Statistical Analysis Plan

Post-Operative Outcomes following the Treatment of Kidney Stones with the MONARCH™ Platform, Urology

Protocol Number: 2023-URO-0001
Protocol Version: C, November 28, 2023

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1 Introduction

This is the Statistical Analysis Plan (SAP) for the final analysis of data collected under Protocol 2023-URO-0001. This SAP describes in detail the statistical methodology and statistical analyses for this protocol.

1.1 Study Objectives

The aim of the study is to assess the successful completion of robotic mini-Percutaneous Nephrolithotomy (PCNL) using the MONARCH™ Platform, Urology. This study will also assess stone clearance (Post-Operative Day 30) and the safety profile following this procedure.

1.2 Study Design

This is a prospective, single arm observational multicenter study to collect outcomes data on the robotic-assisted mini-PCNL removal of kidney stones using the MONARCH™ Platform, Urology system.

The study originally intended to enroll up to 60 subjects across up to 3 sites. Each enrolled subject will be followed up to 90 days ± 14 days post procedure. Enrollment was stopped prior to reaching the original maximum of 60 subjects for business reasons that were unrelated to subject safety.

2 Treatment Assignment

This is a single-arm study where all enrolled subjects will have the MONARCH™ system utilized for removal of kidney stones via a mini-PCNL procedure.

3 Randomization and Blinding Procedures

As this is a single-arm study, no randomization occurred, and no blinding procedures were required.

4 Interval Windows

Interval windows for the purpose of analysis in this study are not defined outside of those already specified in the protocol for visit scheduling where the collection of data for the primary and safety endpoints occurs.

Table 1 Schedule of Assessments in the protocol specifies the following visits and windows where applicable:

- Screening/baseline: completed not more than 120 days prior to the procedure
- Procedure Day
- Follow-Up, Day 1
- Post-operative 30-day follow-up (± 7 days)

- Post-operative 90-day follow-up (± 14 days)

Any information entered in the electronic Case Report Forms (eCRFs) at a given visit will correspond to the scheduled visit. There will be no assigning of observations to time points outside of the visit to which they are recorded in the eCRFs.

5 Levels of Significance

No hypotheses were specified for this study and no p-values are being calculated, therefore no level of significance is specified. All estimation of endpoints will be performed using 95% confidence intervals where indicated below.

6 Analysis Sets

The summary of all performance and safety endpoints will be performed on the set of subjects in whom the MONARCH™ system is utilized during the procedure. This will be labeled as the Full Analysis Set (FAS) and will be identified by having a time recorded in the "When was the Ureteroscope introduced (timestamp)?" field on the Procedure: Ureteroscopy and Percutaneous Access eCRF.

7 Sample Size Justification

The study was originally planned to enroll up to 60 subjects. No formal hypothesis was being tested and therefore the sample size determination was not based on a statistical power calculation, but rather was considered sufficient to inform a baseline assessment on early post-operative outcomes.

8 Statistical Analysis Methods

8.1 General Conventions

Subject data will be summarized in tables and presented in further detail in listings. All eCRF data will be listed per subject for all subjects. Descriptive statistical analyses will be provided for pre-specified study endpoints. Summaries for continuous variables will include a minimum of number of observations (n), mean, standard deviation, median, minimum, and maximum. Summaries for categorical variables will include number and percentage.

Analyses will be conducted using SAS software. During the course of programming of tables for summaries that are described in this SAP, minor modifications may become necessary. Examples of these minor modifications include, but are not limited to, re-wording of a footnote, addition of a footnote, re-labeling of a column, or addition or removal of a column from a listing. In cases where modifications to tables or listings are not related to a change in statistical analysis methodology or conclusions that could be made on the originally proposed

methodology, then no amendment of the SAP is necessary. Changes to planned analyses specified in the protocol or alterations of an approach that is described herein, will require an amendment to the SAP.

Baseline for all parameters will be defined as the last available measurement on or before the procedure date.

8.2 Disposition of Study Subjects

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

8.3 Demographic and Baseline Characteristics

Summary statistics of subject demographics (age, sex, race, and ethnicity) will be presented for the FAS. Vital signs (height, weight, body mass index, systolic blood pressure, diastolic blood pressure, heart rate and ASA score) will be summarized in a similar manner.

Counts and percentages will be provided for medical history terms presented by Medical Dictionary for Regulatory Activities (MedDRA) System Organ Class and Preferred Term. Data collected in the Urologic or Other Relevant Procedure History eCRF will be listed.

Summary statistics will be provided for quantitative parameters collected in the Complete Blood Count (CBC) and Complete Metabolic Panel (CMP) blood draws reported at the Screening/Baseline Visit. Urinalysis and culture test results will be listed.

8.4 Clinical Characteristics

Pre-operative clinical characteristics as well as procedure day measurements will be summarized at both the subject level as well as the kidney stone level given that many subjects present with more than one stone for treatment in the study. At the subject level, counts and percentages will be provided for whether the left or right kidney is being treated, as well as the number of stones per subject. Summary statistics will be provided for cumulative stone burden, defined as the sum of the longest dimension of all stones, estimated percutaneous tract length, and cumulative stone volume which is calculated for each stone as $(\pi/6)$ * x dimension * y dimension * z dimension, then summed across all stones.

At the stone level, counts and percentages will be provided for the pole location and sub-location and summary statistics will be provided for the longest linear dimension and stone radio density.

8.5 Primary Endpoint and Associated Hypotheses

No formal hypotheses are specified for this study.

The primary endpoint is the successful completion of the robotic-assisted kidney stone removal procedure, defined as using robotic-assistance provided by the MONARCH™ Platform, Urology to achieve the following procedure milestones:

- Gain safe concomitant (i.e., retrograde and antegrade) access to the upper urinary tract
- Locate and visualize the kidney stones
- Enable fragmentation of stones by standard of care method
- Evacuate stone fragments and dust
- Complete treatment without need for case conversion, as assessed by the investigator

As indicated in the study protocol, the above bulleted device endpoints will be assessed regardless of clinical outcome (e.g., evacuation of stone fragments and dust may still be achieved by the device even if the patient is not stone free). Additionally, these milestones are considered successfully achieved if done so using robotic assistance provided by the MONARCH™ Platform, Urology at any point during the procedure (e.g., location and visualization of kidney stones may still be achieved with robotic assistance, even if the Investigator occasionally choses to drive the ureteroscope manually due to physician preference.) Alternatively, an early termination of the robotic procedure due to malfunction of the robot, and a subsequent conversion of the case to conventional procedure, would indicate that "complete treatment without need for case conversion, as assessed by the physician" had not been achieved.

The number and percentage of subjects experiencing successful completion will be summarized and an exact 95% confidence interval will be estimated. Counts and percentages will also be provided for each of the four components of the primary endpoint.

8.6 Secondary Endpoints and Associated Hypotheses

The following secondary endpoints are specified for this study:

- Stone free rate (≤ 4 mm residual fragments, measured 30-days post-operative)
- Adverse events through 90-days post-operative, scored on the Clavien-Dindo scale
- Conversion to conventional treatment methods due to study device-related safety event

No associated hypotheses are specified.

The stone free rate will be computed as the percentage of patients who are stone free assessed by computed-tomography (CT) scan at post-operative Day 30. Stone free is defined as having ≤ 4 mm residual cumulative stone burden detected by CT. Patients who are found to not have any residual stone fragments at Day 1, will not undergo a second CT at post-operative Day 30, and will be presumed to be stone free at Day 30 for this calculation. The number and percentage of procedures resulting in a subject who is determined to be stone free at Day 30 will be

summarized and a 95% confidence interval will be estimated. Similar analyses will be performed for the stone-free rate at Day 1.

All adverse events will be captured up to post-operative Day 90, at which point the subject exits the study. Summaries will be provided for all adverse events by MedDRA System Organ Class and Preferred Term. Similar summaries will be provided for device-related AEs, procedure-related AEs, serious adverse events (SAEs), device-related SAEs, and procedure-related SAEs. Adverse events will also be scored on the Clavien-Dindo scale and summaries will be provided by System Organ Class and Preferred Term for events that are graded at III or higher on the Clavien-Dindo scale and then similarly for those that are Grade II or lower in a separate output table.

The number and percentage of procedures converted to conventional stone removal procedures (e.g., ureteroscopy or percutaneous nephrolithotomy) due to the occurrence of a study device-related safety event will be summarized. A qualifying safety event is a study device-related adverse event that occurs during the study procedure that prompts the physician to abort the study procedure and pursue a conventional stone removal procedure.

8.7 Additional Endpoints

Summary statistics will be provided for the following:

- Procedure duration: defined as the difference between “When was the patient’s percutaneous wound closed?” from the Mini-PCNL eCRF and “When is the Cystoscope introduced?” from the Pre-Procedure Setup eCRF
- Cumulative stone burden at the 30-day follow-up visit as well as change in stone burden from the Screening/Baseline visit; Change in cumulative stone burden (%) will also be summarized and is defined as 100*(Change/Baseline). Similar analyses will be presented for cumulative stone volume at the 30-day follow-up visit.
- Efficiency of stone ablation defined as pre-operative stone volume divided by lithotripsy time. Lithotripsy time is defined as the difference between the treatment complete time from the mini-PCNL eCRF and first lithotripsy start time on the Laser Settings eCRF.
- Placement of a stent or nephrostomy tube as well as duration of stent placement in days: defined as the difference between “Date of stent extraction” from the Physical Exam and Vital Signs eCRF at the 30-day visit and “Did you place a ureteral stent in this patient?” from the Mini-PCNL eCRF + 1
- Subject weight post-procedure as well as change from pre-procedure weight
- Length of stay in nights: defined as “Date of hospital discharge” – “Date of hospital admission”
- Selected labs taken immediately post procedure (sodium, creatinine, hematocrit) as well as change from the Screening/Baseline visit
- Total fluoroscopy dosage (mGy) and time (minutes)
- Percutaneous access fluoroscopy dosage (mGy) and time (minutes)

- Wisconsin Stone Quality of Life survey over time as well as change from baseline (overall score and individual domains of social impact, emotional impact, disease impact and vitality impact)
- PROMIS-29 Profile v2.1 survey over time as well as change from baseline (overall score and individual domains of physical function, anxiety, depression, fatigue, sleep disturbance, social role satisfaction, and pain interference).

Counts and percentages will be provided for the following:

- Number and location of post-operative stones at the Day 1 and Day 30 follow-up visits.
- Number of needle attempts
- Need to relocate stones
- Number of Randall's plaques in each of the Upper Pole, Interpole, and Lower Pole as reported in the Investigator Assessment eCRF
- Subjects requiring retreatment for stone removal within the duration of the study, as reported within the Concomitant Procedure eCRF
- Responses to the Investigator Experience surveys regarding the procedure, retrograde instruments, antegrade instruments/controller, and user experience.

8.8 Safety Analyses

Analysis of adverse events is described in Section 8.6.

Listings will be provided for concomitant medications, concomitant procedures, physical examination findings and vital signs during follow-up.

8.9 Plans for Interim Analysis

No interim analysis was planned for this study that had the intention of altering study design or execution. Three summaries of data were provided to support abstract writing that described the initial experiences of the device use in subjects at the respective sites.

8.10 Handling of Missing Data

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

8.11 Adjustments for Multiplicity

No adjustments for multiplicity are necessary for this study given the absence of any formal hypothesis testing.

8.12 Sensitivity Analyses

No sensitivity analysis is planned for this study.

8.13 Subgroup Analysis

No subgroup analysis is planned for this study.

8.14 Assessment of Site Homogeneity

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

8.15 Exploratory Analyses

Counts and percentages (labeled as the “stone free rate”) will be provided for the number of procedures where post-operative cumulative stone burden is in the following categories: 0 mm, ≤ 2 mm, and ≤ 4mm. Analyses of the following cohorts will be performed:

- All subjects receiving the study procedure
- Pre-operative stone burden (1-2 cm), representing “intermediate-sized stones”
- Pre-operative stone burden (1-3 cm), representing “classic mini-PCNL stones”
- Pre-operative stone burden (1-4 cm), representing “targeted patient pool”
- Pre-operative stone burden (> 2 cm), representing “classic PCNL stones”
- Pre-operative stone burden (> 4 cm), representing “very large-sized stone”

Summary statistics will be presented for the total volume of fluid input from the MONARCH™ fluidics pump and total volume of fluid collected in the waste management system.

9 Data Monitoring Committee (DMC)

No Data Monitoring Committee was planned or utilized during this study.

End of Document

2023-URO-0001 SAP

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