in the United States to ensure at least 112 subjects were treated for gastric procedures and at least 131 subjects were treated for lung resection procedures. An adaptive approach to sample size re-estimation will occur after approximately 50% of the originally planned sample size in each group has been enrolled.

2 Treatment Assignment

This is a single-arm study where all enrolled subjects will plan have the ECHELON SLR utilized during the surgical procedure.

3 Randomization and Blinding Procedures

As this is a single-arm study, no randomization will occur, and no blinding procedures are required.

4 Interval Windows

Interval windows will not be defined outside of those already specified in the protocol for visit scheduling. The final visit occurs approximately 19 weeks after surgery,. The protocol Schedule of Events specifies a window of 14 days around the scheduling of follow-up visits, and any information entered in the eCRFs at this visit will correspond to the associated visit. There will be no assigning of observations to time points outside of the visit to which they are recorded in the eCRFs. However, if an adverse event occurs at an unscheduled visit, it will be entered as a unscheduled visit.

5 Levels of Significance

Each ofthe two hypotheses will be evaluated using a one-sided significance level of 0.025 and the overall level of significance across the study will be controlled at a value that does not exceed 0.05. Estimation of all additional endpoints will be performed using 95% confidence intervals.

6 Analysis Sets

The summary of all performance and safety endpoints will be performed on the set of subjects in whom the ECHELON SLR is utilized during the surgical procedure. The summary of all primary and secondary endpoints will be performed by procedure group and in total.

7 Sample Size Justification

For the gastric procedure group, a sample size of at least 99 subjects is required to have a minimum of 80% power for rejecting the null hypothesis when the expected rate of the primary endpoint is 7% based on current available literature. Similarly, for the lung resection group, a sample size of at least 116 subjects is required to have a minimum of 80% power for rejecting the null hypothesis when the expected rate of the primary endpoint is 6% based on current available literature. Each calculation is determined using the Normal approximation with a one-sided significance level of 0.025 and makes the assumption of a 20% reduction in the expected rate of the primary endpoint with the ECHELON SLR. The performance goal-based hypotheses specified in Section 8.4.1 are based on establishing acceptable initial performance of the ECHELON SLR by ruling out a doubling of the expected risk that has been reported in the literature for these procedures. Accounting for an anticipated dropout rate as high as 12.5% in each procedure group leads to an initial planned sample size of 112 subjects in the gastric group and 131 subjects in the lung resection group.

Given the lack of available clinical data on the performance of the ECHELON SLR, an adaptive approach to sample size re-estimation will occur after approximately 50% of the originally planned sample size has been enrolled into each procedure group. The purpose of this interim analysis will be to estimate the rate of the primary endpoint in each group or concurrently to estimate the size of the relative reduction of this endpoint relative to the values reported in current literature. The current sample size calculation assumes an expected background rate of 7% in the gastric group, 6% in the lung resection group, and that a 20% relative reduction will be observed with the ECHELON SLR. Based on the values observed at the interim analysis time points for each group, the within-group sample sizes will be re-estimated. A sample size of 200 subjects has been set as the maximum sample size that will be pursued following the interim analysis and sample size re-estimation process in the gastric group and a maximum of 231 subjects has been set in the lung resection group.

The sample size re-estimation for each group will apply the methodology described in Lan and Trost[1] and Wang, Keller, and Lan[2]. Following that methodology, the prespecified conditional power lower limit for futility is set at 10%, and the upper limit for maintaining the original sample size is set at 80%. Specifically, if the conditional power evaluated at the time of the interim analysis is ≤ 0.10, the trial within that procedure group will be stopped for futility and the null hypothesis will be accepted. If the conditional power is ≥ 0.80, then the study will continue to its originally planned completion with no sample size adjustment. If the conditional power is between 0.10 and 0.80, the sample size will be increased so as to maintain the conditional power at a target of 0.80 under the current trend of the data, up to the maximum values specified above.

As discussed in Lan and Trost, given that the lower limit of conditional power for futility is at least 0.10, the Type I error rate is controlled at the nominal level, and no adjustment to the planned significance level of 0.025 is required under this approach.

8 Analyses to be Conducted

8.1 General Conventions

Categorical variables will be summarized descriptively by frequencies and associated percentages. Continuous variables will be summarized descriptively by number of subjects, mean, standard deviation, median, minimum, and maximum. Confidence intervals will also be provided for procedure-related variables.

Analyses will be conducted using SAS software. Analyses will be performed first using gastric data to populate tables and listing or parts of the tables and listing relevant to gastric. When the full data is available, a combined analyses (gastric and lung) will be conducted next. During the course of programming of tables that are mocked up in this SAP, minor modifications may become necessary. Examples of these minor modifications include, but are not limited to, re-wording of a footnote, addition of a footnote, re-labeling of a column, or addition or removal of a column from a listing. In

cases where modifications to tables or listings are not related to a change in statistical analysis methodology or conclusions that could be made on the originally proposed methodology, then no amendment of the SAP is necessary. Any final analyses that differ from what has been specified in this document will be identified within the final statistical output and documented within the clinical study report.

8.2 Disposition of Study Subjects

Subject disposition will be summarized in total and by procedure group using counts and percentages. The number and percentage of subjects completed and discontinued will be tabulated along with specific reasons for discontinuation.

8.3 Demographic, Baseline, and Surgical Characteristics

Summary statistics of subject demographics (age, gender, race, and ethnicity) will be presented in total and by procedure group. Similar summaries will also be provided in table and/or listing for baseline and surgical characteristics including but not limited to body mass index, surgical procedure, smoking history, ASA physical status classification, type of procedure conducted ,procedure duration,occurrence of blook transfusion, edocutter firing , air leak duration in lung resection..

8.4 Primary and Secondary Endpoints and Associated Hypotheses

8.4.1 Primary Endpoint and Associated Hypotheses

The primary endpoint for this study is the incidence of device-related AEs through the 70-day post-procedure follow-up visit. Specific device-related AEs that will be captured and counted toward the primary endpoint are listed below.

- Gastric
    - Bleeding (defined as below)
        - Occurrence of post-operative blood transfusion deemed related to bleeding at the staple line; or
        - Return to operating room before 70-day post-procedure follow-up visit due to bleeding deemed related to the staple line;
    - Leak (defined as below)
        - Occurrence of intra-operative or post-operative gastrointestinal leak related to the staple line as documented intra-operatively, by clinical exam, or radiographically;
    - Stricture (defined as below)
        - Occurrence of stricture documented radiographically or by endoscopy along the staple line;
- Lung Resection
    - Prolonged air leak deemed related to the staple line (defined as below)
        - Greater than postoperative day 7 (procedure=day 0);

- Empyema (defined as below)
  - Purulent fluid collection in the pleural space documented radiographically, excluding chronic empyema

The following hypotheses will be evaluated for the primary endpoint for gastric procedures:

$$H0: pG \geq 14.0\%$$
$$H1: pG < 14.0\%$$

Where pG is the percentage of subjects experiencing at least one occurrence of bleeding, leak, or stricture through 70 days. A 95% confidence interval will be calculated for pG based on the sample proportion of subjects experiencing the endpoint using the Normal approximation to the Binomial distribution and the upper limit of this confidence interval will be compared to 14.0% to evaluate the above hypotheses. A p-value will be determined based on the same Normal approximation methodology.

A similar methodology will be applied to the data observed in lung procedures to evaluate the following hypotheses:

$$H0: pL \geq 12.0\%$$
$$H1: pL < 12.0\%$$

Where pL is the percentage of subjects experiencing at least one occurrence of prolonged air leak or empyema through 70 days.

8.4.2 Secondary Endpoints and Associated Hypotheses

The secondary performance endpoints for this study are listed below.

- Number of study devices replaced during surgery due to slipping or bunching or not properly loaded onto stapler cartridge; and
- Device questionnaire by procedure group (gastric and lung resection) to capture usability.

8.4.3 Additional Endpoints

No additional endpoints defined for this study.

8.5 Safety Analyses

The primary safety endpoint in this study is the occurrence of device-related AEs. All device-related and procedure-related AEs reported during the study will be coded to MedDRA. All reported AEs will be summarized by MedDRA system organ class and preferred term by procedure group and in total. Separate summaries will be provided for device-related and procedure-related AEs. Serious AEs will be summarized in a similar manner. All adverse events considered unlikely, possibly, probably, or causally related to the device or the procedure will be collected during this study and are defined in the following subsections.

8.5.1 Adverse Event

An AE is defined as any untoward medical occurrence, regardless of its relationship to the study device or the study procedure. An untoward medical occurrence includes any new, undesirable

medical experience or worsening of a pre-existing condition, which occurs throughout the duration of the clinical study.

8.5.2 Adverse Device Effect

An adverse device effect (ADE) is an AE related to the use of a study device. This includes any AE resulting from insufficient or inadequate IFU, deployment, implantation, installation, operation, or any malfunction of the study device. An ADE may also include any event resulting from user error or from intentional misuse of the study device

8.5.3 Serious Adverse Event

It is the Investigator's responsibility to determine the "seriousness" of a reportable AE.
A SAE is defined as an AE (as defined in Section 8.5.1) that results in any of the following:

- Death;
- A life-threatening illness or injury;
- A permanent impairment of a body structure or a body function;
- Required in-patient hospitalization or prolongation of existing hospitalization;
- Resulted in medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function; or
- Led to a fetal distress, fetal death, or a congenital abnormality or birth defect.

8.5.4 Serious Adverse Device Effect (SADE)

A serious ADE (SADE) is an ADE that has resulted in any of the consequences characteristic of a SAE or that might have led to any of these consequences if suitable action had not been taken or intervention had not been made or if circumstance had been less opportune.

8.5.5 Unanticipated Serious Adverse Device Effect (USADE)

An unanticipated serious adverse device effect (USADE) is an effect which, by its nature, incidence, severity or outcome, has not been identified. An anticipated SADE is an effect which by its nature, incidence, severity, or outcome, has been identified in the IFU

8.6 Plans for Interim Analysis

One interim analysis in each procedure group is planned for sample size re-estimation. Details are provided in Section 7 above. Study enrollment may continue while the interim analysis is ongoing.

8.7 Handling of Missing Data

All summaries will be performed only on subjects undergoing the scheduled procedure and only observed data will be summarized. There will be no imputation of data for early terminated subjects or for missing data within the database for the primary evaluation of the hypotheses specified above.

8.8 Sensitivity Analysis

For subjects missing data at Visit 4 (70 ± 14 Days Post Procedure Follow Up visit), a sensitivity analysis will be conducted to evaluate whether the results hold under imputation using multiple imputation approach. A Fully Conditional Specification (FCS) method that employ conditional distribution of each primary endpoint variable will be implemented using proc mi to impute device specific AE at Visit 4. The following baseline variables: age, gender, and race, as well the the device-related and procedure-related AEs at Visit 2 (Procedure through discharge visit) will be used to inform the pattern of missingness. One hundred imputed datasets will be generated for each primary endpoint. SAS procedures genmod will be employed to obtain the relevantparameter estimates from each dataset. The resulting one hundred estimates for each primary endpoint will be combined using SAS procedure mianalyze.

8.9 Subgroup Analysis

Descriptive summaries are planned to be provided for each procedure within the lung resection group (lobectomy, segmentectomy, etc.). Subgroup analyses may be performed for additional groups pending the distributions of baseline demographic or clinical characteristics. These analyses will be exploratory, and summary statistics for the procedure-related parameters will be provided for each subgroup.

8.10 Assessment of Site Homogeneity

No summaries or adjustments by study site are planned for this study.

9 Data Monitoring Committee (DMC)

No Data Monitoring Committee is planned or will be utilized during this study.

10 Change In The Conduct Of The Study or Planned Analysis

N/A

11 REFERENCES

1. Lan, K. K. G., & Trost, D. C. (1997). Estimation of parameters and sample size re-estimation. In *Proceedings-Biopharmaceutical Section American Statistical Association* (pp. 48-51). American Statistical Association.
2. Wang, C., Keller, D. S., & Lan, K. K. G. (2002). Sample size re-estimation for binary data via conditional power. In *American Statistical Association Proceedings of the Joint Statistical Meetings* (pp. 3621-3626).

Appendix: Table Shells and List of Listings to be Generated

Table shells are provided below for all summaries to be generated for this study. These shells are a guide to the general layout of data to be presented. Minor modifications can be made to suit existing programs or macros that are available. Additionally, a list of all listings to be created is provided corresponding to the eCRFs that are used during this study. All fields collected will be listed.

Table 1
Subject Disposition
All Subjects

	Gastric	Lung Resection	Total
Signed Informed Consent	xx	xx	xx
Analysis Set	xx	xx	xx
Completed 70 day Visit	xx (xx.x%)	xx (xx x%)	xx (xx.x%)
Completed the Study	xx (xx.x%)	xx (xx x%)	xx (xx.x%)
Discontinued from the Study	xx (xx.x%)	xx (xx x%)	xx (xx.x%)
Reason for Discontinuation			
Withdrawal of consent	xx (xx.x%)	xx (xx x%)	xx (xx.x%)
Adverse Event	xx (xx.x%)	xx (xx x%)	xx (xx.x%)
Death	xx (xx.x%)	xx (xx x%)	xx (xx.x%)
Lost to Follow-up	xx (xx.x%)	xx (xx x%)	xx (xx.x%)
Site or Study Termination	xx (xx.x%)	xx (xx x%)	xx (xx.x%)
Other	xx (xx.x%)	xx (xx x%)	xx (xx.x%)

All percentages are calculated using the number of subjects in the Analysis Set as the denominator.

Programming note: Only categories actually observed in the database need to be displayed for Reason for Discontinuation.
Programmin note: First analysis will populate only the Gastric column. The Lung and Total columns will be populated when all data is available.

Table 2
Subject Demographics and Vital Signs
Analysis Set

Characteristic	Gastric (N = ##)	Lung Resection (N = ##)	Total (N = ##)
Age at Consent (yrs)			
N	xx	xx	xx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx x (xx.x)
Median (Min, Max)	xx.x (xx, xx)	xx.x (xx, xx)	xx.x (xx, xx)
Gender, n (%)			
Male	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Female	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Unknown	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Ethnicity, n (%)			
Hispanic or Latino	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Not Hispanic or Latino	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Not Reported	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Race, n (%)			
Race 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
……	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Height (cm)			
n	xx	xx	xx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx x (xx.x)
Median (Min, Max)	xx.x (xx, xx)	xx.x (xx, xx)	xx.x (xx, xx)
Weight (kg)			
n	xx	xx	xx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx x (xx.x)
Median (Min, Max)	xx.x (xx, xx)	xx.x (xx, xx)	xx.x (xx, xx)
Body mass index (kg/m^2)			
n	xx	xx	xx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx x (xx.x)
Median (Min, Max)	xx.x (xx, xx)	xx.x (xx, xx)	xx.x (xx, xx)

Denominator and percentages are based on subjects with non-missing data.

Programmin note: First analysis will populate only the Gastric column. The Lung Resection and Total columns will be populated when all data is available.

Table 3
Medical History By System Organ Class and Preferred Term
Analysis Set

System Organ Class	Preferred Term	Gastric (N = ##)	Lung Resection (N = ##)	Total (N = ##)
Total		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
System Organ Class 1		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Preferred Term 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Preferred Term 2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Preferred Term 3	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
System Organ Class 2		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Preferred Term 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Preferred Term 2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
System Organ Class 3		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Preferred Term 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Preferred Term 2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Preferred Term 3	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
System Organ Class 4		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Preferred Term 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Preferred Term 2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Programmin note: First analysis will populate only the Gastric column. The Lung Resection and Total columns will be populated when all data is available.

Table 4
Backgrond Information -ASA Score and Smoking Status
Analysis Set

Characteristic	Gastric (N = ##)	Lung Resection (N = ##)	Total (N = ##)
ASA Score			
I	xx (xx.x%)	xx (xx.x%)	xx (xx x%)
II	xx (xx.x%)	xx (xx.x%)	xx (xx x%)
III	xx (xx.x%)	xx (xx.x%)	xx (xx x%)
IV	xx (xx.x%)	xx (xx.x%)	xx (xx x%)
V	xx (xx.x%)	xx (xx.x%)	xx (xx x%)
Smoking Status			
Current smoker	xx (xx.x%)	xx (xx.x%)	xx (xx x%)
Former smoker	xx (xx.x%)	xx (xx.x%)	xx (xx x%)
Never smoked	xx (xx.x%)	xx (xx.x%)	xx (xx x%)

Programmin note: First analysis will populate only the Gastric column. The Lung Resection and Total columns will be populated when all data is available.

Table 5.1
Background Information – Gastric Procedure Group
Analysis Set

Characteristic	Gastric (N = ##)
Pirmary Indication	
Weight loss	xx (xx.x%)
Metabolic	xx (xx.x%)
Weight loss and Metabolic	xx (xx.x%)
Tumor (benign)	xx (xx.x%)
Tumor (malignant)	xx (xx.x%)
Ulcer	xx (xx.x%)
Other	xx (xx.x%)
Procedure Performed	
Sleeve gastrectomy	xx (xx.x%)
Partial gastrectomy	xx (xx.x%)
Gastric wedge restriction	xx (xx.x%)
Subtotal gastrectomy	xx (xx.x%)
Roux-en-Y gastric bypass	xx (xx.x%)
Other	xx (xx.x%)

Table 5.2
Background Information – Lung Resection Procedure Group
Analysis Set

Characteristic	Lung Resection (N = ##)
Pirmary Indication	
Malignancy	xx (xx.x%)
COPD	xx (xx.x%)
Primary non-malignant lung disease (non-COPD)	xx (xx.x%)
Persistent pneumothorax (including blebs)	xx (xx.x%)
Other	xx (xx.x%)
Procedure Performed	
Lobectomy	xx (xx.x%)
Segmentectomy	xx (xx.x%)
Wedge resectomy	xx (xx.x%)
Lung volume reduction surgery	xx (xx.x%)
Other	xx (xx.x%)

Programmin note: This table will be populated later when data is available.

Table 6
Intra-Operative Information
Analysis Set

Characteristic	Gastric (N = ##)	Lung Resection (N = ##)	Total (N = ##)
Procedure Duration (hours)			
n	xx	xx	xx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)
Median (Min, Max)	xx.x (xx, xx)	xx x (xx, xx)	xx.x (xx, xx)
Surgical approach			
Open	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Laparoscopic	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Robotic	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Conversion to Open Procedure?			
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Volume of Estimated Blood Loss			
n	xx	xx	xx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)
Median (Min, Max)	xx.x (xx, xx)	xx x (xx, xx)	xx.x (xx, xx)
Intervention for Intraoperative Bleeding?			
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Type of Hemostatic Intervention Used			
Hemoclips	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Staples	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Sutures	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Monopolar Energy Product	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Advanced Energy Product	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Fibrin Sealants	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Compression	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

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Programmin note: First analysis will populate only the Gastric column. The Lung Resection and Total columns will be populated when all data is available.

Table 7
Intraoperative Leak Information – Gastric
Analysis Set

Characteristic	Gastric (N = ##)
Presence of intraoperative leak?	
Yes	xx (xx.x%)
No	xx (xx.x%)
Action taken	
Revision to staple line	xx (xx.x%)
Oversow leak point	xx (xx.x%)
Sealant to leak point	xx (xx.x%)
Other	xx (xx.x%)
Repeat leak test performed?	
Yes	xx (xx.x%)
No	xx (xx.x%)
Repeat leak test result	
Leak	xx (xx.x%)
No leak	xx (xx.x%)

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Table 8
Air Leak Information – Lung Resection
Analysis Set

Characteristic	Lung Resection (N = ##)
Air leak related to staple line observed?	
Yes	xx (xx.x%)
No	xx (xx.x%)
Duration of leak (Days)	
n	xx
Mean (SD)	xx.x (xx.x)
Median (Min, Max)	xx x (xx, xx)
Intervetion for Leak Needed?	
Yes	xx (xx.x%)
No	xx (xx.x%)
Type of Intervention	
Watchful Waiting	xx (xx.x%)
Valve	xx (xx.x%)
Pleurodesis	xx (xx.x%)
Surgical Revision	xx (xx.x%)
Other	xx (xx.x%)
Intervetion Succesful?	
Yes	xx (xx.x%)
No	xx (xx.x%)

Programmin note: This table will be populated later when data is available.

Table 9
AE Related to Air Leak Information – Lung Resection
Analysis Set

Characteristic	Lung Resection (N = ##)
AE related to Air leak staple line observed?	
Yes	xx (xx.x%)
No	xx (xx.x%)
Duration of AE related to leak (Days)	
n	xx
Mean (SD)	xx.x (xx.x)
Median (Min, Max)	xx.x (xx, xx)

Programmin note: This table will be populated later when data is available.

Table 10
Device Questionnaire -Part 1
Analysis Set

Characteristic	Gastric (N = ##)	Lung Resection (N = ##)	Total (N = ##)
Previous Buttress Device Used, n (%)			
GORE® SEAMGUARD®	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Baxter Peri-Strips Dry	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Endo GIA™ Reinforced Reload	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Less manipulation or movement compared to previous device, n (%)			
1 – Strongly Disagree	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
2 – Slightly Disagree	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
3 – Neutral	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
4 – Slightly Agree	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
5 – Strongly Agree	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Greater confidence the device will deliver best result compared to previous device, n (%)			
1 – Strongly Disagree	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
2 – Slightly Disagree	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
3 – Neutral	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
4 – Slightly Agree	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
5 – Strongly Agree	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Greater confidence in simplicity of set up compared to previous device, n (%)			
1 – Strongly Disagree	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
2 – Slightly Disagree	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
3 – Neutral	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
4 – Slightly Agree	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
5 – Strongly Agree	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Less frustration with device compared to previous device, n (%)			
1 – Strongly Disagree	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
2 – Slightly Disagree	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
3 – Neutral	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
4 – Slightly Agree	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
5 – Strongly Agree	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Denominator and percentages are based on number of vessels transected in each group.

Programmin note: First analysis will populate only the Gastric column. The Lung Resection and Total columns will be populated when all data is available.

Table 10
Device Questionnaire – Part 2
Analysis Set

Characteristic	Gastric (N = ##)	Lung Resection (N = ##)	Total (N = ##)
Less waste compared to previous device, n (%)			
1 – Strongly Disagree	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
2 – Slightly Disagree	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
3 – Neutral	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
4 – Slightly Agree	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
5 – Strongly Agree	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Satisfaction of operative flow compared to previous device, n (%)			
1 – Very dissatisfied	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
2 – Dissatisfied	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
3 – Neither dissatisfied nor satisfied	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
4 – Satisfied	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
5 – Very satisfied	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Satisfaction of manipulation and repositioning compared to previous device, n (%)			
1 – Very dissatisfied	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
2 – Dissatisfied	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
3 – Neither dissatisfied nor satisfied	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
4 – Satisfied	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
5 – Very satisfied	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Likey to recommend to a colleague, n (%)			
1 – Strongly Disagree	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
2 – Slightly Disagree	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
3 – Neutral	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
4 – Slightly Agree	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
5 – Strongly Agree	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Denominator and percentages are based on number of vessels transected in each group.

Programmin note: First analysis will populate only the Gastric column. The Lung Resection and Total columns will be populated when all data is available.

Table 11
Length of Stay Summary
Analysis Set

Characteristic	Gastric (N = ##)	Lung Resection (N = ##)	Total (N = ##)
Discharge Location			
Home	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Skilled nursing facility	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Long-term care	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Hospice care	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Length of Stay (days)			
n	xx	xx	xx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)
Median (Min, Max)	xx x (xx, xx)	xx.x (xx, xx)	xx.x (xx, xx)

Programmin note: First analysis will populate only the Gastric column. The Lung Resection and Total columns will be populated when all data is available.

Table 12
All Adverse Events by System Organ Class and Preferred Term
Analysis Set

System Organ Class	Preferred Term	Gastric (N = ##)	Lung Resection (N = ##)	Total (N = ##)
Total		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
System Organ Class 1		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Preferred Term 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Preferred Term 2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Preferred Term 3	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
System Organ Class 2		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Preferred Term 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Preferred Term 2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
System Organ Class 3		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Preferred Term 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Preferred Term 2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Preferred Term 3	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
System Organ Class 4		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Preferred Term 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Preferred Term 2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Programmin note: First analysis will populate only the Gastric column. The Lung Resection and Total columns will be populated when all data is available.

The following tables will have the same format as Table 12:

Table 13	All Serious Adverse Events by System Organ Class and Preferred Term Analysis Set
Table 14	Adverse Events Related to the Study Device by System Organ Class and Preferred Term Analysis Set
Table 15	Serious Adverse Events Related to the Study Device by System Organ Class and Preferred Term Analysis Set
Table 16	Unanticipated Serious Adverse Event related to the Study Device by System Organ Class and Preferred Term Analysis Set

Table 17
Primary Endpoint Summary
Analysis Set

Characteristic	Gastric (N = ##)	Lung Resection (N = ##)	Total (N = ##)
Specific Device-related AEs [1]			
Yes, n (%)	xx (xx x%)	xx (xx.x%)	xx (xx.x%)
95% Confidence Interval [2]	(xx.x%, xx.x%)	(xx.x%, xx.x%)	(xx x%, xx.x%)

[1] Device-related AEs through the 70-day post-procedure follow-up visit.
[2] 95% CI is calculated using the Normal approximation to the Binomial distribution

Programmin note: First analysis will populate only the Gastric column. The Lung Resection and Total columns will be populated when all data is available.

Table 18
Primary Endpoint Summary
Analysis Set

Procedure	Specific Device-related AEs [1] N (%)
Lung Resection	
Prolonged Air Leak Greater than Day 7 Postoperative	xx (xx.x%)
Empyema	xx (xx.x%)
Gastric	
Bleeding	xx (xx.x%)
Leak	xx (xx.x%)
Stricture	xx (xx.x%)

[1] Specific Device-related AEs through the 70-day post-procedure follow-up visit

Programmin note: First analysis will populate only the Gastric column. The Lung Resection and Total columns will be populated when all data is available.

Table 19
Primary Endpoint Summary
Analysis Set

Procedure	Specific Device-related AEs [1] Gastric	Specific Device-related AEs [1] Lung Resection
Total Number of Specific Device-related AEs [1]	xxx	xxx
ASA Score		
I	xx (xx.x%)	xx (xx.x%)
II	xx (xx.x%)	xx (xx.x%)
III	xx (xx.x%)	xx (xx.x%)
IV	xx (xx.x%)	xx (xx.x%)
V	xx (xx.x%)	xx (xx.x%)
Smoking Status		
Current smoker	xx (xx.x%)	xx (xx.x%)
Former smoker	xx (xx.x%)	xx (xx.x%)
Never smoked	xx (xx.x%)	xx (xx.x%)

[1] Specific Device-related AEs through the 70-day post-procedure follow-up visit

Programmin note: First analysis will populate only the Gastric column. The Lung Resection and Total columns will be populated when all data is available.

Table 20
Primary Endpoint By Procedure Performed Summary
Analysis Set

Procedure	Specific Device-related AEs [1] Lung Resection
Total Number of Specific Device-related AEs [1]	xxx
Procedure Preformed	
Lobectomy	xx (xx.x%)
Segmentectomy	xx (xx.x%)
Wedge resectomy	xx (xx.x%)
Lung volume reduction surgery	xx (xx.x%)
Other	xx (xx.x%)

[1] Specific Device-related AEs through the 70-day post-procedure follow-up visit

Programmin note: This table will be populated later when data is available.

Table 21
Primary Endpoint Summary
Analysis Set

Procedure	Specific Device-related AEs [1] N (%)
Lung Resection	
Prolonged Air Leak Greater than Day 7 Postoperative	xx (xx.x%)
Empyema	xx (xx.x%)
Gastric	
Bleeding	xx (xx.x%)
Leak	xx (xx.x%)
Stricture	xx (xx.x%)

[1] All AEs through the 70-day post-procedure follow-up visit

Programmin note: First analysis will populate only the Gastric column. The Lung Resection and Total columns will be populated when all data is available.

Table 21
Protocol Deviations
Analysis Set

Characteristics	Gastric (N = ##)	Lung Resection (N = ##)	Total (N = ##)
Total Number of Protocol Deviations	xxx	xxx	xxx
Specific Types of Protocol Deviations [1]			
AE/SAE	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Assessment related	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Informed Consent Related	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Inclusion/Exclusion Criteria	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Study Procedure Related	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Visit related	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Sponsor Assessment of Protocol Deviations [1]			
Minor	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Major	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Number (%) of Subjects With at Least 1 Protocol Deviation [2]	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

1. Denominator used is the total number of protocol deviations reported.
2. Denominator used is the total number of subjects in the column header.

Programmin note: First analysis will populate only the Gastric column. The Lung Resection and Total columns will be populated when all data is available.

The following listings will be generated for this study:

Listing 1	Inclusion/Exclusion Criteria All Subjects
Listing 2	Demographics All Subjects
Listing 3	Vital Signs All Subjects
Listing 4	Medical History All Subjects
Listing 5	Surgical History All Subjects
Listing 6	Background Information 1 All Subjects
Listing 7	Background Information 2 All Subjects
Listing 8	Malignancy Form All Subjects
Listing 9	Neo-Adjuvant Chemotherapy All Subjects
Listing 10	Neo-Adjuvant Radiation All Subjects
Listing 11	Inclusion/Exclusion Criteria Procedure Day All Subjects
Listing 13	Intraoperative Data All Subjects
Listing 14	Endocutter Firing All Subjects
Listing 15	Intervention for Intraoperative Bleeding All Subjects

Listing 16	Chest Tube Summary All Subjects
Listing 17	Air Leak Information All Subjects
Listing 18	Lung Resection Assessment All Subjects
Listing 19	Device Questionnaire All Subjects
Listing 20	Gastric Primary Assessment (Pre-Discharge) All Subjects
Listing 21	Additional Intraoperative Details – Gastric Only All Subjects
Listing 22	Unscheduled Visit All Subjects
Listing 23	Discharge All Subjects
Listing 24	Gastric Primary Assessment (Post-Discharge) All Subjects
Listing 25	Post-Procedure Follow-Up All Subjects
Listing 26	Adverse Events All Subjects
Listing 27	Concomitant Procedures All Subjects
Listing 28	Concomitant Medications All Subjects
Listing 29	Protocol Deviations All Subjects
Listing 30	Radiation Therapy All Subjects

Listing 31	Blood Transfusion Detail All Subjects
Listing 32	Subject Completion/Discontinuation All Subjects

Programmin note: Listign for Gastric will be generated first. The Lung Resection listing will be generated when all data is available.

Signature Page for VTMF-17296895, V-TMF Version: 1.0
ESC_2018_03---Statistical Analysis Plan-17 Jun 2022

[redacted]	[redacted]
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[redacted]	[redacted]

Signature Meaning:
To verify that the content is accurate and true to the best of my knowledge.