Johnson&Johnson MedTech

Statistical Analysis Plan (SAP)

Safety and Effectiveness Evaluation of the OMNYPULSE™ Catheter with the TRUPULSE™ Generator for treatment of Paroxysmal Atrial Fibrillation (PAF) Omny-IRE

Protocol Version: 2.3

SAP Revision: 3.0
SAP Revision Date: 28/JUL/2025

Safety and Effectiveness Evaluation of the OMNYPULSE™ Catheter with the TRUPULSE™ Generator for treatment of Paroxysmal Atrial Fibrillation (PAF)
Protocol Version: 2.3

The following individuals have reviewed this version of the Statistical Analysis Plan and are in agreement with the content:

Signature Page

Study Biostatistician:

PPD
Lead Biostatistician

PPD		PPD	
(Print)		(Sign)	Date

Head of Biostatistics:

PPD
Medical Device and Sector CSS Lead BPDM

PPD		PPD	
(Print)		(Sign)	Date

Franchise Clinical Study Lead:

PPD
Clinical Research Leader

PPD		PPD	
(Print)		(Sign)	Date

Franchise Clinical Platform Lead:

PPD
Senior Director Clinical Research

PPD		PPD	
(Print)		(Sign)	Date

Revision History

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		CCI [redacted]
V 3.0	28/JUL/2025	

List of Acronyms and Abbreviations

Acronym/ Abbreviation	Expanded Term
AAD	Antiarrhythmic Drug
AE	Adverse Event
AF	Atrial Fibrillation
AFEQT	Atrial Fibrillation Effect on Quality of Life
AFL	Atrial Flutter
AT	Atrial Tachycardia
CE	Conformite Europeenne
CEC	Clinical Events Committee
CIP	Clinical Investigation Plan
CSR	Clinical Study Report
CT	Computed Tomography
CTI	Cavotricuspid Isthmus
DMC	Data Monitoring Committee
ECG	Electrocardiogram
EE	Esophageal Endoscopy
EP	Electrophysiology
FDA	Food and Drug Administration
FU	Follow-Up
HRQoL	Health Related Quality of Life
IRE	Irreversible Electroporation
LA	Left Atrium
mITT	Modified Intent to Treat
MMSE	Mini Mental State Examination
MRA	Magnetic Resonance Angiogram
MRI	Magnetic Resonance Imaging
mRS	Modified Rankin Scale
NA	Neurological Assessment
NIHSS	National Institute of Health Stroke Scale
NSC	Non-Study Catheter
PAE	Primary Adverse Event
PAF	Paroxysmal Atrial Fibrillation
PEE	Primary Effectiveness Endpoint
PF energy	Pulsed Electric Field Energy
PP	Per Protocol
PV	Pulmonary Vein
PVI	Pulmonary Vein Isolation
QoL	Quality of Life
RF	Radiofrequency
SADE	Serious Adverse Device Effect
SAE	Serious Adverse Event

Acronym/ Abbreviation	Expanded Term
SAP	Statistical Analysis Plan
USADE	Unanticipated Serious Adverse Device Effect

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1 Study Design

This study is a prospective, multi-center, single-arm, pre-market clinical evaluation utilizing the OMNYPULSE™ Bi-Directional Catheter in conjunction with the guiding sheath and the TRUPULSE™ Generator, for the treatment of symptomatic paroxysmal atrial fibrillation (PAF) with pre-specified goals for safety and effectiveness.

The main study will enroll 135 evaluable subjects who have symptomatic PAF and are candidates for atrial fibrillation ablation. To minimize the learning curve effect on the evaluation of safety and effectiveness of the OMNYPULSE™ Bi-Directional Catheter, up to 50 Roll-In subjects will be enrolled in the study. These subjects will not be counted in the main study, and data for Roll-In subjects will be analyzed separately from the main study.

During the study, all subjects will be followed for 12 months after index procedure. All subjects will be evaluated at 7 days (Day 7-9), 1 month (Day 23-37), 3 months (Day 76-104), 6 months (Day 166-194), and 12 months (Day 335-379) following the index ablation procedure (Day 0).

The primary safety and effectiveness endpoint will be evaluated using the data available at the time of the 3-month follow-up. The hypothesis testing of the primary endpoints will be performed when all subjects complete their 3-month follow-up. A Clinical Study Report (hereinafter, 3-Month CSR) will be submitted as part of the CE mark application dossier.

After the 3-Month CSR submission, the primary safety and primary effectiveness endpoints, along with associated sensitivity analyses, may be summarized descriptively using the complete follow-up data, if there are any updates on the primary endpoint outcome data. No hypothesis testing will be conducted for the primary endpoints in the final CSR.

Regarding all other study endpoints, they will be summarized descriptively using the full follow-up data. The final analysis results will be compiled and presented in the Final CSR (hereinafter, Final CSR).

Embedded within the main study, there will be a Neurological Assessment (NA) subset, a cardiac Computed Tomography (CT) or Magnetic Resonance Angiogram (MRA) image subset, an Esophageal Endoscopy (EE) subset, and a Pulmonary Vein Isolation (PVI) durability subset. These subsets are intended to delineate safety and assess lesion durability 2-3 months following ablation. Each subset will consist of 30 subjects. The same subjects may participate in all four (4) subsets.

2 Treatment Assignment

This is a single-arm study. All subjects will be treated with the OMNYPULSE™ Bi-Directional Catheter (D-1430-05-SI) and the TRUPULSE™ Generator (D-1417-01-IC), along with any related components and accessories needed for the ablation procedure.

3 Randomization and Blinding Procedures

This study is a non-randomized single-arm study. Therefore, masking of treatment assignment for operators and subjects will not be performed. To minimize operational bias, the study will maintain screening logs at each site to ensure that eligible subjects are considered for participation in the study.

4 Levels of Significance

The type-I error rate for the analyses of the two primary endpoints is controlled each at a one-sided 2.5% level. The hypotheses of the primary endpoints will be tested at the full alpha level of 0.025, and only if there is a success, the hypothesis testing of the secondary endpoint will be performed at the same alpha level. This gate-keeping approach will control the overall type-I error rate at a one-sided 2.5%.

5 Analysis Sets

5.1 **Main Study**

For the analysis of study endpoints, the analysis sets defined in the following will be used:

- **Safety Analysis Set**: CCI [redacted]
- **Modified Intent-To-Treat (mITT) Analysis Set**: CCI [redacted]
- **Per Protocol (PP) Analysis Set**: CCI [redacted]

CCI [redacted]

- CCI [redacted]

- **Neurological Assessment (NA) Analysis Set:** CCI [redacted]

- **Esophageal Endoscopy (EE) Analysis Set:** CCI [redacted]

- **Cardiac CT/MRA Analysis Set:** CCI [redacted]

- **PVI Durability Analysis Set:** CCI [redacted]

CCI [redacted]

5.2 **Roll-In**

- **Roll-In Analysis Set:** CCI [redacted]

6 Sample Size Justification

CCI [redacted]

CCI

[redacted]

CCI

[redacted]

- **Total Sample size:**

The sample size of this study is mainly driven by the hypothesis test for the primary safety endpoint. The total sample size for this study will be 135 evaluable subjects, CCI [redacted]

A total of 135 evaluable subjects will be included in the main study. Each of the four (4) subsets (NA, CT/MRA, EE and PVI durability) will target 30 subjects and will be integrated within the main study. Additionally, 30-50 subjects will be enrolled in the Roll-In analysis set. CCI [redacted]

7 Statistical Analysis Methods

7.1 General Conventions

Descriptive summaries for continuous variables will include the number of observations with available data, along with the mean, standard deviation, median, 25% percentile, 75% percentile, minimum, and maximum values. As for categorical variables, the reporting will include the count and the corresponding percentage. Percentages will be based on the number of subjects with available data.

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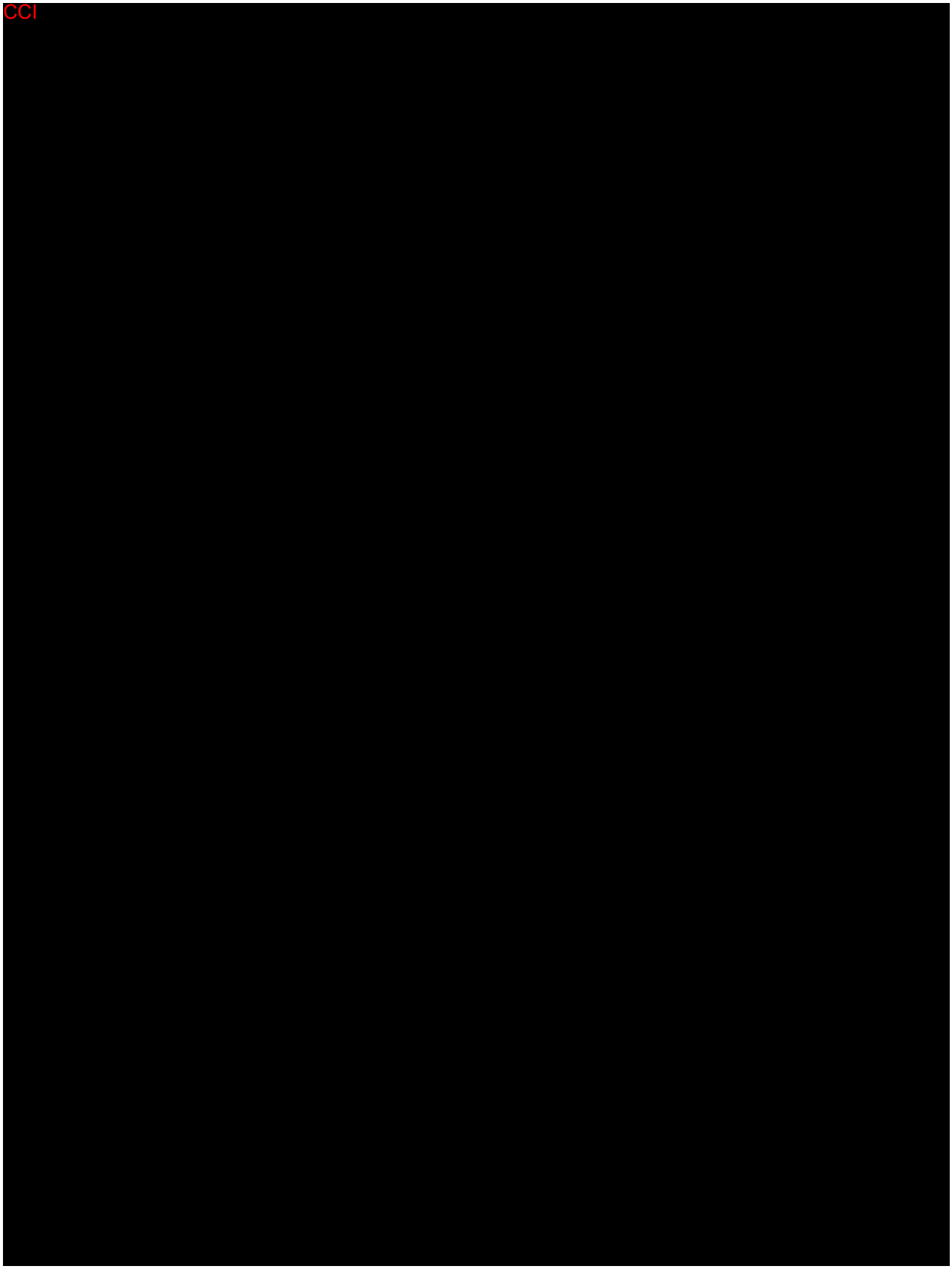
CCI [redacted]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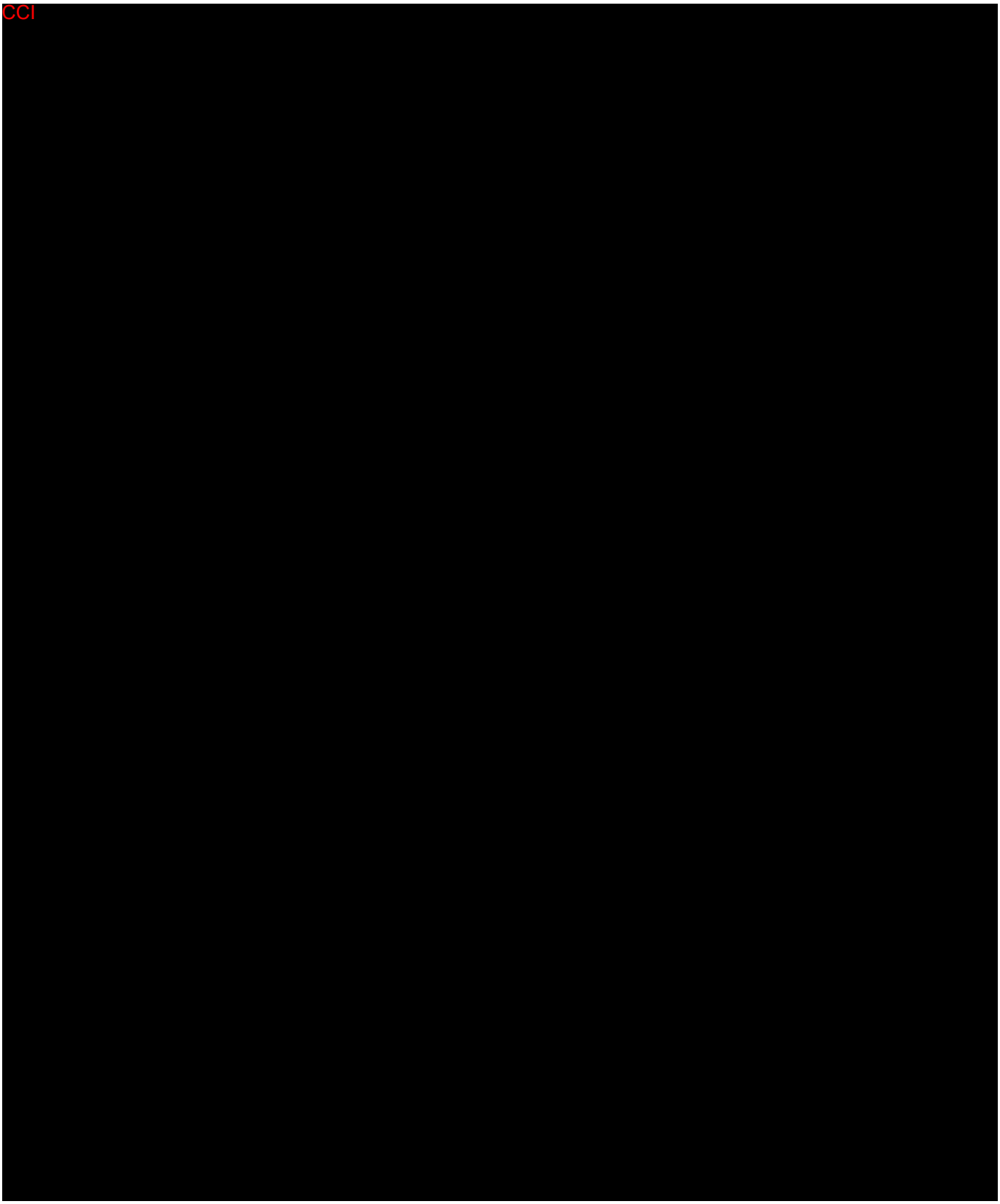

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7.2 Disposition of Study Subjects

Subject disposition and accountability of the study subjects will be summarized descriptively for all enrolled subjects. The definition of disposition categories mentioned in section 19.5 of the study protocol will be used to categorize subjects.

7.3 Demographic and Baseline Characteristics

Subject demographics, medical history, previously failed and actively taking AADs utilization, and other baseline data will be summarized descriptively for all enrolled subjects. CCI

[redacted]

7.4 Endpoints and Associated Hypotheses

7.4.1 Primary Safety Endpoint

The primary safety endpoint is the occurrence of primary adverse events (PAEs) within 7 days of the index ablation procedure with the OMNYPULSE™ Catheter and TRUPULSE™ generator, except device or procedure related death, pulmonary vein (PV) stenosis, and atrio-esophageal fistula, which may also be considered as primary adverse event if occurring greater than one week (7 days) and less than or equal to 90 days post-procedure (section 7.4.1 in the Protocol). Cardiac Tamponade/Perforation occurring up to 30 days post AF ablation process procedure will also be considered a PAE (section 7.4.1 in the Protocol). The PAE rate will be compared against a performance goal of 12%.

The hypotheses to be tested for this evaluation are:

H_0: $P_S \geq 0.12$ vs. H_A: $P_S < 0.12$,

where P_S denotes the rate of early onset primary adverse events.

7.4.2 Primary Effectiveness Endpoint

The primary effectiveness endpoint (PEE) for a subject is acute procedural success, which is achieved by electrical isolation of clinically relevant targeted PVs (confirmed by entrance block) after adenosine/isoproterenol challenge at the end of the index ablation procedure (section 7.4.1 in the Protocol). Use of

a non-study device to achieve PVI is considered an acute procedural failure. The primary acute effectiveness success rate will be compared against a performance goal of 90%.

The hypotheses to be tested for this evaluation are:

H_0: $P_E \leq 0.90$ vs. H_A: $P_E > 0.90$,

where P_E denotes the rate of acute procedure success.

7.4.3 Secondary Effectiveness Endpoint

The secondary effectiveness endpoint is 12-month effectiveness success, which is defined as freedom from documented (symptomatic and asymptomatic) atrial arrhythmia episodes including atrial fibrillation (AF), atrial tachycardia (AT), or atrial flutter (AFL, of unknown origin*). The AF/AT/AFL episodes will be assessed based on the electrocardiographic data (≥ 30 seconds on arrhythmia monitoring device) during the effectiveness evaluation period (91-365 days post the index procedure). Acute procedural failure (i.e., failure to achieve entrance block with the study device in any of the clinically relevant targeted PVs) will also be deemed a 12-month effectiveness failure. The secondary effectiveness success rate will be compared against a performance goal of 50%.

The hypotheses to be tested for this evaluation are:

H_0: $P_{12m} \leq 0.50$ vs. H_A: $P_{12m} > 0.50$,

where P_{12m} denotes the proportion of subjects who are failure-free at 12 months follow-up.

**AFL of unknown origin is defined as all AFL except those CTI dependent AFL as confirmed by 12-lead electrocardiogram (ECG) or entrainment maneuvers in an EP study.*

7.4.4 Additional Endpoints

No formal statistical hypothesis will be formulated and tested for the additional endpoints. Additional details are described in section 7.11 in the SAP.

7.4.4.1. Additional Procedural Endpoints

- Total procedure time, PVI time, PF application time and mapping time
- Number of PF applications by left and right PV and by subject
- Total fluoroscopy time
- Total study catheter left atrial dwell time
- Ablation settings used

7.4.4.2. Additional Safety Endpoints

- Occurrence of Serious Adverse Device Effects (SADEs)
- Occurrence of Unanticipated (Serious) Adverse Device Effects (USADEs)
- Occurrence of Serious Adverse Events (SAEs) within 7 days (early-onset), 8-30 days (peri-procedural), and >30 days (late onset) of index ablation procedure
- Occurrence of non-serious adverse events (non-SAEs)

7.4.5 Additional Effectiveness Endpoints

- **Single Procedural Success** is defined as freedom from documented symptomatic atrial arrhythmia (AF, AT or AFL of unknown origin*) episodes based on electrocardiographic data (≥30 seconds on arrhythmia monitoring device) during the effectiveness evaluation period (Day 91-Day 365) following a single index ablation procedure. Subjects who had repeat procedure(s) for the study arrhythmia post the index procedure will be deemed failures of this endpoint.

- **Freedom from documented symptomatic atrial arrhythmia (AF, AT or AFL of unknown origin*):** The time to first documented symptomatic atrial arrhythmia (AF, AT or AFL) recurrence based on electrocardiographic data (≥30 seconds on arrhythmia monitoring device) during the effectiveness evaluation period (Day 91-Day 365) at 12 months post the index procedure.

  Acute procedural failure (i.e., failure to confirm entrance block in all PVs except those that are silent and/or cannot be cannulated post-procedure, use of non-study catheter for PV isolation, and failure to have energy delivery with the study device due to ablation system malfunctions) will also be considered a failure.

- **Freedom from documented (symptomatic and asymptomatic) atrial arrhythmia (AF, AT or AFL of unknown origin*) with additional failure models:** The time to first documented (symptomatic and asymptomatic) atrial arrhythmia (AF, AT or AFL) based on electrocardiographic data (≥30 seconds on arrhythmia monitoring device) during the effectiveness evaluation period (Day 91-Day 365). The following criteria will also be deemed failures:

  - Failure to achieve acute procedural success.
  - Taking a new Antiarrhythmic Drug (AAD) (Class I / Class III) for atrial tachyarrhythmia (AF, AT or AFL of unknown origin*) or taking a previously failed Class I/III AAD at a greater than the highest ineffective historical dose for AF/AFL/AT during the effectiveness evaluation period (Day 105* – Day 365).
  - Greater than 1 repeat ablation for AF/AT or AFL of unknown origin* in the blanking period or any repeat ablation for AF/AT or AFL of unknown origin* during the effectiveness evaluation period.

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- **Use of a non-study device** for the purpose of PVI (i.e., touch-up) among all clinically relevant targeted PVs.

- **Acute reconnection** defined as any pulmonary vein reconnection during the index procedure identified by adenosine/isoproterenol challenge among all clinically relevant targeted PVs.

- **Repeat ablation procedures** for left atrial arrhythmia (AF, AT or AFL of unknown origin*) within the 12-month FU period.

- **Quality of Life (QoL)** is defined as the change of QoL assessed by comparing the Atrial Fibrillation Effect on Quality-of-Life (AFEQT™) scores before and at 3, 6 and 12- months after the ablation procedure.

- **Hospitalization for cardiovascular events** through 12 months follow-up compared to 12 months prior to baseline.

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7.5 Analysis of Primary Endpoints

The primary safety and acute effectiveness endpoints will be evaluated based on 3-month follow-up and procedural data respectively. The hypothesis testing of these primary endpoints will be performed once all subjects treated with the OMNYPULSE™ catheter and TRUPULSE™ Generator have completed their 3-month follow-up. The results will be reported in the 3-Month CSR. Additionally, the Final CSR will include descriptive statistics based on the final complete follow-up data, if there is any primary endpoint data change after the database extraction for the 3-Month CSR. The 3-Month CSR will be submitted as a part of the CE mark application dossier.

7.5.1 Primary Safety Endpoint

The primary safety endpoint will be analyzed using the 3-month PAE rate.

Analysis Method:
The primary safety endpoint will be evaluated using an exact test for a binomial proportion at a one-sided significance level of 2.5%. If the upper bound of the exact two-sided 95% confidence interval of the primary safety endpoint rate is less than the performance goal of 12%, the study will be considered to have demonstrated safety. The study has met its primary safety endpoint.

The hypothesis testing will be performed in the mITT analysis set. Subjects with non-missing PAE outcome data will be included in the primary analysis. The number of events, number of subjects who experience PAEs, and percentage of subjects who experience PAEs will be reported, along with the exact two-sided 95% confidence interval.

To investigate the robustness of the analysis result, sensitivity analyses including estimation of the PAE rate in the Safety analysis set, worst-case and best-case scenario analyses, and tipping point analysis will be performed in the Safety and mITT analysis sets. Details are provided in Section 7.6.1.

As all primary safety endpoint outcomes will be determined based on the 3-month follow-up date per protocol definition of PAEs, all Clinical Events Committee (CEC)-adjudicated PAE cases will be considered final at the 3-Month CSR.

If there are any changes to the PAE data in the final 12-month follow-up data, the data will be summarized descriptively using the mITT and Safety analysis sets and reported in the Final CSR. Descriptive statistics may also be presented for Roll-In analysis set.

7.5.1.1. Primary Effectiveness Endpoint

The primary effectiveness endpoint of acute effectiveness will be evaluated using the exact test for binomial proportion at a one-sided significance level of 2.5%. If the lower bound of the exact two-sided 95% confidence interval of the acute effectiveness success rate is greater than the performance goal of 90%, the study will be considered to have demonstrated effectiveness. The study has met its primary effectiveness endpoint.

The hypothesis testing will be performed in the PP analysis set. Subjects with non-missing acute effectiveness outcome data will be included in the primary analysis. Subjects who are discontinued (i.e., no energy delivered with the study catheter/system) due to study device related reasons will be considered acute effectiveness failures, regardless of the PV isolation achieved or not. Subjects who are discontinued due to non-study device related reasons will be considered missing outcomes.

To investigate the robustness of the analysis result, sensitivity analyses including estimation of the acute procedure success rate in the mITT analysis set, worst-case and best-case scenario analyses, and tipping point analysis will be performed in the mITT and PP analysis sets. Details are provided in Section 7.6.2.

As all acute effectiveness endpoint outcomes will be determined on Day 0 (i.e., date of the index procedure), all data will be considered final at the 3-Month CSR. There will be updates made to the primary acute effectiveness descriptively if any changes are present in the Final CSR. Descriptive statistics may be presented for Roll-In subjects.

7.5.2 Criteria for Study Success

The study will be considered a success if both primary safety and acute effectiveness endpoints are met based on the 3-month follow-up data.

7.6 Sensitivity Analyses

The sensitivity analyses will be performed for the primary endpoints based on the 3-month follow-up data.

7.6.1 Primary Safety Endpoint

Sensitivity to Analysis Sets

CCI [redacted]

Best-Case Scenario

CCI [redacted]

Worst-Case Scenario

CCI [redacted]

Tipping Point Analysis

CCI [redacted]

CCI [redacted]

7.6.2 Primary Effectiveness Endpoint

Sensitivity to Analysis Sets

CCI [redacted]

Best-Case Scenario

CCI [redacted]

Worst-Case Scenario

CCI [redacted]

Tipping Point Analysis

CCI [redacted]

7.7 Subgroup Analyses

In order to provide additional characterization and interpretation of the primary endpoints, the following subgroup analyses will be performed. CCI [redacted]

- **Baseline Characteristics**
  - Age group: <65 vs. ≥65 years

- Sex: Male vs. Female
- CHA_2DS_2-VASc Score: $\leq$2 vs. >2

7.8 Handling of Missing Data

7.8.1 Primary Safety Endpoint

CCI [redacted]

7.8.2 Primary Effectiveness Endpoint

CCI [redacted]

7.8.3 Secondary Effectiveness Endpoint

CCI [redacted]

[redacted]

7.9 Adjustments for Multiplicity

The secondary endpoint will only be tested if both primary endpoints are met CCI [redacted] C C

[redacted]

[redacted]

CCI [redacted]

7.10 Analyses of Secondary Endpoints

If success is achieved in both the primary safety and acute effectiveness endpoints, then the secondary effectiveness will be evaluated using the Kaplan-Meier estimate.

CCI [redacted] The testing of the hypothesis for the secondary effectiveness endpoint after the success of the primary endpoints are met ensures family-wise error rate is controlled at a 2.5% level.

The secondary effectiveness endpoint will be tested in the PP analysis set when all subjects have completed their 12-month follow-up. The analyses results will be reported in the final CSR.

The following additional analysis will be performed for the secondary effectiveness endpoint based on 12-month follow-up data:

- **Sensitivity to Analysis Set**

CCI [redacted]

- **Exact Test for Binomial Proportion Analysis**

CCI [redacted]

- **Best-case Scenario**

CCI [redacted]

[redacted]

CCI [redacted]

- **Worst-case Scenario**

CCI [redacted]

[redacted]

7.11 Additional Endpoint Analyses

No formal statistical hypothesis will be formulated and tested for the additional endpoints. Descriptive statistics will be provided on all additional endpoints in the analysis sets specified below.

7.11.1 Additional Procedural Endpoints

The following procedural data will be summarized descriptively in the PP, mITT, and Roll-In analysis sets:

- Total procedure time, PVI time, PF application time and mapping time
- Number of PF applications by left and right PV and by subject
- Total fluoroscopy time
- Total study catheter left atrial dwell time
- Ablation settings used

7.11.2 Additional Safety Endpoints

The following analyses for the additional safety endpoints will be summarized descriptively in Safety, mITT, and Roll-In analysis sets as the total number of events, number of subjects with events, and percentage of subjects with events:

- Occurrence of Serious Adverse Device Effects (SADEs)
- Occurrence of Unanticipated (Serious) Adverse Device Effects (USADEs)

- Occurrence of Serious Adverse Events (SAEs) within 7 days (early-onset), 8-30 days (peri-procedural), and >30 days (late onset) of index ablation procedure
- Occurrence of non-serious adverse events (non-SAEs)

7.11.3 Additional Effectiveness Endpoints

The following analyses for additional effectiveness endpoints will be summarized descriptively in the PP, mITT, and Roll-In analysis sets after all study subjects completed the 12-month follow-up. CCI [redacted]

- **Single Procedural Success** is defined as freedom from documented symptomatic atrial arrhythmia (AF, AT or AFL of unknown origin*) episodes based on electrocardiographic data (≥30 seconds on arrhythmia monitoring device) during the effectiveness evaluation period (Day 91-Day 365) following a single index ablation procedure. Subjects who had repeat procedure(s) for the study arrhythmia post the index procedure will be deemed failures of this endpoint. CCI [redacted]

- **Freedom from documented symptomatic atrial arrhythmia (AF, AT or AFL of unknown origin*):** Kaplan-Meier estimates and plots will be used to characterize the time to first documented symptomatic atrial arrhythmia (AF, AT or AFL) recurrence based on electrocardiographic data (≥30 seconds on arrhythmia monitoring device) during the effectiveness evaluation period (Day 91-Day 365) at 12 months post the index procedure.

  Acute procedural failure (i.e., failure to confirm entrance block in all PVs except those that are silent and/or cannot be cannulated post-procedure, use of non-study catheter for PV isolation, and failure to have energy delivery with the study device due to ablation system malfunctions) will also be considered a failure.

- **Freedom from documented (symptomatic and asymptomatic) atrial arrhythmia (AF, AT or AFL of unknown origin*) with additional failure models:** Kaplan-Meier estimates and plots will be used to characterize the time to first documented (symptomatic and asymptomatic) atrial arrhythmia (AF, AT or AFL) based on electrocardiographic data (≥30 seconds on arrhythmia monitoring device) during the effectiveness evaluation period (Day 91-Day 365).

  The event-free rate will also be summarized descriptively as the number and percent of subjects free from documented (symptomatic and asymptomatic) atrial arrhythmia (AF, AT or AFL) during the evaluation period. The following criteria will also be deemed failures:

- Failure to achieve acute procedural success.
- Taking a new Antiarrhythmic Drug (AAD) (Class I / Class III) for atrial tachyarrhythmia (AF, AT or AFL of unknown origin*) or taking a previously failed Class I/III AAD at a greater than the highest ineffective historical dose for AF/AFL/AT during the effectiveness evaluation period (Day 105 – Day 365).
- Greater than 1 repeat ablation for AF/AT or AFL of unknown origin* in the blanking period or any repeat ablation for AF/AT or AFL of unknown origin* during the effectiveness evaluation period.

- **Use of a non-study device** for the purpose of PVI (i.e., touch-up) among all clinically relevant targeted PVs. The number and percentage of subjects and number and percent of clinically relevant PVs ablated by a non-study catheter (NSC) for PVI will be summarized.

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- **Acute reconnection** identified by adenosine/isoproterenol challenge among all clinically relevant targeted PVs.

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- **Repeat ablation procedures** for left atrial arrhythmia (AF, AT or AFL of unknown origin*) within the 12-month FU period. Procedures for new CTI dependent flutter in the follow up period are not considered repeat procedures per CIP. Following analyses will be performed to delineate the repeat ablation procedure.

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CCI [redacted]

- **Quality of Life (QoL)** is defined as the change of QoL assessed by comparing the Atrial Fibrillation Effect on Quality-of-Life (AFEQT™) scores before and at 3, 6 and 12- months after the ablation procedure.

CCI [redacted]

The AFEQT questionnaire will only be used in countries with validated languages. These analyses will be conducted for subjects in countries where the AFEQT questionnaires are applied.

- **Hospitalization for cardiovascular events** through 12 months follow-up compared to 12 months prior to baseline. CCI [redacted]

7.12 Subset Analyses

The same subjects will participate in all four (4) subsets, which include a PVI Durability subset, a Neurological Assessment (NA) subset, a Cardiac Computed Tomography (CT) or Magnetic Resonance Angiogram (MRA) image subset and an Esophageal Endoscopy (EE) subset.

The subset analysis will be summarized in individual subset independently after all study subjects completed the 3-month follow-up. Additionally, the subset analysis will be performed again after all study subjects completed the 12-month follow-up if there are any updates after 3-month follow-up and data was presented in the 3-month CSR previously.

7.12.1 Analysis of PVI Durability Endpoint

The percentage of targeted PVs in the index ablation procedure being durably isolated evidenced by confirmation of isolation via electroanatomical mapping 75 days (+/- 15 days) post index ablation procedure.
Percentage of subjects with durably isolated targeted PVs, evidenced by confirmation of isolation via electroanatomical mapping at 75 days (+/- 15 days) post index ablation procedure.

These analyses will be performed in the PVI Durability analysis set.

7.12.2 Analysis of NA Endpoint

The following analyses of neurological evaluations will be conducted and summarized descriptively. The analysis will be performed in the Neurological Assessment (NA) analysis set.

- **Neurological Exam:** CCI [redacted]
- **Cerebral Emboli:** CCI [redacted]
- **Mini Mental State Examination (MMSE):** CCI [redacted]
- **National Institute of Health Stroke Scale (NIHSS):** CCI [redacted]
- **Modified Rankin Scale (mRS):** CCI [redacted]

7.12.3 Analysis of CT/MRA Endpoint

Incidence of PV stenosis in the CT/MRA subset up to 3 months post-ablation will be summarized with the number and percentage of subjects experiencing PV stenosis as defined by the core lab. The analysis will be performed in the Cardiac CT/MRA analyses set.

7.12.4 Analysis of EE Endpoint

The listing of subjects experiencing esophageal thermal lesions in the region of the contact area between the esophagus and LA as determined by post-procedure endoscopy and assessed by the core lab will be reported. The analysis will be performed in the EE analyses set.

8 Handling of Deviations from Planned Analyses

In the event of unforeseen challenges or data issues preventing the execution of the planned statistical analyses, a description of the reason will be provided in the methods section of the clinical study report ensuring transparency. Additional analyses not specified in the Statistical Analysis Plan that are conducted to support the evaluation of the study will be described in the clinical study report. This approach aims to uphold the integrity of the study's findings while providing comprehensive insights into any changes made to the statistical analysis methods.

9 Data Monitoring Committee (DMC)

A Data Monitoring Committee (DMC) will assess subjects' data for safety on frequent intervals and make recommendations on study adaptations as described in the DMC Charter. There will be no formal interim analysis (sample size analysis or early success analysis).

10 References

1. Spertus, J., et al., Development and validation of the Atrial Fibrillation Effect on QualiTy-of-Life (AFEQT) Questionnaire in patients with atrial fibrillation. Circ Arrhythm Electrophysiol, 2011. 4(1): p. 15-25.

2. Folstein, M.F., S.E. Folstein, and P.R. McHugh, “Mini-mental state”: A practical method for grading the cognitive state of patients for the clinician. Journal of Psychiatric Research, 1975. 12(3): p. 189-198.

3. Schlegel, D., et al., Utility of the NIH Stroke Scale as a predictor of hospital disposition. Stroke, 2003. 34(1): p. 134-7.

4. Wilson, J.T., et al., Improving the assessment of outcomes in stroke: use of a structured interview to assign grades on the modified Rankin Scale. Stroke, 2002. 33(9): p. 2243-6.

OmnyIRE SAP v3.0_FINAL

Final Audit Report 2025-08-06

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"OmnyIRE SAP v3.0_FINAL" History

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2025-07-28 - 6:48:49 PM GMT- PPD

PPD authenticated with Adobe Acrobat Sign.
Challenge: The user clicked on the signature field: 'Signature Field 2'.
2025-07-28 - 6:56:50 PM GMT

Document e-signed by PPD

Signing reason: I am approving this document

Signature Date: 2025-07-28 - 6:57:03 PM GMT - Time Source: server- PPD

Email viewed by PPD

2025-07-28 - 7:01:53 PM GMT- PPD

PPD authenticated with Adobe Acrobat Sign.

Challenge: The user clicked on the signature field: 'Signature Field 3'.

2025-07-28 - 7:03:09 PM GMT

PPD authenticated with Adobe Acrobat Sign.

Challenge: The user clicked on the signature field: 'Signature Field 3'.

2025-07-28 - 7:03:39 PM GMT

PPD authenticated with Adobe Acrobat Sign.

Challenge: The user clicked on the signature field: 'Signature Field 3'.

2025-07-28 - 7:04:05 PM GMT

Document e-signed by PPD

Signing reason: I am approving this document

Signature Date: 2025-07-28 - 7:04:15 PM GMT - Time Source: server- PPD

Email viewed by PPD

2025-08-01 - 3:30:11 AM GMT- PPD

Email viewed by PPD

2025-08-03 - 2:07:36 PM GMT- PPD

Email viewed by PPD

2025-08-05 - 10:06:45 PM GMT- PPD

PPD authenticated with Adobe Acrobat Sign.

Challenge: The user clicked on the signature field: 'Signature Field 4'.

2025-08-06 - 8:53:49 AM GMT

Document e-signed by PPD

Signing reason: I am approving this document

Signature Date: 2025-08-06 - 8:54:06 AM GMT - Time Source: server- PPD

Agreement completed.

2025-08-06 - 8:54:06 AM GMT