
# Statistical Analysis Plan

## Q-fficiency IDE #G180176

## Evaluation of QDOT MICRO™ Catheter for Pulmonary Vein Isolation (PVI) in Subjects with Paroxysmal Atrial Fibrillation (PAF)

## Protocol # BWI_2017_07 (v 5.0)

## The Variable Flow Study

**Version 2.0**

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History of Changes:

| **Version— Date** | **Description** |
|---|---|
| V 1.0 - 13 April 2021 | Original document submitted to the FDA |
| V 2.0 – 22 July 2021 | 1. The second stage of borrowing approach in Section 7.4 was updated to ensure that the borrowing from the Main study is less than the number of subjects with outcomes in the Variable Flow study for each strata. |

# Contents

## List of Abbreviations

| | |
|---|---|
| AAD | antiarrhythmic drug |
| AF | atrial fibrillation |
| AFEQT | Atrial Fibrillation Effect on Quality-of-life |
| AFL | atrial flutter |
| AT | atrial tachycardia |
| DCCV | Direct Current cardioversion |
| DMC | Data Monitoring Committee |
| mITT | Modified Intent-To-Treat |
| PAE | primary adverse event |
| PAF | paroxysmal atrial fibrillation |
| PG | performance goal |
| PP | per-protocol |
| PV | pulmonary vein |
| PVI | pulmonary vein isolation |
| RF | radiofrequency |
| SAE | serious adverse event |
| UADE | unanticipated adverse device effects |

# 1 STUDY DESIGN

QDOT MICRO IDE (IDE # G180176) is a prospective, non-randomized, pre-market clinical evaluation of the QDOT MICRO™ Catheter to demonstrate the safety and effectiveness against performance goals. The trial includes 1.) Main study: subjects treated using the nMARQ RF generator with constant flow rate (8mL/min) for QMODE+ applications, and 2.) Variable Flow study: subjects treated with the nMARQ RF generator with variable flow rate (4-15 ml/min) for QMODE+ applications.

The goal of the Variable Flow study is to demonstrate safety and effectiveness for the variable flow configuration of the device. A total of 92 enrolled subjects is planned. Enrollment in the Variable Flow study will begin when enrollment in the main study is completed.

The analysis for the Main study is a stand-alone analysis and it is not dependent on data from the Variable Flow study. The results from the Variable Flow study will only be used for additional claims on the safety and effectiveness of the variable flow feature of the device.

# 2 TREATMENT ASSIGNMENT

All subjects in the Variable Flow study will be treated using the QDOT MICRO™ catheter with variable flow rate.

# 3 RANDOMIZATION AND BLINDING PROCEDURES

All subjects will receive treatment with the QDOT MICRO catheter using variable flow rate. Therefore, no masking of treatment assignment for operators and subjects will be performed.

However, several measures will be employed to minimize operational bias:

- Screening logs will be maintained at sites to confirm consecutive eligible subjects are considered for participation in the study
- Sponsor personnel directly involved in the conduct of the study will not have access to intermediate aggregated summaries of primary safety and effectiveness endpoint data until preparation for filing for approval

# 4 LEVEL OF SIGNIFICANCE

Both primary safety and effectiveness endpoints will be tested at the one-sided 2.5% significance level. All confidence intervals will be presented at the 95% confidence level unless otherwise specified.

# 5 ANALYSIS SETS

The following analysis sets will be used for the Variable Flow study:

- **Safety Analysis Set**: The Safety analysis set will include all enrolled subjects in the Variable Flow study who have the investigational device inserted, regardless of RF energy delivery.

- **Modified Intent-To-Treat (mITT) Analysis Set**: The mITT analysis set will consist of all enrolled subjects in the Variable Flow study who meet all eligibility criteria and have the investigational device inserted. Subjects in this analysis set who are discontinued due to reasons related to the QDOT MICRO™ catheter will be considered as acute effectiveness failures; subjects who are discontinued due to reasons not related to the QDOT MICRO™ catheter will not be considered as acute effectiveness failures.

- **Per Protocol (PP) Analysis Set**: The PP analysis set will include subjects in the Variable Flow study who satisfy the following criteria:
    - Enrolled and meet eligibility criteria
    - Have undergone RF ablation
    - Are treated with the study catheter, and have been treated for the study related arrhythmia
    - without major protocol deviations:
        - Missing all protocol-specified electronic effectiveness monitoring
        - Esophageal monitoring is not done per protocol and risk is not mitigated
        - Not following the required waiting period of 20 minutes before pacing procedures, and/or infusion of cardiac medications to induce AF/reconnection is not performed before entrance block confirmation
        - Undergoing the ablation procedure with a constant flow rate in place of the variable flow rate

# 6 SAMPLE SIZE JUSTIFICATION

The final analyses for primary safety and effectiveness endpoints in the Variable Flow study will apply Bayesian methods using a beta-binomial model with data borrowing from the Main study using a propensity score-integrated power prior approach. Based on a PG of 14% for the primary safety endpoint and a PG of 50% for the primary effectiveness endpoint, and allowing borrowing up to 91 subjects from QDOT MICRO (IDE # G180176) Main study, the sample size of 92 subjects in the Variable Flow study provides close to 80% power at a one-sided significance level of 2.5% to declare success for both the safety and effectiveness endpoints, assuming the true PAE rate is 7% and the true effectiveness failure-free rate is 65%. It is also assumed that there is a 5% and 12%

attrition rate for the safety and effectiveness endpoints in the Variable Flow study, respectively. More details about the borrowing strategy are provided in section 7.4.

# 7 STATISTICAL ANALYSIS METHODS

## 7.1 General Conventions

Standard descriptive summaries for continuous variables will include the number of observations with data, mean, standard deviation, median, 25% percentile, 75% percentile, minimum and maximum values. For categorical variables, the count and percentage will be provided. Percentages will be based on the number of subjects without missing data.

## 7.2 Subject Disposition

Disposition and accountability of the study subjects will be summarized descriptively for the subject categories defined in section 9.5 of the protocol.

## 7.3 Demographic and Baseline Characteristics

Subject demographics, medical history, AAD use history and other baseline data will be summarized descriptively for all enrolled subjects as well as subjects in the Safety, mITT and PP analysis sets.

## 7.4 Borrowing Approach

A propensity score-integrated power prior approach will be used to borrow data from the Main study for evaluating safety and effectiveness of the Variable Flow study. The borrowing approach follows the method described in Yue, L. et al[1], and ensures that we only borrow data from subjects in the Main study who are similar to the subjects in the Variable Flow study in terms of their baseline characteristics. The catheter design and the procedure workflow with the exception of the flow rate are identical between the Main study and the Variable Flow study. Preclinical and bench testing concluded comparable performance of the catheter for constant or variable flow rates. Accordingly, data from up to 91 subjects in the Main study will be borrowed for the Variable Flow study.

The following two-stage strategy will be used for borrowing :

1st Stage (Build the propensity score model) :

Using mITT analysis set, the propensity score model will be developed using assignment to the two studies (Main study vs. Variable Flow study) as the outcome, and demographics and

[1] Wang C, Li H, Chen WC, Lu N, Tiwari R, Xu Y, Yue L. Propensity score-integrated power prior approach for incorporating real-world evidence in single-arm clinical studies. Journal of Biopharmaceutical Statistics. 2019, 29:5, 731-748.

baseline characteristics as covariates in a logistic regression model. Covariates to be included are the following :

a. Demographics : age (age≥ 75, age 65-74 years, and age < 65), gender, BMI
b. Baseline : left ventricle ejection fraction, LA diameter
c. Medical conditions prior to enrollment: hypertension, thromboembolic events including stroke/TIA, Type II diabetes, obstructive sleep apnea (OSA), pericardial effusion, mitral valve regurgitation, and type of arrythmia, congestive heart failure, vascular disease history
d. History of symptomatic paroxysmal AF: total duration of PAF, total number of episodes in the past 12 months
e. Previous treatment for arrhythmia: pharmacological cardioversion (PCV), direct current cardioversion (DCCV), catheter ablation procedure, number of previously failed AADs

An independent statistician who has no access to the main study outcomes will be identified after enrollment is complete but prior to completion of follow-up in the Variable Flow study to build the propensity score model. For the modeling, any missing data or outliers (e.g. a subject with loop recorder may have a excessively large value for the history of symptomatic paroxysmal AF) will be imputed by randomly drawing from the distribution of the corresponding covariate.

2nd Stage (Determine Borrowing) :

Once the propensity score model is built by the independent statistician, the Sponsor will proceed to determine borrowing. This will be done after completion of enrollment in the Variable Flow study but prior to completion of follow-up. Let $N$ denote one subject less than the number of subjects in the mITT analysis set in the Variable Flow study :

I. The subjects in the Main study will be trimmed if their propensity scores are outside of the range of propensity scores for the subjects in the Variable Flow study.
II. Subjects will be grouped into 5 strata (quintiles) based on the propensity score ranking such that the same number of Variable Flow study subjects are in each propensity score stratum.
III. The balance of covariate distributions will be assessed graphically between subjects in the Main study and the Variable Flow study.
IV. The similarity measurement ($r_s$) will be calculated using the Kolmogorov-Smirnov ($KS$) distance for each propensity score stratum. Let $KS_s$ denotes the maximum distance between the empirical distribution functions of the observed propensity score in the Main study and the Variable Flow study for the $s$-th stratum. Then the similarity measurement for the $s$-th stratum will be obtained by

$$r_s = 1 - KS_s.$$

V. The number of subjects to be borrowed from the Main study in each stratum will be based on similarity to the Variable Flow study. The standardized similarity measurement for each stratum is obtained by $r_s/\sum r_s$ and the number of Main study subjects to be borrowed from each stratum is obtained by $Nr_s/\sum r_s$.

Let $n_{s,Main}$ and $n_{s,Flow}$ be the number of subjects in the Main study and the Variable Flow study in the $s$-th stratum, respectively. For the Variable Flow study, subjects with missing outcomes will be excluded to obtain the following posterior distributions. The power term controlling the amount of information borrowed from the Main study for each stratum is obtained by $\alpha_s = \min\left(\frac{Nr_s/\sum r_s}{n_{s,Main}}, 1\right)$.

Let $y_{s,Flow}$ and $y_{s,Main}$ be the number of subjects with PAEs in the Variable Flow study and the Main study respectively in the $s$-th stratum. Assuming non-informative Beta(0.5, 0.5) prior for safety, the resulting posterior distribution for the safety endpoint for each stratum is $\text{Beta}(0.5 + Y_{s,borrow} + y_{s,Flow}, 0.5 + NY_{s,borrow} + (n_{s,Flow} - y_{s,Flow}))$, where $Y_{s,borrow} = \min(\alpha_s \times y_{s,Main}, y_{s,Flow})$ and $NY_{s,borrow} = \min(\alpha_s \times (n_{s,Main} - y_{s,Main}), (n_{s,Flow} - y_{s,Flow}))$.

Let $x_{s,Flow}$ and $x_{s,Main}$ be the number of subjects that are failure-free through 12 months in the Variable Flow study and the Main study respectively in the $s$-th stratum. Similarly, assuming non-informative Beta(1, 1) for the effectiveness endpoint, the resulting posterior distribution for the effectiveness endpoint for each stratum is $\text{Beta}(1 + X_{s,borrow} + x_{s,Flow}, 1 + NX_{s,borrow} + (n_{s,Flow} - x_{s,Flow}))$, where $X_{s,borrow} = \min(\alpha_s \times x_{s,Main}, x_{s,Flow})$ and $NX_{s,borrow} = \min(\alpha_s \times (n_{s,Main} - x_{s,Main}), (n_{s,Flow} - x_{s,Flow}))$. Only subjects with non-missing endpoint data in the main arm will be included for borrowing in the corresponding endpoint analyses. The posterior distributions of the primary endpoints are obtained by a weighted average of the posterior distributions across the 5 strata using equal weights.

### 7.5 Analysis of Primary Safety Endpoint

The primary adverse event (PAE) rate will be compared against a performance goal of 14% by testing the following hypotheses:

$$H_0: p_s \geq 0.14 \qquad vs \qquad H_A: p_s < 0.14\,,$$

where $p_s$ is the PAE rate (please refer to the study protocol for the definition of the primary safety endpoint). The mITT Analysis Set is the primary analysis set for the primary safety endpoint.

The primary analysis for the primary safety endpoint will be based on data from the Variable Flow study with borrowing from the mITT analysis set in the Main study, and will apply Bayesian methods and use a beta-binomial model.

The primary safety endpoint will be met if

$$\Pr(p_S < 0.14|y,n) > 0.975$$

where $p_s$ is the PAE rate. If the posterior probability of the safety rate being less than 14% is greater than 0.975 then the study will be considered to have demonstrated safety for the variable flow rate.

The following additional sensitivity analyses will be performed by updating the resulting posterior distribution for the safety endpoint for each stratum in the 2nd stage in Section 7.4 after accounting for missing data. Since the power term $\alpha_s$ controlling the borrowing does not depend on the missing outcome, the posterior distribution for the safety endpoint for each stratum is updated by incorporating the missing safety outcomes according to each scenario. Borrowing from the main study remains unchanged from the primary analysis, i.e., sensitivity analyses will be performed for missing primary endpoint data in the Variable Flow study.

- **Tipping Point Analysis**

Tipping point analysis will be performed for the primary safety endpoint in the mITT analysis set to assess the impact of missing outcomes in the Variable Flow study on the primary safety analysis. The posterior distribution will be updated each time to evaluate whether a tipping point is identified.

### 7.6 Analysis of Primary Effectiveness Endpoint

The primary effectiveness endpoint will be assessed by testing the following hypothesis:

$$H_0: p_E \leq 0.50 \qquad vs \qquad H_A: p_E > 0.50\,,$$

where $p_E$ is the effectiveness success rate. The mITT Analysis Set is the primary analysis set for the primary effectiveness endpoint.

The primary analysis for the primary effectiveness endpoint will use complete follow-up data from the Variable Flow study with borrowing from the mITT analysis set in the Main study, and apply Bayesian testing using a beta-binomial model.

The primary effectiveness endpoint will be considered as success if

$$\Pr(p_E > 0.5|x,n) > 0.975$$

where $p_E$ is the 12-month effectiveness rate.

If the posterior probability of the effectiveness rate being greater than 50% is higher than 0.975, then the study will be considered to have demonstrated effectiveness of the device.

The Variable Flow study will be considered achieving study success when both the primary safety and primary effectiveness performance goals are met. The following additional

analyses will be performed at the time of the final effectiveness analysis. Similar to the safety sensitivity analyses, the posterior distribution for the effectiveness endpoint for each stratum is updated by incorporating the missing effectiveness outcomes according to each scenario. Borrowing from the main study remains unchanged from the primary analysis, i.e., sensitivity analyses will be performed for missing primary endpoint data in the Variable Flow study.

- **Tipping Point Analysis**

Tipping point analysis will be performed for the primary effectiveness endpoint in the mITT analysis set to assess the impact of missing outcomes in the Variable Flow study on the primary effectiveness analysis. The posterior distribution will be updated each time to evaluate whether a tipping point is identified.

## 7.7 Analysis of Secondary Endpoints

No formal statistical hypothesis and inferential statistics will be formulated and performed for the secondary endpoints. Descriptive statistics will be provided on all secondary safety endpoints in the Safety analysis set in the Variable Flow study. Similarly, the secondary Effectiveness endpoints will be summarized descriptively in the PP analysis set in the Variable Flow study. The following analyses will be completed when all subjects complete their 12-month follow-up.

### 7.7.1 Analysis of Secondary Safety Endpoint

The following analyses for the secondary safety endpoints will be conducted in the Safety analysis set in the Variable Flow study.

- Incidence of Unanticipated Adverse Device Effects (UADEs) will be summarized descriptively.
- Incidence of Serious Adverse Events (SAEs) within 7 days (early onset), >7 to 30 days (peri-procedural) and >30 days (late onset) will be summarized descriptively by three timeframes.
- Incidence of bleeding complication (ISTH definitions): major, clinically relevant non-major and minor bleeding
  The ISTH (International Society on Thrombosis and Haemostasis) recommended the following criteria for defining different severity levels of bleeding complications of the atrial fibrillation and non-surgical venous thromboembolism cases [1],
    - Major bleeding: having a symptomatic presentation and 1) Fatal bleeding, and/or 2) Bleeding in a critical area or organ, such as intracranial, intraspinal, intraocular, retroperitoneal, intra-articular or pericardial, or intramuscular with compartment syndrome, and/or 3) Bleeding causing a fall in hemoglobin level of 20 g L−1 (1.24 mmol L−1) or more, or leading to transfusion of 2 or more units of whole blood or red cells

- Clinically relevant non-major bleeding: Any sign or symptom of hemorrhage (e.g., more bleeding than would be expected for a clinical circumstance, including bleeding found by imaging alone) that does not fit the criteria for the ISTH definition of major bleeding but does meet at least 1 of the following criteria: 1) requiring medical intervention by a healthcare professional, 2) leading to hospitalization or increased level of care, 3) prompting a face-to-face (i.e., not just a telephone or electronic communication) evaluation

All bleeding complications after the index procedure will be included in this analysis. The number of bleeding complications, number of subjects with bleeding complications, percentage of subjects with bleeding complications, rate of ISTH-defined major bleeding complications (per person-month) will be presented overall and by ISTH-defined categories (i.e. major, clinically relevant non-major, and minor).

### 7.7.2 Analysis of Secondary Effectiveness Endpoint

Descriptive statistics will be provided on the following endpoints in the PP analysis set in the Variable Flow study.

- **Acute Procedural Success**: confirmation of entrance block in all PVs.

  The number and percentage of subjects with acute procedural success and the corresponding 97.5% exact binomial lower confidence bound will be presented.

- **PV Isolation/ Acute Reconnection/ Touch-Up Application**:

  - **PV isolation at the end of the procedure**

    Percent of subjects and percent of targeted PVs where PVI was achieved at the end of the index procedure, including additional RF application for the PV reconnection if applicable, will be summarized descriptively.

    The achievement of PVI at the end of the procedure will be identified at the following time points, including 1) before the required 20-min waiting period, or 2) after the adenosine challenge was performed, and 3) after additional RF application for PV reconnection, whichever occurs last during the index procedure.

    - Rate of PVI achieved at the end of procedure among targeted veins:

      $$= \frac{number\ of\ targeted\ veins\ reaching\ PVI\ at\ the\ end\ of\ procedure}{total\ number\ of\ targeted\ veins}$$

    - Rate of PVI achieved at the end of procedure among subject:

$$= \frac{number\ of\ subjects\ reaching\ PVI\ at\ the\ end\ of\ procedure}{total\ number\ of\ subjects\ undergone\ ablation\ procedure}$$

- **PV isolation using QMODE+ as only ablation strategy**

Percent of subjects and percent of targeted PVs where PVI was achieved at the end of the index procedure by using only the QMODE+ during the procedure will be summarized descriptively.

- Rate of PVI achieved by using QMODE+ only among targeted veins:

$$= \frac{number\ of\ targeted\ veins\ reaching\ PVI\ at\ the\ end\ of\ procedure\ by\ using\ QMODE+only}{total\ number\ of\ targeted\ veins}$$

- Rate of PVI achieved by using QMODE+ only among subjects:

$$= \frac{number\ of\ subjects\ reaching\ PVI\ at\ the\ end\ of\ procedure\ by\ using\ QMODE+only}{total\ number\ of\ subjects\ who\ underwentablation\ procedure}$$

- **PVs isolation after first encirclement (evaluated prior to the 20-minute waiting period and adenosine challenge)**

Percent of subjects and percent of targeted PVs where PVI was achieved before the required 20-min waiting period, regardless the additional application was applied to remove the PV reconnection or not, will be summarized descriptively.

- Rate of PVI achieved prior to 20-min waiting period among targeted veins:

$$= \frac{number\ of\ targeted\ veins\ reaching\ PVI\ prior\ to\ 20-min\ waiting\ period}{total\ number\ of\ targeted\ veins}$$

- Rate of PVI achieved prior to 20-min waiting period among subjects:

$$= \frac{number\ of\ subjects\ reaching\ PVI\ prior\ to\ 20-min\ waiting\ period}{total\ number\ of\ subjects\ who\ underwent\ ablation\ procedure}$$

- **PV isolation after first encirclement without acute reconnection (evaluated after waiting period and adenosine challenge)**

Percent of subjects and percent of targeted PVs where PVI was achieved after the adenosine challenge and with no additional RF applications to remove PV reconnection will be summarized descriptively.

- Rate of PVI achieved after adenosine challenge among targeted veins:

$$= \frac{number\ of\ targeted\ veins\ reaching\ PVI\ after\ adnosine\ challenge\ and\ without\ acute\ reconnection}{total\ number\ of\ targeted\ veins}$$

- Rate of PVI achieved after adenosine challenge among subject:

$$= \frac{number\ of\ subjects\ reaching\ PVI\ after\ adenosine\ challenge\ and\ without\ acute\ reconnection}{total\ number\ of\ subjects\ who\ underwentblation\ procedure}$$

- **Acute PV reconnection after first encirclement**

Percent of subjects and percent of targeted PVs where PV reconnection was observed after the adenosine challenge will be summarized descriptively.

- Rate of acute PV reconnection among targeted veins:

$$= \frac{number\ of\ targeted\ veins\ with\ PV\ reconnection\ after\ adenosine\ challenge}{total\ number\ of\ targeted\ veins}$$

- Rate of acute PV reconnection among subject:

$$= \frac{number\ of\ subjects\ with\ PV\ reconnection\ after\ adenosine\ challenge}{total\ number\ of\ subjects\ who\ underwent\ ablation\ procedure}$$

- **PVs with touch-up (i.e. touch-up or ablation for acute reconnection)**

Percent of subjects and percent of targeted PVs where additional RF applications was applied to remove PV reconnection, regardless the timing of PVI or the confirmation of the entrance block, will be summarized descriptively.

- Rate of PV touch-up among targeted veins:

$$= \frac{number\ of\ targeted\ veins\ with\ touch-up\ RF\ application}{total\ number\ of\ subjects\ who\ underwent\ ablation\ procedure}$$

- Rate of PV touch-up among subjects:

$$= \frac{number\ of\ subjects\ with\ touch-up\ RF\ application}{total\ number\ of\ subjects\ who\ underwent\ ablation\ procedure}$$

- **Repeat ablation procedures during 12-month period post procedure**

- **Rate of repeat procedures**

All repeat ablation procedures after the index procedure will be summarized. The number of repeat procedure, number of subjects undergoing repeat procedure, percentage of subjects undergoing repeat procedure will be presented overall and by timing of the repeat procedure (i.e. during blanking period (Day 1-90), and during the evaluation period (Day 91-365)) and by type of arrhythmia being treated (e.g. AF, AFL, atypical flutter, etc.).

$$= \frac{number\ of\ subjects\ undergoing\ repeat\ ablation\ for\ study\ arrhythmia}{total\ number\ of\ subjects\ who\ underwent\ the\ index\ ablation\ procedure}$$

Additionally, Kaplan-Meier analysis will also be performed to characterize the time to first repeat procedure post the index procedure.

- **PV re-isolated among all the targeted PVs at repeat procedure**

  Percent of PVs that were targeted for ablation at both the index and repeat procedure and reached isolation in the repeat procedure will be presented overall and by timing of the repeat procedure (i.e. during blanking period (Day 1-90), and during the evaluation period (Day 91-365)) and by type of arrhythmia being treated (e.g. AF, AFL, atypical flutter, etc.).

$$= \frac{number\ of\ PV\ reisolated\ at\ repeat\ procedure}{total\ number\ of\ PVs\ being\ targted\ at\ index\ and\ repeat\ procedures}$$

- **Requiring additional lesions for non-PV triggers among the repeat ablation procedures**

  Percent of repeat ablation procedures requiring new linear lesions/ foci lesion which were not ablated in the index procedure will be will be presented overall and by timing of the repeat procedure (i.e. during blanking period (Day 1-90), and during the evaluation period (Day 91-365)) and by type of arrhythmia being treated (e.g. AF, AFL, atypical flutter, etc.).

$$= \frac{number\ of\ repeat\ procedure\ requiring\ new\ linear\ (foci) lesion\ not\ previsouly\ ablated\ in\ the\ index\ procedure}{total\ number\ of\ repeat\ procedures}$$

- **12-Month Single Procedure Success**

  - 12-month Single Procedure Success is defined as freedom from documented AF/AFL/AT recurrence (episodes ≥ 30 secs) during the evaluation period after a single ablation procedure and off AADs. Any repeat ablation procedure or AAD therapy will be deemed effectiveness failure for this analysis.

    The 12-month single procedure success rate will be summarized descriptively. Kaplan-Meier analysis will be performed to characterize the time to the first single procedure failures post the index procedure.

### 7.7.3 Analysis of Additional Endpoint

- **Procedure Data**

Procedural data such as total procedure time, PVI time, RF application time, mapping time, RF application time per lesion, total fluoroscopy time and dose, fluid delivered from the study catheter, location of RF applications, number of RF applications, repeat ablation rate, RF ablation parameters per application, device(s) utilized (per ablation), VISITAG™ Settings, CF range, Power range will be summarized descriptively. These analyses will be conducted using the PP analysis set in the Variable Flow study.

- **Quality of Life**

AFEQT includes 20 questions on a 7-point Likert scale. Questions 1 - 18 evaluate Health Related Quality of Life (HRQoL) and Questions 19- 20 relate to patients' satisfaction with treatment [1].

First 18 questions are also used to calculate Overall AFEQT score and subscale scores across three domains

• Symptoms: Four questions 1 - 4 assess AF related symptoms

• Daily Activities: Eight questions (5 – 12)

• Treatment Concerns: Six questions (13 – 18)

Overall and subscale scores range from 0 to 100. A score of 0 corresponds to complete disability, while a score of 100 corresponds to no disability.

Baseline values and changes from baseline at each time point the questionnaire is administered will be summarized descriptively for the following five scores. The overall AFEQT score and subscale scores across study visits will be plotted.

• Overall AFEQT Score (18 questions)

• Symptom Subscale Score (4 questions)

• Daily Activities Subscale Score (8 questions)

• Treatment Concern Subscale Score (6 questions)

• Treatment Satisfaction Score (2 questions)

These analyses will be conducted in the PP analysis set.

# 8 DATA MONITORING COMMITTEE- FOR INTERIM ANALYSIS

A Data Monitoring Committee (DMC) will be constituted to monitor subject safety. The DMC charter will document the constitution, roles and responsibilities of the committee, sponsor, and the independent statistician.

# 9 STUDY SUCCESS

The study will be considered successful if both primary endpoints are met.