Executive Statistical Analysis Plan Summary

ProstaCare Water Electrolysis System for the Treatment of Benign Prostatic Hyperplasia

Statistical Analysis Plan

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Sponsored by: ProstaCare Singapore Pte. Ltd.

1 Fernvale Close #02-01, Lush Acres, Singapore 797485

1 STUDY OBJECTIVES AND DESIGN

1.1 Study Objectives

a. Primary Objectives

The primary objectives of the study are to:

- Demonstrate that BPH symptoms are improved by 6.5 points or more after use of prostaFix Water Electrolysis System as measured by the IPSS on all subjects at 3 months.
- Demonstrate that the treatment does not cause unacceptable rates of serious adverse events (SAE) associated with use of the device.

b. Secondary Objectives

The secondary objective(s) of the study are:

- To characterize changes in Qmax and PVR, sexual function and quality of life.
- To characterize post-treatment recovery measuring treatment tolerability and medication requirements.
- To measure durability up to 12 months after treatment.
- To characterize prostate size and necrosis via MRI (for the first 10-15 subjects only).
- To characterize all adverse events and technical observations on device performance.

1.2 Study Design

The study design is a prospective, multicenter, multinational, single-arm clinical investigation. A total of up to 50 subjects will be enrolled at 2-5 sites. Subject follow-up visits will be conducted at 2-day (if catheterized post procedure), 1 and 6 weeks, and 3 months to reach the primary endpoint visit analysis. The first few subjects will have fluoroscopic confirmation of electrodes placement before treatment, then fluoroscopy is optional. The first 10-15 subjects will have MRI studies at baseline, and the 1 week and 3-month follow-up visits to assess subject safety and treatment effect, then MRI is optional. Subject discomfort will be assessed throughout the treatment using VAS. Follow-up visits will assess BPH symptoms, uroflowmetry parameters, quality of life and adverse events.

Subjects will continue to attend follow-up visits at 6 months and 12 months after treatment to demonstrate treatment durability. After completion of their 12-month follow-up visit, subjects will have the option to continue study participation into the long-term follow-up phase with a yearly visit up to 5 years post treatment.

2 EFFICACY EVALUATION

2.1 Summary of Planned Analysis

The statistical analysis of efficacy is a within-subject analysis in which the significance of changes from baseline are assessed. No interim analyses are planned.

Initial analysis for the study objective will be performed when all subjects treated have completed their 3-month post-treatment visit and will be repeated at 6- and 12-month post-treatment visits. Analyses for this objective will be performed on an intention-to-treat basis, including all subjects treated under the protocol. Long-term analysis will be performed after completion of the 60-month visit for all remaining subjects.

2.2 Hypothesis to be tested

The primary efficacy objective is to demonstrate that mean IPSS improvement (Δ IPSS) following treatment with the prostaFix Water Electrolysis System exceeds 6.5 points with 95% confidence.

The null and alternative hypotheses associated with this objective can be written as:

$$H_0: \mu_{\Delta IPSS} \leq 6.5 \text{ points}$$

$$H_A: \mu_{\Delta IPSS} > 6.5 \text{ points}$$

where $\mu_{\Delta IPSS}$ is the true underlying value of mean ΔIPSS following a treatment at the 3-month visit and 6.5 points is an objective performance goal (OPG). The objective is met at a given time point by rejection of the null hypothesis in a one-sided t-test at the 5% significance level.

2.3 Sample Size Justification

The SAS proc power procedure was used to estimate the sample size required to reject the null hypothesis with 90% power at the one-sided 5% significance level in a paired t-test. The specific alternative hypothesis and standard deviation of the change in IPSS used in the calculation was derived from the feasibility study and other studies of devices for BPH. This suggested a mean change in IPSS of 10 points and a standard deviation of 6 points could be expected for this device.

Given these assumptions, a sample size of 27 subjects would provide adequate power to reject the null hypothesis. Allowing for a 10% attrition rate, a total of 30 subjects are required for this study. Actual number of subjects enrolled will range from 40-50.

3 SAFETY EVALUATION

An overall summary of TEAEs will be made including the number and percentage of subjects with any TEAE, any severe TEAE, and any TEAE related to the device, any TEAE related to the procedure, serious TEAE and serious adverse device effect (SADE). A treatment-emergent adverse event (TEAE) is defined as an adverse event with a start date on or after the date of the treatment. In this summary, severe means CTC grade 3 or greater and related means possibly, probably or definitely related.

For the primary safety objective, the percentage of all subjects treated under the protocol who have been affected by one or more SADEs will be calculated along with the Clopper-Pearson exact binomial 95% confidence interval for this percentage. SADEs will also be summarized by term.