RESET Study
PRospective Study to Evaluate EffectivenesS With the NURO™ PErcutaneous Tibial Neuromodulation System in Patients With OAB
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Statistical Analysis Plan

Clinical Investigation Plan Title	P**R**ospective Study to **E**valuate Effectiveness**S** with the NURO™ P**E**rcutaneous **T**ibial Neuromodulation System in Patients with OAB (RESET)
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1. Version History

Version	Summary of Changes	Author(s)/Title
1.0	• Not Applicable, New Document	Fiona Kan, Principal Statistician

2. List of Abbreviations and Definitions of Terms

Abbreviation	Definition
ICF	Informed Consent Form
MedDRA	Medical Dictionary for Regulatory Activities
MESA	Medical, Epidemiological, and Social Aspects of Aging
OAB	Overactive Bladder
OABq	Overactive Bladder Symptom Quality of Life Questionnaire
PGI-I	Patient Global Impression of Improvement
PPBC	Patient Perception of Bladder Condition
PTNM	Percutaneous Tibial Neuromodulation
PTNS	Percutaneous Tibial Nerve Stimulation
RESET	P**R**ospective Study to **E**valuate Effectivenes**S** with the NURO™ P**E**rcutaneous **T**ibial Neuromodulation System in Patients with OAB
SADEs	Serious Adverse Device Effects
SAGA	Self-Assessment Goal Achievement Questionnaire
SAP	Statistical Analysis Plan
TENS	Transcutaneous Electrical Nerve Stimulation
UF	Urgency Frequency
UTI	Urinary Tract Infection
UUI	Urinary Urge Incontinence

3. Introduction

This prospective, multicenter, single arm study evaluates changes from baseline in OAB symptoms as measured by voiding diaries and patient reported outcomes through 12 PTNM therapy sessions. The purpose of this Statistical Analysis Plan (SAP) is to document the statistical analysis plan for Final Report.

4. Study Objectives

4.1. Primary Objective

The primary objective of this study is to demonstrate a statistically significant reduction from baseline through 12 percutaneous tibial neuromodulation (PTNM) therapy sessions in the number of urinary urge incontinence (UUI) episodes per day.

4.2. Secondary Objectives

Secondary objectives include:

- Reduction from baseline through 12 PTNM therapy sessions in number of voids per day
- Change from baseline through 12 PTNM therapy sessions in quality of life as measured by the Overactive Bladder Symptom Quality of Life Questionnaire (OABq).

4.3. Additional Measures

Additional measures include:

- Incidence of device or therapy/procedure-related adverse events
- Nocturia / Nighttime voiding frequency
- Urgency including the Urgency Perception Scale (UPS)
- Patient-reported Outcomes:
    - Self-Assessment Goal Achievement Questionnaire (SAGA)
    - Patient Perception of Bladder Condition (PPBC)
    - Patient Global Impression of Improvement (PGI-I)

5. Investigation Plan

This is a prospective, multicenter, open-label study evaluating the use of PTNM in OAB drug naïve patients with UUI.

5.1. Study Population

The intended study population is subjects with UUI who have not tried an OAB medication. In addition, subjects must not have received advanced therapy treatment options for OAB (botulinum toxin injections, sacral neuromodulation or PTNS/PTNM).

5.2. Subject Enrollment

Subjects are considered enrolled at the time the study-specific Informed Consent Form (ICF) is signed. Each subject must meet all of the inclusion criteria and no exclusion criteria to be eligible to participate in this study. Any subject meeting an exclusion criterion will be excluded from study participation.

5.3. Inclusion Criteria

To be eligible to participate in the study, a subject must meet all of the following inclusion criteria:

1. 18 years of age or older

2. Diagnosis of OAB and associated symptoms of UUI and qualify with at least 3 episodes of mild, moderate, or severe urgency demonstrated on a 3-day urinary voiding diary
3. Experiencing UUI symptoms for at least 3 months
4. No prior treatment with anticholinergics/antimuscarinics or beta 3-agonists medications to treat OAB
5. Willing and able to accurately complete voiding diaries and questionnaires, attend visits, and comply with the study protocol
6. Willing and able to provide signed and dated informed consent

5.4. Exclusion Criteria

A potential subject who meets any of the following criteria will be excluded from participating in the study:

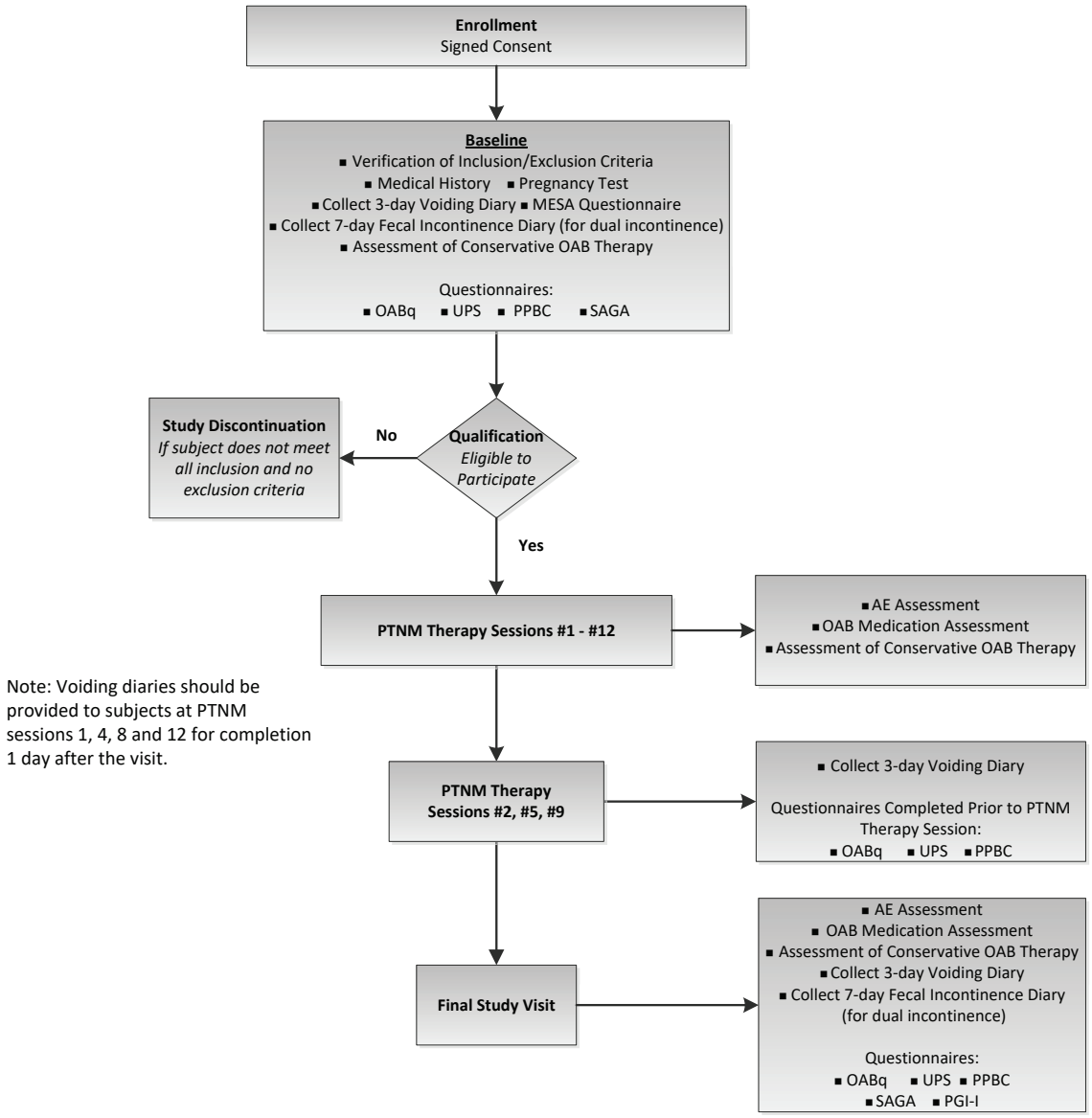
1. Have received anticholinergics/antimuscarinics or beta 3-agonists medications to treat OAB or advanced therapy treatment options for OAB (botulinum toxin injections, sacral neuromodulation, or percutaneous tibial nerve stimulation/neuromodulation)
2. Primary stress incontinence or mixed incontinence where the stress component overrides the urge component (see enrollment/baseline requirements for use of the MESA urinary incontinence questionnaire)
3. Have implantable pacemakers or implantable defibrillators
4. Use of transcutaneous electrical nerve stimulation (TENS) in pelvic region, back or legs
5. Women who are pregnant or planning to become pregnant during the course of the study (women of child-bearing potential must undergo a pregnancy test, with a clear negative result, prior to first PTNM session)
6. Characteristics indicating a poor understanding of the study or characteristics that indicate the subject may have poor compliance with the study protocol
7. Nerve damage that could impact either tibial nerve or pelvic floor function.
8. Subjects prone to excessive bleeding
9. Inadequate skin integrity in the area of PTNM needle placement
10. History of diabetes unless the diabetes is well-controlled through diet and/or medications
11. Have symptomatic urinary tract infection (UTI)

12. Participation in any research study involving or impacting gynecologic, urinary or renal function within the 4-week period prior to or plans to participate during study enrollment

5.5. Study Procedures

Subjects are considered enrolled at the time the study-specific ICF is signed. Each subject must meet all of the inclusion criteria and no exclusion criteria to be eligible to continue participation in this study. Following qualification using a 3-day baseline urinary voiding diary, MESA urinary incontinence questionnaire and pregnancy test (if applicable), subjects will undergo 12 PTNM therapy sessions, administered weekly (± 3 days), utilizing the NURO system. Urinary voiding diaries (3-day) to assess efficacy measures and quality of life questionnaires will be completed as indicated in Figure 1-1: Study Procedures. The study is expected to last approximately 14 weeks per subject following the enrollment visit. Subjects will be exited from the study after the final study visit is complete.

Figure 1-1: Study Procedures



6. Determination of Sample Size

This study is designed to evaluate the reduction from baseline in the number of UUI episodes per day after the 12th PTNM therapy session. The OrBIT trial by Peters et al (2009)[1] compared the effectiveness of PTNS to extended-release tolterodine. This study reported an average reduction of UUI at 12 weeks compared to baseline in the PTNS arm was 1 episode per day with a standard deviation of 2.2. The following assumptions were used for the sample size calculations: reduction of 0.75 UUI episodes/day from baseline, one-sample t-test with two-sided α=0.05, 90% power, and an estimated standard deviation of 2.2 incontinence episodes/day. Based on these assumptions, a sample size of 93 subjects would be required to demonstrate a statistically significant reduction from baseline. To account for an

attrition of approximately 20% during the study, a sample size of up to 120 subjects is required for this study.

The sample size requirement of 93 for the primary objective is also adequate to assess the secondary objectives of number of voids per day and quality of life measured by OABq. In the OrBIT trial by Peters et al (2009)[1], the average reduction of voids at 12 weeks compared to baseline in the PTNS arm was 2.4 voids per day with a standard deviation of 4.0. Based on a one-sample t-test, with α=0.05 two-sided, 90% power, 44 subjects with urgency frequency (UF) are required to demonstrate a statistically significant reduction from baseline if using a conservative estimate of a reduction of 2.0 voids per day with a standard deviation of 4.0. In the InSite study, among all implanted subjects 63% of the urinary incontinence (UI) subjects had both UI and UF at baseline. Therefore, 93 subjects should ensure the sample size needed for the secondary objective of UF based on this assumption.

In the OrBIT trial by Peters et al (2009)[1], the average improvement from baseline of HRQL from OABq for PTNS at 12 weeks was 25.3±21.5. Based on a one-sample t-test, with α=0.05 two-sided, 90% power, 15 subjects are required to demonstrate a statistically significant reduction from baseline when using a conservative estimate of average improvement of 20 points at 12 weeks with a standard deviation of 22. Therefore, 93 subjects should ensure the sample size needed for the secondary objective of OABq.

7. Statistical Methods

7.1. Study Subjects

7.1.1. Disposition of Subjects

Subject disposition will be summarized by study visit in a flow diagram. Discontinuation will be summarized by visit and discontinuation reasons will be provided.

7.1.2. Clinical Investigation Plan (CIP) Deviations

CIP deviations occurring during the study will be summarized by deviation type.

7.1.3. Analysis Sets

Throughout the document, all qualified subjects refer to subjects who meet inclusion/exclusion criteria.

Subjects used for analyses are described in each objective under Section 7.9.

7.2. General Methodology

The analysis methods are provided under each subsection in Section 7.9. In all analyses when p-value is calculated, a statistical test is deemed significant if the P value is less than 0.05.

7.3. Center Pooling

Data from all study centers will be pooled for the analysis. There are no planned statistical methods to test for treatment differences among centers. The study will be conducted at approximately 15 sites in

the US. Initial site enrollment is not planned to exceed 20% of the total number of subjects that are qualified for the study; however, this may be increased based on the Sponsor's discretion. This is intended to reduce the possibility that a site with atypical results will be overly influential in the overall study results.

7.4. Handling of Missing, Unused, and Spurious Data and Dropouts

For the primary objective and secondary objectives, primary analysis method will be based on the completers dataset, with no imputation of missing data. Sensitivity analyses with various missing data handling approaches will be conducted as described in Section 7.9.1. Secondary objectives will be analyzed in a similar matter as detailed in Section 7.9.2.

7.5. Adjustments for Multiple Comparisons

This is a single arm study, with a primary objective to evaluate the efficacy of PTNM on UUI episodes per day at the 12th PTNM session from baseline. No adjustments for multiple comparisons were made in this study.

7.6. Demographic and Other Baseline Characteristics

Demographics and other baseline characteristics will be summarized for subjects who are qualified for the study and receive PTNM treatment including:

- Age, gender, race and ethnicity
- Diagnosis, years since diagnosis
- Body Mass Index (BMI)
- Medical history
- Surgery history
- Conservative therapies for OAB
- Baseline UUI episodes per day, baseline voids per day (for UF subjects only), average degree of urgency, average nighttime voiding frequency and nocturia.

7.7. Treatment Characteristics

Motor and sensory response during therapy sessions will be summarized by PTNM session. If multiple sessions are used to complete a session visit, the motor and sensory response values from the last session in that visit will be used for summary.

During the study, if a subject starts an OAB medication following the first PTNM therapy session, a deviation form will be completed and the medication will be captured on the OAB medication form.

7.8. Interim Analyses

No interim analysis was planned for this study.

7.9. Evaluation of Objectives

7.9.1. Primary objective

This study will assess the efficacy of PTNM on UUI episodes collected using a voiding diary. The primary objective is to demonstrate a statistically significant reduction between baseline and following the 12th PTNM therapy session in the number of UUI episodes per day.

Hypothesis

Ho: µ12th PTNM therapy session = µbaseline

Ha: µ12thPTNM therapy session ≠ µbaseline

Where µbaseline and µ12th PTNM therapy session are average UUI episodes per day at baseline and following the 12th PTNM therapy session respectively.

Endpoint definition

The average UUI episodes per day collected at baseline and following the 12th and final PTNM therapy session will be used as the endpoint for the primary objective. Average UUI episodes per day will be calculated by summing all reported leaks and dividing by the total number of days of diaries.
For a diary to be included in the analysis, it needs to have complete leak and/or void episode entries for at least one day. For any reported episode if leak or void is not indicated, the diary of that day will not be included.

Data collection and analysis methods

Diary data collected at baseline and after the 12th PTNM therapy session will be used for the primary endpoint analysis. Reduction in average UUI episodes per day from baseline will be calculated for each subject after the 12^{th} PTNM. The paired t-test or the Wilcoxon signed-rank test will be used to evaluate the changes after testing for data normality by calculating Shapiro-Wilk W statistic. A statistical test is deemed significant if the P value is less than 0.05. Primary analysis method will be completers (with no imputation of missing data). Sensitivity analyses will be conducted with the adjusted worst-case method and per protocol analysis.

Determination of subjects for analysis

Qualified subjects with diary data from both baseline and the 12th PTNM therapy session will be included in the primary analysis for this objective.

In additional to the primary analysis, two sensitivity analyses will be performed:

- Adjusted worst-case analysis, in which,
    a. For subjects who received the study therapy and withdrew early due to device or therapy/procedure -related adverse events, or treatment unsuccessful, the 12th PTNM therapy session data point will be set to subject's baseline assessment.
    b. For subjects who received the study therapy and exit the study early due to all other reasons (i.e. adverse events not related to the device or therapy), and for subjects who missed the 12th PTNM therapy session or fail to provide the relevant data for 12th PTNM therapy session, the Last Observation Carried Forward (LOCF) method will be used to impute the missing data.
    c. Subjects who exit the study prior to the initial NURO PTNM therapy session will be excluded from this sensitivity analysis
- Per protocol sensitivity analysis which will be based on the completers dataset, but will exclude those subjects who take OAB medications in the study. Use of OAB medications will be captured as a protocol deviation.

Besides PTNM session 12, diary data are also collected for PTNM Session #1, #4, and #8. Reduction in number of UUI episodes from baseline will be summarized for each follow up visit (PTNM session #1, #4, #8 and #12) when the diary data is collected with no imputation of missing data (completers analysis).

7.9.2. Secondary objectives

7.9.2.1. Secondary objective #1

This objective is to assess the reduction in number of voids per day from baseline following 12 PTNM therapy sessions.

Endpoint definition

The average number of voids per day collected from baseline and following the 12th PTNM therapy session will be used for analysis of this objective. Average voids per day will be calculated by summing all reported voids and dividing by the total number diary days. For a diary to be included in the analysis, it needs to have complete leak and/or void episode entries for at least one day. For any reported episode if leak or void is not indicated, the diary of that day will not be included.

Data collection and analysis methods

Diary data from both baseline and following the 12th PTNM therapy session will be included in the analysis. Reduction in average voids per day from baseline will be calculated for each subject at 12th PTNM. A paired t-test or the Wilcoxon signed-rank test will be used to evaluate the changes after 12th PTNM therapy session from baseline after testing for data normality by calculating Shapiro-Wilk W statistic.

Determination of subjects for analysis

This objective will be assessed in qualified subjects with ≥ 8 voids per day at baseline, who has diary data at both baseline and 12th PTNM session.

In additional to the primary analysis which includes subjects with diary data from baseline and 12th PTNM therapy session, the same sensitivity analyses as described in the primary objective will be performed for secondary objective #1.

Besides PTNM session 12, diary data are also collected for PTNM Session #1, #4, and #8. Reduction in number of voids per day from baseline will also be summarized by the PTNM session (session #1, #4, #8 and #12) when the diary data is collected.

7.9.2.2. Secondary objective #2

This objective is to assess the change from baseline through 12 PTNM therapy sessions in quality of life as measured by the OABq Questionnaire. This objective will be assessed in subjects with OABq data at baseline and after 12th PTNM therapy session.

Endpoint definition

OABq Questionnaire collected from baseline and the 12th PTNM therapy session will be used for analysis of this objective.

Data collection and analysis methods

OABq Questionnaire collected from baseline and the 12th PTNM therapy session will be used for analysis of this objective. OABq consists a symptom bother scale and four health related quality of life (HRQL) subscales (Coping, Concern, Sleep and Social interaction). They will be scored according to published scoring criteria[2]. Symptom bother scale and 4 HRQL subscales are measured as 0-100 using a range percentile transformation on the summed value from individual listed items. The HRQL score is a calculated score with a range from 0 to 100 using a range percentile transformation on the summed value from 4 subscales (Coping, Concern, Sleep and Social interaction). For the subscale analyses, if < 50% of the scale items are missing, the scale should be retained with the mean scale score of the items present used to impute a score for the missing items. If ≥ 50% of the items are missing, no scale score

should be calculated, the subscale score should be considered missing. If a subscale score is missing, the HRQL Total score cannot be calculated. These scores will be analyzed for changes from baseline to the 12th PTNM. Calculation of change from baseline will be computed subtracting baseline values from the 12th PTNM values. A paired t-test or the Wilcoxon signed-rank test will be used to evaluate the changes after the 12th PTNM therapy session from baseline after testing for data normality by calculating Shapiro-Wilk W statistic.

Determination of subjects for analysis

This objective will be assessed in all qualified subjects who receive PTNM therapy and have OABq questionnaire data available at both baseline and the 12th PTNM session.

In additional to the primary analysis which includes subjects with diary data from baseline and 12th PTNM therapy session, the same sensitivity analyses as described in primary objective will be performed for secondary objective #2.

Improvement in OABq from baseline will also be summarized at by the PTNM session (session #1, #4, #8 and #12) when this data is collected.

7.9.3. Additional Measures

7.9.3.1. Incidence of device-related or therapy/procedure-related adverse events

Objective:

To summarize the device-related or therapy/procedure-related adverse events for all subjects who receive the PTNM therapy.

Endpoint definition

Device-related and therapy/procedure-related adverse events are defined as possible, probable and causal relationship to study procedure, NURO external neurostimulator, therapy session kit, and stimulation as reported on the event case report form (CRF). The sponsor assessment on the event is documented in the Medtronic Use Only CRFs. When there are differences in event CRF reporting and MUO CRFs, both will be reported in the final report, and the events summaries will be based on more conservative approach: for example, if it is reported as device related and not assessed as such in MUO CRF, the event will be counted as device related in event summaries.

Data collection and analysis methods

Device-related and therapy/procedure-related adverse events will be summarized by MedDRA preferred terms for all qualified subjects who receive the PTNM therapy. Number of subjects and percent of

subjects in each preferred term will be reported. These events will be further summarized by serious events and non-serious events.

Determination of subjects for analysis

All qualified subjects who receive the PTNM therapy will be included in the analysis.

7.9.3.2. Nocturia/ Nighttime voiding frequency

Objective:

To summarize the reductions in nocturia and nighttime voiding frequency from baseline by PTNM session when data is collected.

Endpoint definition

Nocturia is measured as the number of times the subject is woken from sleep to void. Nighttime frequency is measured as number of voids during nighttime sleep.

Data collection and analysis methods

Nighttime voiding and nocturia are collected on diaries for baseline visit, 1st, 4th, 8th and 12th PTNM sessions. Reduction in average night time voids per day and nocturia per day will be calculated for each subject from baseline to each PTNM session when diary data is collected. Average night time voids per day will be calculated by summing all reported night time voids and dividing by the total number of days of diaries. Average nocturia per day will be calculated by summing all reported nocturia episodes and dividing by the total number of days of diaries. For a diary to be included in the analysis, it needs to have complete leak and/or void episode entries for at least one day. For any reported episode if leak or void is not indicated, the diary of that day will not be included.

Determination of subjects for analysis

Reduction of nocturia and nighttime voiding frequency from baseline will be calculated for all qualified subjects who receive PTNM therapy and report baseline nighttime voiding and nocturia data respectively.

7.9.3.3. Urgency including the Urgency Perception Scale (UPS)

Objective:

To summarize UPS at baseline and by PTNM sessions for subjects who receive PTNM therapy.

Endpoint definition:

UPS is a three-category scale to measure the urgency perceptions based on subjects' experience when they have a desire to urinate.

Data collection and analysis methods:

UPS data are collected for baseline and the 1st, 4th, 8th and 12th PTNM sessions. Number of subjects and percent of subjects in each category of the scale will be summarized by visit.

As an additional analysis to look at urgency besides UPS, urgency is also collected for diary episodes such as no urgency, mild, moderate and severe. The following scores will be assigned to each urgency degree: 0= no urgency; 1=mild; 2=moderate; 3=severe. Average urgency score will be calculated by summing urgency scores for leaking episodes and dividing by the total number of leaks in 3-day voiding diary when urgency is reported. Average urgency score will be reported at baseline and 1st, 4th, 8th and 12th PTNM sessions. For a diary to be included in the analysis, it needs to have complete leak and/or void episode entries for at least one day. For any reported episode if leak or void is not indicated, the diary of that day will not be included.

Determination of subjects for analysis:

All qualified subjects who receive PTNM therapy and have data available will be included in the analysis.

7.9.3.4. Patient reported outcomes

- Self-Assessment Goal Achievement Questionnaire (SAGA)

Objective:

To summarize SAGA first visit at baseline and SAGA follow-up collected at final visit after 12th PTNM session for subjects who receive PTNM therapy.

Endpoint definition:

The SAGA questionnaire asks subjects to rank, in order of importance for standard urology symptom goals using a scale of 0-5 and allows for other personal goals to be included[3]. In SAGA follow-up assessment, it includes a scale of -2 to 2 to report on achievement of each symptom goal and other personal goal(s). The questionnaire includes an assessment question of "Overall, to what extent have you achieved your goals" on a scale of 0-4.

Data collection and analysis methods:

SAGA data are collected for baseline (goal-assessment; ranking) and follow-up (goal-achievement) after the 12th session.

SAGA data will be analyzed for subjects who receive the PTNM therapy and have data at baseline and follow-up after the 12th session. Baseline data will be summarized by importance of symptom goals for

each fixed symptom goal. Number of subjects and percent of subjects in each rating from not very important to very important for each fixed goal will be reported.

In the SAGA follow-up, SAGA goal achievement for each fixed goal will be tabulated from much worse than expected to much better than expected. The assessment on overall question on goal achievement will be summarized from "Did not achieve my goals at all" to "Exceeded my goals".

For the SAGA follow-up, goal attainment scores will be calculated according to the formula provided by Kiresuk and Sherman[4] (T-scores with mean=50 and SD=10) for 9 fixed goals. Additionally, weights will be applied to goal achievement ratings based on the baseline level of importance attached to each goal. Descriptive statistics for the T-scores will be reported. A mean T-score of 50 represents an outcome of goal achievement. Scores>50 are interpreted as exceeding goal and scores <50 as only somewhat or partially achieving goal[5].

Determination of subjects for analysis:

All qualified subjects who receive PTNM therapy with both SAGA first and SAGA follow-up data will be included in the analysis.

- Patient Perception of Bladder Condition (PPBC)

Objective:

To summarize PPBC at baseline and by PTNM sessions for subjects who receive PTNM therapy.

Endpoint definition

PPBC is a 6-point scale to describe the subject's bladder condition from bladder condition not causing problem to causing many severe problems.

Data collection and analysis methods

PPBC data are collected for baseline and the 1st, 4th, 8th and 12th PTNM sessions. Number of subjects and percent of subjects in each condition of the scale will be summarized by visit.

Determination of subjects for analysis

All subjects who are treated by the PTNM therapy and have data available will be included in this analysis.

- Patient Global Impression of Improvement (PGI-I)

Objective:

To summarize PGI-I collected at the end of the study.

Endpoint definition

PGI-I is a single question asking the patient to rate their urinary condition as compared with prior to beginning treatment on a scale from 1 (very much better) to 7 (very much worse).

Data collection and analysis methods

This questionnaire is collected following the 12th PTNM session. Number of subjects and percent of subjects in each of 7 categories will be presented for subjects with data available, especially the number and percent of subjects who report “Very much better” and “Much better” will be provided. Furthermore, three categories with “Very much better” and “Much better”, “A little better” combining into “Better”; “No change” as “Same”; and “A little worse”, “Much worse”, and “Very much worse” combining into “Worse” will be analyzed. Additionally, descriptive statistics including mean, standard deviation, and median will be provided.

Determination of subjects for analysis

All qualified subjects who receive PTNM therapy and have data available will be included in this analysis.

7.10.Safety Evaluation

In the study, reportable Adverse Events are collected. All serious, device related, therapy/procedure related and all device deficiencies are considered as reportable for this study. The sponsor assessment is documented in the Medtronic Use Only (MUO) CRFs. When there are differences in event CRF reporting and MUO CRFs, both will be reported in the final report, and the events summaries will be based on more conservative approach: for example, if it is reported as device related and not assessed as such in MUO CRF, the event will be counted as device related in event summaries.

Incidence of device-related and therapy/procedure-related adverse events will be summarized as detailed in Section 7.9.3.

Serious AEs (SAEs), regardless of device-related, therapy/procedure-related or not, will also be summarized for all enrolled subjects.

Device Deficiency will be summarized for qualified subjects who receive PTNM therapy. Additionally, Narratives of SADEs (Serious Adverse Device Effects) will be provided.

7.11.Changes to Planned Analysis

There are no changes to planned analyses as specified in the protocol.

8. Validation Requirements

Statistical programming code for programming code that affects the result of the main analysis for the primary objective as specified in Section 7.9.1 will be validated using Level I validation (peer reviewer independently programs output and then compares the output with that generated by the original Statistical Programmer). Programming code that affects the result of the main analysis for the secondary objectives as specified in Section 7.9.2 will be validated using Level II validation (peer reviewer reviews the code; where appropriate, performs manual calculations or simple programming checks to verify the output). In addition, those main analyses that are planned for publication are validated with Level II

validation. Level III validation (original Statistical Programmer performs a visual inspection of the code and output to confirm functionality) may be used for any previously validated program where only minor/administrative changes were made (eg, change the location of the data directory).

9. References

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