COVER PAGE

Statistical Analysis Plan	
Title	Safety and Performance of the Motorized Spiral Endoscope (PowerSpiral) in Subjects indicated for small-bowel enteroscopy or Endoscopic Retrograde Cholangio-Pancreatography (ERCP) in Subjects with surgically altered gastrointestinal anatomy: A PMCF Registry
Short Title or Acronym	The SAMISEN study (**SA**fety and Performance of the **M**otorIzed **S**piral **EN**doscope)
NCTNumber	NCT05129449

Final
STATISTICAL ANALYSIS PLAN
Study SAMISEN Phase B

Title: *(as per protocol/amendment)*	Safety and Performance of the Motorized Spiral Endoscope (PowerSpiral) in Subjects indicated for small-bowel enteroscopy or Endoscopic Retrograde Cholangio-Pancreatography (ERCP) in Subjects with surgically altered gastrointestinal anatomy: a PMCF Registry.
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Date:	08/June/2023

Note: This statistical analysis plan was prepared by SCO:SSiS using the SAP template Version 1 of SCO:SSiS

Abbreviations

Abbreviation	Description
AE	Adverse event
DT	Prototype table for descriptive statistics
FAS	Full analysis set
FT	Prototype of frequency table
GL	Prototype for general listings
ITT	Intent-to-treat
ND/UNK/NA	Not determined / unknown / not applicable
PP	Per-protocol
SAE	Serious adverse event
SOC	System organ class

Table of Contents

1 Relevant Documents and Standards

1.1 Protocol Version and Amendments

The statistical analysis plan is based on final version 03 of the study protocol of study SAMISEN dated June 28th, 2021 (CIP#: 2018-GI(OEKG) – 01).

1.2 Applicable Standards

None.

1.3 Review Report

<text>

1.4 Other Documents

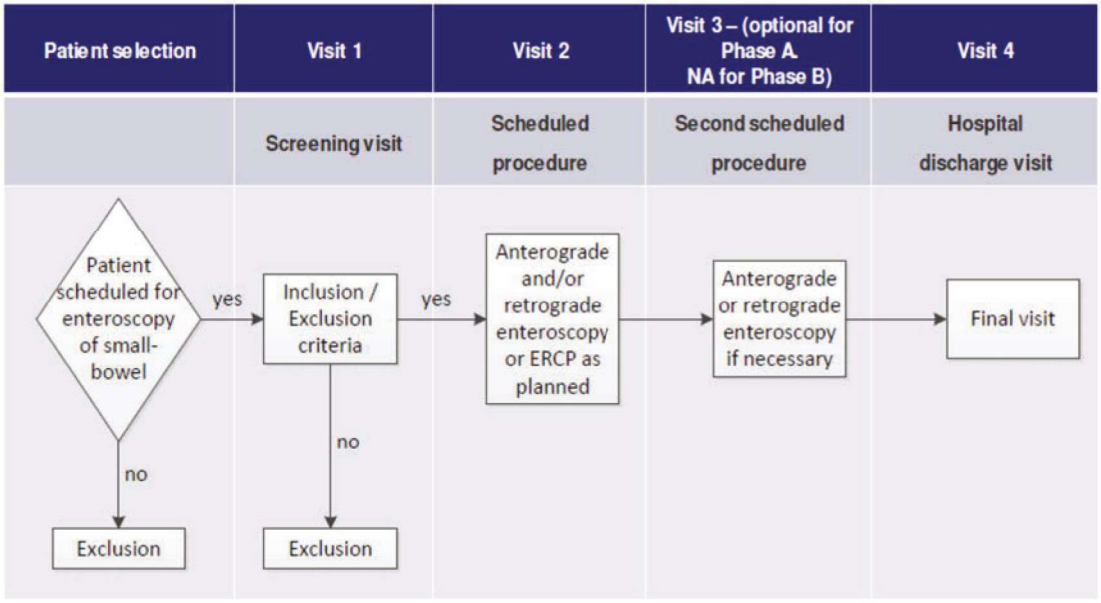
None.

2 Study Design and Objectives

2.1 Study Design

SAMISEN is an international, multicenter, open label, non-randomized, prospective, observational open-label study. Phase B has an exploratory study design for data collection in ERCP conducted with PowerSpiral.

2.2 Flow chart of study activities



2.3 Study Objectives

The main objective of this registry is to collect data on the safety and performance of the new motorized PowerSpiral device when used as intended by the manufacturer. It is assumed that the new device and its safety profile is non-interior to preceding generations of balloon assisted enteroscopes.
As clinical performance and efficacy is equally important for the user this study also collects efficacy and handling data of the new device.

2.4 Efficacy Variables

The efficacy parameters are defined as follows:

- **Total success rate**: Defined as the combined percentage of enteroscopy success rate, biliary cannulation success rate and procedural (therapeutic) success rate, i.e., the number of therapeutic successes divided by the number of patients who received an enteroscopy.
- **Enteroscopy success rate**: Defined as the percentage of procedures with the ability to reach the major papilla or the biliary anastomosis, i.e., the number of successful enteroscopies divided by the number of patients who received an enteroscopy.
- **Biliary cannulation success rate**: Defined as the percentage of procedures with the ability to selectively cannulate the bile duct and conduct a cholangiography, i.e., the number of successful cannulations divided by the number of successful enteroscopies.
- **Therapeutic (procedural) success rate**: Defined as the percentage of procedures in which the intended treatment could be successfully completed, i.e., the number of therapeutic successes divided by the number of successful bile cannulations.
- **Total procedure time**: Time from start of oral insertion to final withdrawal of the device.
- **Enteroscopy time**: Time from start of oral insertion to reaching the papilla or the biliary anastomosis.
- **User feedback** and assessment of handling characteristics and other logistical aspects regarding:
    - Handling of PowerSpiral
    - Instrument insertion of PowerSpiral
    - Precision of positioning during therapy of PowerSpiral
    - Time needed for procedure of PowerSpiral
    - Staff and resources needed for procedure of PowerSpiral

2.5 Safety Variables

The following safety variables will be collected:

- Enteroscopy-associated serious adverse events during and after enteroscopy procedure
- ERCP-related serious adverse events (Dumonceau et al., 2020)
- Sedation/anesthesia related serious adverse events
- Other serious adverse events (procedure or product related)
- Adverse events during enteroscopy and ERCP procedure
- Adverse events of interest are: bleeding, mucosal damage and pancreatitis (including hyperamylasemia)

2.6 Coding dictionaries

- Adverse events: IMDRF current version
- Baseline findings: not applicable
- Medical history: not applicable
- Medication: not applicable

3 Statistical Evaluation

3.1 Populations for Analysis

All patients who did not undergo at least one enteroscopy will be considered as dropouts. Dropouts will be excluded from any statistical analyses.

Two different analysis populations will be defined:
The **safety population (SAF)** will consist of all patients who underwent at least one enteroscopy.

The **ITT population (ITT)** will comprise all patients who underwent at least on enteroscopy and did not have any major protocol deviation.

The safety analysis will be performed on the safety population (SAF), which consists of all patients who underwent at least one enteroscopy.
Efficacy analyses will be based on the intent-to-treat (ITT) population, which includes all patients

- who underwent at least one enteroscopy and
- who had not major protocol deviations.

3.2 Interim analyses

No interim analyses planned.

3.3 Subgroup analyses

The following subgroups will be additionally considered in the analysis of the primary endpoint:

- Type of indication (Stone treatment / Stricture treatment)
- Type of reconstructive surgery (Billorth II gastrectomy / Whipple's duodenopancreatectomy Roux-en-Y / Gastric bypass / Hepaticojejunostomy)
- Presence/absence of biliodigestive anastomosis (reimplanted papilla)
- First 10 cases per investigator versus subsequent cases (to account for learning curve)

3.4 Derived Data and Data Sets

3.4.1 Rules for incomplete data

Missing data will not be replaced.

3.4.2 Rules for efficacy

None.

3.4.3 Rules for adverse events

Seriousness: 0 ≈ 'no', 1 ≈ 'yes'.

Attribution of the AE to the PowerSpiral Device
A frequency table will be presented showing the information on attribution of the AE to the PowerSpiral device using the categorization given on the CRFs:
1 ≈ 'not related', **2** ≈ 'unlikely', 3 ≈ 'possible', **4** ≈ 'probable', **5** ≈ 'causal relationship'.
Moreover, this categorization will be used in data listings.

3.4.4 Rules for laboratory data

Not applicable.

3.4.5 Rules for vital signs

Not applicable.

3.4.6 Rules for physical examination

Not applicable.

3.4.7 Other rules

None.

3.5 Demography, Medical History, Concomitant Medication, Study Procedures

Descriptive statistics (n, mean, standard deviation, median, 25th and 75th percentiles, minimum and maximum) will be calculated for quantitative variables; frequency counts by category will be given for qualitative variables. Confidence intervals will be given where appropriate. If not stated otherwise, these intervals will be two sided in each case and provide 95% confidence. Individual listings will be provided for each parameter examined in this study.

Concomitant medication and medical history will be listed only (if no codes are available).

3.6 Efficacy Analysis

The following efficacy analyses will be performed based on the ITT population:

- The total success rate (the number of therapeutic successes divided by the number of patients who received an enteroscopy) will be computed alongside with its 95% Clopper-Pearson confidence interval.
- The enteroscopy success rate (percentage of procedures with the ability to reach the major papilla or the biliary anastomosis) will be presented alongside its 95% Clopper-Pearson confidence interval.
- The biliary cannulation success rate (percentage of procedures with the ability to selectively cannulate the bile duct and conduct a cholangiography in relation to all cases with enteroscopy success) will be presented alongside its 95% Clopper-Pearson confidence interval.
- The therapeutic (procedural) success rate (percentage of procedures in which the intended treatment could be successfully completed after successful cannulation) will be presented alongside its 95% Clopper-Pearson confidence interval.
- The total procedure time (period in minutes needed to complete the procedure) will be summarized descriptively.
- The enteroscopy time will be summarized descriptively.
- The outcomes for the items in the user feedback for the judgement of handling characteristics and other aspects will be tabulated in frequency tables.

3.7 Safety Analysis

3.7.1 Adverse Events

The frequencies of adverse events, serious adverse events and device deficiencies will be reported in summary tables. These tables will show the number of subjects per group presenting a (serious) adverse event and the incidence of its occurrence.

Tabulations will be provided for system organ class and stratified by relation to the investigational product. Any withdrawals from the study due to adverse events will be reported. All measures taken due to adverse events will be reported.

AEs of special interest
- Number of patients with pancreatitis (including hyperamylasemia)
- Number of patients with bleeding
- Number of patients with mucosal damage

For pre-treatment events summary tables and listings will be provided.

3.7.2 Laboratory Data

Not applicable.

3.7.3 Vital Signs

Vital signs will be analyzed descriptively by visit including changes from baseline.

3.7.4 ECG Data

Not applicable.

3.7.5 Other Safety Data

Physical examination at baseline will be analyzed descriptively by summary tables. Listings will be provided.

3.8 Other Analyses

None.

3.9 List of all tables / listings / figures with their location in Clinical Study Report

DT = Descriptive statistics table with n, mean, standard deviation, median, 25th and 75th percentiles, minimum and maximum

FT = Frequency table with absolute and relative frequencies, for the primary endpoint, 95% confidence intervals will be added

GL = General listing of parameters with patient ID, center, analysis population in each listing.

Description of table / figure / listing	Type
Tables	
11.1.1 Patient Disposition - All Enrolled Population Reference: annCRF, In- and Exclusion Criteria Parameters: Patients with entries Analyses: Absolute and relative frequencies	FT
11.1.2 Analysis Populations - All Enrolled Population Reference: None Parameters: Analyses populations (SAF, ITT) Analyses: Absolute and relative frequencies	FT
11.1.3 In- and Exclusion criteria fulfilled? - SAF Reference: annCRF, In- and Exclusion Criteria Parameters: Categorical parameters Analyses: Absolute and relative frequencies	FT
11.1.4 Visit Schedules - SAF Reference: annCRF, Visit Dates Parameters: Median time from enrollment to discharge Analyses: Descriptive analyses	DT
11.1.5.1 Demographics and Baseline Characteristics - Continuous Parameters - SAF Reference: annCRF, Demographic Data Parameters: Age Analyses: Descriptive analyses	DT
11.1.5.2 Demographics and Baseline Characteristics - Categorical Parameters - SAF Reference: annCRF, Demographic Data Parameters: Sex Analyses: Absolute and relative frequencies	FT
11.1.6 Surgical Altered Upper GI Anatomy - SAF Reference: annCRF, Information about surgical altered upper GI anatomy Parameters: Types of upper GI surgery Analyses: Absolute and relative frequencies	FT
11.1.7.1 Details About The Biliary Indication for ERCP - SAF Reference: annCRF, Details about the biliary indication for ERCP Parameters: Suspicious finding, suspected diagnosis, other Analyses: Listing of free text	GL
11.1.7.2 Initially Planned Procedure with PowerSpiral - SAF Reference: annCRF, Initially planned procedure with PowerSpiral Parameters: Stricture treatment, stone treatment, other Analyses: Absolute and relative frequencies	FT

Description of table / figure / listing	Type
11.1.7.3 Initially Planned Procedure with PowerSpiral, Other – SAF Reference: annCRF, Initially planned procedure with Power Spiral Parameters: Other, please specify Analyses: Listing of free text	GL
11.1.8.1 Procedure with PowerSpiral - Categorical Parameters - SAF Reference: annCRF, Procedure with PowerSpiral, Procedural Information Parameters: categorical parameters Analyses: Absolute and relative frequencies	FT
11.1.8.2 Procedure with PowerSpiral - Continuous Parameters - SAF Reference: annCRF, Procedure with PowerSpiral, Procedural Information Parameters: Number of staff needed, length of procedure, time to reach papilla or biliary anastomosis, time scope out, enteroscopy duration, total procedure duration, total radiation dose Analyses: Descriptive statistics	DT
11.1.8.3 Therapeutic Interventions – Intervention Type - SAF Reference: annCRF, Therapeutic interventions during the procedure Parameters: Intervention type Analyses: Absolute and relative frequencies	FT
11.1.8.4 Therapeutic Interventions – Other Intervention - SAF Reference: annCRF, Therapeutic interventions during the procedure Parameters: Other intervention, please specify Analyses: Listing of free text	GL
11.1.8.5 Therapeutic Interventions – Continuous Parameters - SAF Reference: annCRF, Therapeutic interventions during the procedure Parameters: Number of stents, calculated duration Analyses: Descriptive statistics	DT
11.2.1 Assessment After Procedure - Categorical Parameters - ITT Reference: annCRF, Assessment after procedure Parameters: Intervention successful, therapeutic management plan modified during procedure Analyses: Absolute and relative frequencies	FT
11.2.2 Assessment After Procedure - Listing of Diagnoses - ITT Reference: annCRF, Assessment after procedure Parameters: Final diagnosis/assessment after ERCP Analyses: Listing of free text	GL
11.2.3 Evaluation of Procedure - Categorical Parameters - ITT Reference: annCRF, Evaluation Parameters: Handling, instrument insertion, precision, time needed, staff and resources needed Analyses: Absolute and relative frequencies by category (worse, similar, better)	FT

Description of table / figure / listing	Type
11.2.4 Evaluation of Procedure - Total Success Rate - ITT Reference: SAP section 3.6 Parameters: Total success rate Analyses: Absolute and relative frequencies, confidence interval	FT
11.2.5 Evaluation of Procedure - Total Enteroscopy Success Rate - ITT Reference: SAP section 3.6 Parameters: Total enteroscopy success rate Analyses: Absolute and relative frequencies, confidence interval	FT
11.2.6 Evaluation of Procedure - Biliary Cannulation Success Rate - ITT Reference: SAP section 3.6 Parameters: Biliary cannulation success rate Analyses: Absolute and relative frequencies, confidence interval	FT
11.2.7 Evaluation of Procedure - Therapeutic (Procedural) Success Rate - ITT Reference: SAP section 3.6 Parameters: Therapeutic (procedural) success rate Analyses: Absolute and relative frequencies, confidence interval	FT
11.3.1.1 Adverse Events during procedure - SAF Reference: annCRF, (Serious) adverse events during procedure Parameters: Trigger question on AEs Analyses: Absolute and relative frequencies	FT
11.3.1.2.1 Adverse Events by category - SAF Reference: annCRF, Adverse event, Adverse event details Parameters: Adverse event category Analyses: Absolute and relative frequencies	FT
11.3.1.2.2 Serious Adverse Events by category - SAF Reference: annCRF, Adverse event, Adverse event details Parameters: Adverse event category Analyses: Absolute and relative frequencies	FT
11.3.1.3 Adverse Events by category - Listing of other AEs - SAF Reference: annCRF, Adverse event, Adverse event details Parameters: Free text Analyses: Listing of free text	GL
11.3.1.4.1 Adverse Events - Relatedness - SAF Reference: annCRF, Adverse event, Adverse event details Parameters: Relatedness Analyses: Absolute and relative frequencies	FT

Description of table / figure / listing	Type
11.3.1.4.2 Serious Adverse Events - Relatedness - SAF Reference: annCRF, Adverse event, Adverse event details Parameters: Relatedness Analyses: Absolute and relative frequencies	FT
11.3.1.5.1 Adverse Events - Seriousness - SAF Reference: annCRF, Adverse event details Parameters: Seriousness and seriousness components (e.g. death), outcome Analyses: Absolute and relative frequencies	FT
11.3.1.5.2 Adverse Events - Seriousness – SAF Reference: annCRF, Adverse event details Parameters: Seriousness and seriousness components Analyses: Listing of free text	GL
11.3.1.6.1 Adverse Events - Therapy - SAF Reference: annCRF, Adverse event details Parameters: Therapy Analyses: Absolute and relative frequencies	FT
11.3.1.6.2 Adverse Events - Listing of Therapy - SAF Reference: annCRF, Adverse event details Parameters: Other, please specify Analyses: Listing of free text	GL
11.3.1.7.1 Adverse Events - Relatedness - SAF Reference: annCRF, Adverse event details Parameters: Related to enteroscopy, ERCP, sedation, PowerSpiral device Analyses: Absolute and relative frequencies	FT
11.3.1.7.2 Serious Adverse Events - Relatedness - SAF Reference: annCRF, Adverse event details Parameters: Related to enteroscopy, ERCP, sedation, PowerSpiral device Analyses: Absolute and relative frequencies	FT
11.3.1.7.3 Adverse Events - Listing of Device Deficiencies - SAF Reference: annCRF, Adverse event details Parameters: Device deficiency Analyses: Listing of free text	GL
11.3.1.8.1 Adverse Events - AEs of special interest - SAF Reference: SAP section 3.7.1 Parameters: Adverse event Analyses: Absolute and relative frequencies	FT
11.3.1.8.2 Serious Adverse Events - AEs of special interest - SAF Reference: SAP section 3.7.1 Parameters: Adverse event Analyses: Absolute and relative frequencies	FT

Description of table / figure / listing	Type
11.3.2.1 Hospital Discharge - Categorical Parameters - SAF Reference: annCRF, Hospital discharge Parameters: Categorical parameters Analyses: Absolute and relative frequencies	FT
11.3.2.2 Hospital Discharge - Listing of Comments - SAF Reference: annCRF, Hospital discharge Parameters: Remarks Analyses: Listing of free text	GL
11.3.3.1 Physical Examination - Continuous Parameters - SAF Reference: annCRF, Physical Examination Parameters: Height, Weight, Heart Rate, Blood Pressure (RR), Analyses: Descriptive statistics	DT
11.3.3.2 Physical Examination - Categorical Parameters - SAF Reference: annCRF, Physical Examination Parameters: ECG performed, Clinical standard panel of laboratory parameters, ASA category, Abnormalities detected by region, Analyses: Absolute and relative frequencies	FT
11.3.3.3 Physical Examination - Verbatims of abnormalities detected - SAF Reference: annCRF, Physical Examination Parameters: Abnormalities detected by region Analyses: Listing of free text	GL
11.4.1 Concomitant Medication - Anticoagulants - SAF Reference: annCRF, Concomitant medication Parameters: Acetylsalicylic acid, Anticoagulants, anticoagulation discontinued prior to /during the procedure? Analyses: Absolute and relative frequencies	FT
11.4.2 Concomitant Medication - Number of Anticoagulants - SAF Reference: annCRF, Concomitant medication Parameters: Specification of number of anticoagulants Analyses: Descriptive statistics	DT
11.4.3 Concomitant Medication - Listing of Anticoagulants - SAF and cSAF Reference: annCRF, Concomitant medication Parameters: Anticoagulants Analyses: Listing of free text	GL
Listings	

Description of table / figure / listing	Type
11.5.1 Listing of Patient Disposition and Analyses Populations - All Enrolled Population Reference: annCRF, Visit Date Parameters: Patients with entries Analyses: Listing	GL
11.5.2 Listing of In- and Exclusion criteria - All Enrolled Population Reference: annCRF, In- and Exclusion Criteria Parameters: Categorical parameters Analyses: Listing	GL
11.5.3 Listing of Demographic Data - All Enrolled Population Reference: annCRF, Demographic Data Parameters: Age, sex Analyses: Listing	GL
11.5.4 Listing of Physical Examination - All Enrolled Population Reference: annCRF, Physical examination Parameters: Height, weight, heart rate, blood pressure, ECG performed, clinical standard panel of laboratory parameters, ASA category, abnormalities detected Analyses: Listing	GL
11.5.5 Listing of Information About Surgical Altered Upper GI Anatomy - All Enrolled Population Reference: annCRF, Information about surgical altered upper GI anatomy Parameters: Specification of GI surgery Analyses: Listing	GL
11.5.6 Listing of Concomitant Medication - All Enrolled Population Reference: annCRF, Concomitant medication Parameters: all Analyses: Listing	GL
11.5.7 Listing of Previous Diagnostic Workup - All Enrolled Population Reference: annCRF, Previous diagnostic workup Parameters: all Analyses: Listing	GL
11.5.8 Listing of Details About the Biliary Indication for ERCP - All Enrolled Population Reference: annCRF, Details about the biliary indication for ERCP Parameters: all Analyses: Listing	GL
11.5.9 Listing of Procedure with PowerSpiral - All Enrolled Population Reference: annCRF, Procedure with PowerSpiral Parameters: all Analyses: Listing	GL

Description of table / figure / listing	Type
11.6.1 Listing of Assessment After Procedure - All Enrolled Population Reference: annCRF, Procedure with PowerSpiral - Assessment after procedure Parameters: all Analyses: Listing	GL
11.6.2 Listing of Evaluation of Procedure - All Enrolled Population Reference: annCRF, Evaluation Parameters: all Analyses: Listing	GL
11.7.1 Listing of Hospital Discharge - All Enrolled Population Reference: annCRF, Hospital discharge Parameters: all Analyses: Listing	GL
11.7.2 Listing of Adverse Events - All Enrolled Population Reference: annCRF, Adverse Events Parameters: all Analyses: Listing	GL

4 Revision History

Not applicable.