Cover Page

Study Title

Prostatic Artery Embolization (PAE) for Treatment of Signs and Symptoms of Benign Prostatic Hyperplasia (BPH)

NCT:02026908

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Protocol Version V 6.10.2019

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STUDY SUMMARY

Title	**Prostatic Artery Embolization (PAE) for Treatment of Signs and symptoms of Benign Prostatic Hyperplasia (BPH)**
Short Title	PAE for BPH
Protocol Number	V 6.10.19
Phase	Pilot study
Methodology	Open labeled, non-randomized feasibility study
Study Duration	We estimate it will take approximately 4 years or 48 months to fully enroll and complete the study.
Study Center(s)	Single Center, Northwestern: (Northwestern University, Northwestern Memorial Hospital and Northwestern Memorial Faculty Foundation)
Objectives	Primary Objective: Evaluate the safety of PAE for the treatment of lower urinary tract symptoms (LUTS) attributed to BPH.
Number of Subjects	60
Diagnosis and Main Inclusion Criteria	Subjects with LUTS secondary to BPH refractory to/contraindicated for medical treatment
Study Product(s)	Embosphere Microspheres, Merit Medical, given intra-procedurally
Duration of administration	Dose given one-time during interventional radiology PAE procedure, given by and at the discretion of the interventional radiologist PI or Sub-I's
Statistical Methodology	Descriptive Statistics will be employed.

STUDY OBJECTIVES

Primary Objectives

Endpoint #1: Patient safety

The Primary Objective of this pilot study is to evaluate the safety of PAE for the treatment of LUTS attributed to BPH. Primary Safety Endpoints include:

1. A reduced incidence and severity of adverse events compared with historical TURP morbidity rates. These include genitourinary events (i.e., events associated with the urinary tract and/or the surrounding genital region)

2. Damage to the bladder floor, trigone, sphincters, and rectum

3. Incontinence as defined by International Continence Society (ICS) male IS score of at least +6 from baseline.

4. Infections

5. Secondary surgical interventions

6. All transient post-procedure events (i.e. *catheter dwelling time)*

7. Deaths

Endpoint #2: Objective clinical endpoints (measured at baseline, 4 weeks, 12 weeks, 6 and 12 months)

1. Change in International Prostate Symptom Score (IPSS)

2. Change in QoL bother question

3. Change in BPH impact index

4. Change in Qmax (*peak and total void volume at each follow-up visit)*

Secondary Objectives

1. Change in Post Void Residual (PVR) volumes:

Measure PVR at each follow-up visit to monitor impairment or improvement of bladder emptying due to the treatment or disease progression.

2. Change in Detrusor Muscle Pressure (Pdet) at Peak Urine Flow (Qmax)

3. Change in International Index of Erectile Function (IIEF-EF) domain:

Both BPH and many of its therapies adversely affect sexual function. Use validated, gender-specific measure of sexual function assessed at each follow-up visit.

4. Change in Male Sexual Health Questionnaire (MSHQ)

5. Change in Prostate volume: Many devices intended to treat BPH, such as TUMT, can reduce prostatic volume.

6. Cystoscopic appearance of the prostatic urethra

Endpoints

Preliminary Safety (Primary Endpoints) will be assessed during treatment and at post-treatment intervals of 1, 3, 6 and 12 months. Preliminary effectiveness (Secondary Endpoint) will be evaluated based on International Prostate System Score (IPSS) and cystoscopic visualization of the subject's urethra, prostate and bladder based on the timeline listed in the protocol.

Annual Long-term follow-up

Patients will be followed for up to 4 additional years after the 12-month visit (visit 6) for the following evaluations:

-physical examination including vital signs, weight and GU evaluation

-blood (comprehensive chemistry panel, PSA, Free PSA)

laboratory evaluations

- urinalysis and urine culture to be done 1-2 weeks prior to cystoscopy and urodynamic testing at this visit

-PSA and free PSA

-DRE

-urodynamic testing including the same parameters as at baseline

-IPSS

-IIES

-MSHQ

-concomitant medications

-toxicity evaluation

-documentation of any new treatments for BPH and/or LUTS

Patients unwilling to come to clinic will be asked to complete the IPSS and IIEF questionnaires and provide information of any new treatments for BPH and/or LUTS by telephone, email or mail. Information on medications and adverse events will not be captured during the long-term follow-up period following the 12-month visit.

Study Design

Overall Clinical Study Design

This pilot study will be a single center, open labeled, non-randomized feasibility study to evaluate the initial safety of the PAE for the treatment of symptomatic BOO. 60 adult male subjects will be enrolled in this study.

All investigators and sub-investigators participating in this study have signed the Investigator Signature Page document. No additional investigators will be added until this agreement is signed. A new agreement will be signed by each investigator for every new version of the protocol created and approved by the IRB.

The first 10 subjects of this study will receive PAE adjusted by the investigators for volume and dose. These subjects will be treated under Monitored Anesthesia Care (MAC) anesthesia to ensure the investigator's complete control and to reduce implementation variables. The investigator will utilize real-time angiogram images of the prostate to direct the placement/movement of the microspheres throughout the targeted prostate treatment volume. These first 10 subjects will be carefully monitored for adverse events to establish preliminary safety of initial dosing plan. Once safety of the technique is established after the first 10 patients, MAC will only be used when medically necessary.

STATISTICAL ANALYSIS

General Considerations

General considerations: continuous variables will be summarized as n, mean, standard deviation, median, minimum and maximum. Categorical variables will be summarized as the number and percentage of patients in each category

Sample Size and Accrual

This is a single center pilot proof of concept study aiming to evaluate the safety, efficacy, and tolerability of PAE for the treatment of signs and symptoms BPH. A small number of subjects will be recruited for this purpose (50 subjects). The first 10 subjects will receive PAE adjusted for volume and dose. They will be carefully monitored for adverse events to establish preliminary safety of initial dosing plan. We estimate it will take approximately years to recruit, treat, and complete follow up on 60 subjects.

No large randomized studies using PAE to treat BPH have been done to date. The sample size has been chosen to evaluate PAE using a US population. The results of the study will provide critical preliminary data to later guide in powering a more statistically robust, and larger randomized controlled trial in the future.

Demographic and Baseline Characteristics

-age, gender, race, ethnicity

-baseline BPH/LUTS characteristics (prostate volume), PSA, free PSA, maximum flow rate (Qmax), average flow rate, detrusor muscle pressure (Pdet), voided volume, total time of voiding and post void residual volume (PVR)

-concurrent medications

-prior BPH/LUTS therapy

Safety and Outcome Analysis

Clinical and outcome measures will be compared to baseline. These included IPSS, IIEF, urodynamic test changes and prostate volume.

Duration of Procedure

Parameters to be recorded include during of procedure, number of Embosphere vials used, radiation exposure, catheter/wire used and amount of contrast.

Peak Urine Flow (Qmax)

Peak urine flow (Qmax) from urodynamic assessments will be summarized comparing baseline to follow-up measurements.

Post void residual (PVR)

PVR from urodynamic assessments will be summarized comparing baseline to follow-up measurements.

Detrusor muscle pressure (Pdet)

Pdet from urodynamic assessments will be summarized comparing baseline to follow-up measurements**.**

International Index of Erectile Function (IIEF)

IIEF will be summarized comparing baseline to follow-up measurements. Each subscale (erectile function, orgasmic function, sexual desire, intercourse satisfaction, overall satisfaction). Each subscale will be summarized separately at each time point (visit).

Prostate Specific Antigen (PSA)

PSA will be summarized comparing baseline to measurements at each follow-up visit.

Additional Variables from Urodynamic Testing

Average flow rate, voided urine volume and total time of voiding from the urodynamic assessments will be summarized and compared to follow-up time points (visits).

Laboratory evaluations

Summary statistics for baseline and change from baseline will be summarized.

Vital signs

Summary statistics for baseline and change from baseline will be summarized.

Cystoscopy

Cystoscopy results will be summarized for baseline and all subsequent cystoscopies.