Abbott	Statistical Analysis Plan Cover Page

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JETi Registry

JET Enhanced Thrombectomy intervention (JETi) Registry

Statistical Analysis Plan (SAP)

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Statistical Analysis Plan

TABLE OF CONTENTS

1.0 SYNOPSIS OF STUDY DESIGN 4
1.1 Purpose of the Statistical Analysis Plan 4
1.2 Clinical Investigation Objectives 4
1.3 Clinical Investigation Design 4
1.4 Endpoints 4
1.4.1 Primary Endpoints 4
1.4.1.1 Arterial Subjects 4
1.4.1.2 Venous Subjects 5
1.4.2 Descriptive Endpoint(s) 5
1.4.2.1 All Subjects 5
1.4.2.2 Arterial Subjects 6
1.4.2.3 Venous Subjects 7
2.0 ANALYSIS CONSIDERATIONS 8
2.1 Analysis Populations 8
2.2 Statistical Methods 8
2.2.1 Descriptive Statistics for Continuous Variables 8
2.2.2 Descriptive Statistics for Categorical Variables 8
2.3 Endpoint Analysis 9
2.3.1 Primary Endpoint(s) 9
2.3.1.1 Arterial Subjects 9
2.3.1.2 Venous Subjects 9
2.3.2 Descriptive Endpoint(s) Analyses 10
[redacted]
2.6 Timing of Analysis 11
[redacted]
2.9 Handling of Missing Data 11
2.10 Poolability Issue 12
[redacted]
3.0 DESCRIPTIVE ENDPOINTS AND ADDITIONAL DATA 12

[redacted]

3.1 Baseline and Demographic Characteristics 12
3.2 Adverse Events 12
3.3 Subject Early Termination 13
3.4 Protocol Deviation 13
4.0 DOCUMENTATION AND OHER CONSIDERATIONS 13
5.0 ACRONYMS AND ABBREVIATIONS 14
6.0 REFERENCES 15
7.0 APPENDICES 15

1.0 SYNOPSIS OF STUDY DESIGN

1.1 Purpose of the Statistical Analysis Plan

This statistical analysis plan (SAP) is intended to provide a detailed and comprehensive description of the planned methodology and analysis to be used for [redacted] the JETi Registry clinical investigation. This plan is based on the [redacted] Clinical Investigation Plan.

1.2 Clinical Investigation Objectives

The objective of the JETi Registry is to collect real-world data on the safety, performance, and clinical benefits of the JETi System for the treatment of thrombosis in the peripheral vasculature.

1.3 Clinical Investigation Design

The JETi Registry is a prospective, single-arm, multicenter study to collect real-world data on the safety, performance, and clinical benefits of the JETi System for the treatment of acute and subacute thrombosis in the peripheral vasculature. This is a post-market study and will register approximately 280 subjects at approximately 30 centers globally. Subjects participating in this registry will be followed through their 12-month follow up visit. [redacted] After JETi procedure, subjects will be evaluated at discharge, 30 days, and 12 months.

1.4 Endpoints

1.4.1 Primary Endpoints

1.4.1.1 Arterial Subjects

For subjects treated for arterial or arteriovenous thrombosis, the primary endpoints are:

- **Clot removal grade** for each JETi-treated target vessel(s) from pre-JETi angiogram to post-JETi angiogram (post-JETi thrombectomy and prior to any adjunctive therapies to treat underlying culprit lesions) per the grades in **Table 1** (vessel basis). The independent imaging core laboratory will be responsible for assessing this endpoint.

Table 1. Clot Removal Grade

Grade I	< 50% reduction
Grade II	50 - <95% reduction
Grade III	95 – 100% reduction

- **Composite of JETi-related major adverse events** (MAEs), defined as the following JETi-related events: device-related death, major amputation of the treated limb (arterial subjects only), or major bleeding up to 30 days post-JETi procedure and as adjudicated by a clinical events committee (CEC) (subject basis).

[redacted]

1.4.1.2 Venous Subjects

For subjects treated for lower extremity DVT, the primary endpoints are

- **Percent of treated vessel(s) with ≥ 75% venous thrombus reduction** from pre-JETi venogram to final venogram (post-JETi AND after any/all adjunctive therapies to treat underlying culprit lesions) via modified Marder score. The independent imaging core laboratory will be responsible for assessing this endpoint.
  If no adjunctive therapies or devices are used after JETi, post-JETi modified Marder score is also final score.
  [redacted]

- **Composite of JETi-related major adverse events** (MAEs), up to 30 days post-JETi procedure, defined as the following JETi-related events, adjudicated by a clinical event committee (CEC): (1) death, (2) symptomatic pulmonary embolism (PE), (3) major bleeding, (4) re-thrombosis of JETi-treated vessel(s).

[redacted]

1.4.2 Descriptive Endpoint(s)

1.4.2.1 All Subjects

- Procedure-related death as adjudicated by a CEC.
- JETi-related AEs collected at discharge, 30 days, and 12 months follow-up, and as adjudicated by a CEC.
- Procedure-related access site complications such as hematoma, pseudoaneurysm (false aneurysm), perforation, as adjudicated by a CEC.

[redacted]

- Treatment Used: The number and percentage of patients having each of the following treatments:
  - JETi mechanical thrombectomy only
  - JETi in combination with one or [redacted]
- Quality of life (QoL) questionnaire: SF-12 at baseline, 30-day and 12-month follow-up.

1.4.2.2 Arterial Subjects

- Clot removal grade for each JETi-treated target vessel from pre-JETi angiogram to final angiogram (post-JETi thrombectomy and after any/all adjunctive therapies and prior to removal of the vascular sheath) per the grades in **Table 1**.
- Components of the MAE including device-related death, major amputation of treated limb (arterial subjects only), and major bleeding up to 30 days post-JETi as adjudicated by a CEC.
- Ankle Brachial Index* (ABI) of treated limb(s) at baseline and 30 days.
- Rutherford* classification at baseline and 30 days.
  ** only applicable to subjects with lower limb arterial thrombus.*
- Rate of re-thrombosis of JETi-treated vessel at 30 days, and 12 months, as assessed by investigator/physician reported.
- Patency as determined by duplex ultrasound at baseline, 30-day, and 12-month follow-up. Note that this endpoint will only apply to subjects treated for arteriovenous thrombus.
- Vessel patency: assessed by the independent imaging core laboratory using the Modified Thrombolysis in Myocardial Infarction (TIMI) classification called TIPI (Thrombo-aspiration in Peripheral Ischemia)[1] (**Table 3**) for each JETi-treated vessel, assessed using angiogram.
  - At post-JETi timepoint (post-JETi thrombectomy and prior to any adjunctive therapies to treat underlying culprit lesions)
  - At final timepoint (post-JETi thrombectomy and after any/all adjunctive therapies and prior to removal of the vascular sheath)

[1] de Donato G, Pasqui E, Sponza M, et al. Safety and Efficacy of Vacuum Assisted Thrombo-Aspiration in Patients with Acute Lower Limb Ischaemia: The INDIAN Trial. *Eur J Vasc Endovasc Surg*. 2021;61(5):820-828. doi:10.1016/j.ejvs.2021.01.004

If no adjunctive therapies or devices are used after JETi, post-JETi TIPI score is also final TIPI score.

Table 3. Thrombo-aspiration in Peripheral Ischemia (TIPI)

Description	TIPI score
No recanalization of the thrombotic occlusion	0
Incomplete or partial recanalization of the thrombotic occlusion with no distal flow	1
Incomplete or partial recanalization of the thrombotic occlusion with any distal flow	2
Complete recanalization of the thrombotic occlusion with normal distal flow	3

- Acute success, as per TIPI score (**Table 3**), per core lab assessment:
  - Device success: Near complete or complete recanalization of occluded vessel, defined as post-JETi TIPI 2-3.
  - Technical success: Near complete or complete recanalization of occluded vessel, defined as final TIPI 2-3, using JETi system and any other adjunctive device or procedures.
  - Procedural success: Technical success with no JETi-related MAEs within 5 days of registration or by discharge, whichever occurs first.

1.4.2.3 Venous Subjects

- Percent of treated vessels with ≥75% clot reduction from pre-JETi venogram to post-JETi venogram (post-JETi thrombectomy and before any adjunctive therapies to treat underlying culprit lesions) via modified Marder score. The independent imaging core laboratory will be responsible for assessing this endpoint.
- For subjects not treated for lower extremity DVT (i,e. upper extremity DVT (UE DVT)), Clot removal grade for each JETi-treated target vessel from pre-JETi venogram to final venogram (post-JETi thrombectomy and after any/all adjunctive therapies and prior to removal of the vascular sheath) per the grades in **Table 1**.
- Components of the JETi-related MAE including up to 30 days post-JETi adjudicated by a CEC death, symptomatic pulmonary embolism (PE), major bleeding and rethrombosis of target vessel(s).
- Re-thrombosis in the JETi-treated vessel(s) at 30-day and 12-month follow up, as assessed by investigator/physician reported, and as adjudicated by CEC.
- The Villalta Post Thrombotic Syndrome (PTS) severity scale at baseline, 30-day, and 12-month follow-up. Note that this assessment will apply only to subjects with lower extremity DVT.

  - Edema component score from the Villalta Post Thrombotic Syndrome (PTS) severity scale at baseline, 30-day, and 12-month follow-up.
- A 7-point Likert Scale for leg pain at baseline, discharge, 30-day, and 12-month follow-up.
- Venous patency and compressibility as determined by duplex ultrasound at baseline, 30-day, and 12-month follow-up.
- Acute success, [redacted] assessed by core laboratory:
  - Device success: Post-JETi thrombus removal grade II-III [redacted]
  - Technical success: Final thrombus removal grade II-III [redacted] where final [redacted] occurs after JETi system and any other adjunctive device or procedures.
  - Procedural success: Technical success with no JETi-related MAEs within 5 days of registration or by discharge, whichever occurs first.

If no adjunctive therapies or devices are used after JETi, post-JETi [redacted] is also final [redacted] score.

[redacted]

2.0 ANALYSIS CONSIDERATIONS

2.1 Analysis Populations

All registered subjects will be included in the analyses. The point of registration in the Registry is when a JETi Catheter is introduced into the intended vasculature of an enrolled subject during the procedure (Day 0). A subject who is enrolled but not registered in this study will be considered as a screen failure.

Consenting up to 5 days post-JETi procedure is acceptable. In these cases, the point of registration will be the same and any procedural information will be entered post-consent, and adverse events (AEs) will be collected retrospectively from the point of registration (Day 0).

2.2 Statistical Methods

2.2.1 Descriptive Statistics for Continuous Variables

For continuous variables (e.g., age, BMI, etc.), results will be summarized with the numbers of observations, means, and standard deviations, with quartiles, minimums, maximums, and 95% confidence intervals, where specified.

2.2.2 Descriptive Statistics for Categorical Variables

For categorical variables (e.g., gender, race, etc.), results will be summarized with subject counts and percentages/rates, with [redacted] 95% [redacted] confidence intervals, when specified.

[redacted]

2.3 Endpoint Analysis

2.3.1 Primary Endpoint(s)

2.3.1.1 Arterial Subjects

For subjects treated for arterial thrombosis [redacted] all endpoints are descriptive. There will be no hypothesis testing, and there are no statistical power considerations.

Primary Effectiveness Endpoint:

Clot removal grade for each JETi-treated target vessel from pre-JETi angiogram to post-JETi angiogram (post-JETi thrombectomy and prior to any adjunctive therapies to treat underlying culprit lesions) per the grades. Summary statistics (number and % of treated vessel) of clot removal grade from pre- to post-JETi thrombectomy will be summarized.

Primary Safety Endpoint:

Composite of JETi-related major adverse events (MAEs), defined as the following JETi-related events: device-related death, major amputation of the treated limb (arterial subjects only), or major bleeding up to 30 days post-JETi procedure and as adjudicated by a clinical events committee (CEC). It will be summarized as the number of events and the percentage of subjects with events.

2.3.1.2 Venous Subjects

[redacted]

Primary Effectiveness Endpoint:

- For subjects treated for lower extremity DVT, the primary effectiveness endpoint is the percent of treated vessel(s) with ≥ 75% venous thrombus reduction from pre-JETi venogram to final venogram (post-JETi AND after any/all adjunctive therapies to treat underlying culprit lesions) via modified Marder score. If no adjunctive therapies or devices are used after JETi, post-JETi modified Marder score is also final score. This endpoint is a binary outcome defined as whether there is 75% reduction in modified Marder score from baseline at the limb level.

[redacted]

[redacted]

Primary Safety Endpoint:

The primary safety endpoint is the composite of JETi-related MAEs, up to 30 days post- JETi procedure (death, symptomatic pulmonary embolism (PE), major bleeding, or re-thrombosis of JETi-treated vessel(s)) for subjects treated for lower extremity DVT and as adjudicated by a clinical events committee (CEC).

It will be summarized as the number of events and the percentage of subjects with events.

[redacted]

2.3.2 Descriptive Endpoint(s) Analyses

All descriptive endpoints will be summarized descriptively.

[redacted]

[redacted]

[redacted] A total of approximately 280 subjects [redacted] will be registered in this Registry.

[redacted]

[redacted]

2.6 Timing of Analysis

Analysis for the primary endpoints will be performed after all registered subjects (within arterial or DVT groups) have reached their 30-day follow-up visit. Analysis for final report will be conducted after all registered subjects have completed the 12-month follow-up visit.

[redacted]

Analysis will be performed separately for arterial and venous subjects.

2.9 Handling of Missing Data

Every effort will be made to acquire all necessary data. Analysis will be based on available data with missing data excluded. Any unused or spurious data will be noted as appropriate in the final report. However, impact of missing data may be assessed in the sensitivity analysis.

[redacted]

2.10 Poolability Issue

The primary endpoints will be assessed for poolability across regions [redacted]

[redacted]

3.0 DESCRIPTIVE ENDPOINTS AND ADDITIONAL DATA

3.1 Baseline and Demographic Characteristics

The following baseline and demographic variables will be summarized for all registered subjects: gender, age, ethnicity, race, medical history, etc.

3.2 Adverse Events

All device-, and procedure-related adverse events and all serious adverse events will be summarized for all registered subjects in this trial in terms of the number of events, the percentage of subjects with events.

[redacted]

[redacted]

3.3 Subject Early Termination

Subject early termination reasons including deaths, withdrawals, lost-to-follow-up, etc. will be summarized at all scheduled visits.

3.4 Protocol Deviation

Protocol deviations will be summarized for subjects in whom a protocol deviation was reported.

4.0 DOCUMENTATION AND OHER CONSIDERATIONS

All analyses will be performed using SAS® for Windows, version 9.4 or higher.

5.0 ACRONYMS AND ABBREVIATIONS

Acronym or Abbreviation	Complete Phrase or Definition
ABI	Ankle Brachial Index
ALI	Acute Limb Ischemia
AV	Arteriovenous
CDT	Catheter Directed Thrombolysis
CEC	Clinical Events Committee
CIP	Clinical Investigation Plan
DVT	Deep Vein Thrombosis
IVC	Inferior Vena Cava
MAE	Major Adverse Event
OUS	Outside of US
PE	Pulmonary Embolism
PG	Performance Goal
PTS	Post Thrombotic Syndrome
QOL	Quality of Life
SAE	Serious Adverse Event
SAP	Statically Analysis Plan
SF-12	Short-Form Health Survey-12
TIMI	Thrombolysis in Myocardial Infarction
TIPI	Thrombo-aspiration in Peripheral Ischemia

6.0 REFERENCES

[redacted]

2. SAS Institute Inc. 2015. SAS/STAT® 14.1 User's Guide. Cary, NC: SAS Institute Inc.

7.0 APPENDICES

APPENDIX A: STATISTICAL ANALYSIS PLAN REVISIONS

[redacted]