Protocol Synopsis

A Post-Market, Prospective, Randomized, Controlled, Multicenter International Study to Assess the Efficacy and Safety of the Temporarily Implanted Nitinol Device (iTind) Compared to the UroLift® System in Subjects with Symptomatic Benign Prostatic Hyperplasia (BPH)	
Short Title	Post-Market Study to Assess iTind Efficacy and Safety in Comparison to UroLift
Study Sponsor	Olympus Corporation of the Americas and Olympus Europa SE & SO.KG
Background and Rationale	The iTind is a minimally invasive temporary device designed to relieve LUTS secondary to BPH. This study is designed to compare the minimally invasive iTind device to the UroLift System.
Study Design	The study is a post-market prospective, multi-center, 1:1 randomized study (iTind: UroLift). Eligible subjects will be randomized to iTind or UroLift. Subject follow-up visits are at two weeks, 1, 3, 6, 12, 18, 24, and 36 months
Test Device / Indications for Use	**iTind** The iTind device is a CE marked and FDA 510(k) cleared minimally invasive device and is indicated for the treatment of male patients with LUTS secondary to BPH. The iTind device is inserted into the prostatic urethra, positioned using a cystoscope and maintained in position by means of an anchoring leaflet. Upon placement, the iTind expands and exerts continuous pressure on the prostatic urethra and bladder neck at the 5, 7, and 12 o'clock positions. Over the next five to seven days, the iTind remodels the tissue by creating three deep longitudinal channels through a localized ischemic response. These three channels allow an improved urinary outflow. The device is subsequently removed.
Active Comparator	**UroLift® System UL400 and UroLift® 2 System** The UroLift System is indicated for the treatment of symptoms due to urinary outflow obstruction secondary to BPH, including lateral and median lobe hyperplasia, in men 45 years of age or older. The UroLift System (UL400) is comprised of two main components: UroLift Delivery Device and UroLift implant. The UroLift 2 System is comprised of two main components: UroLift 2 Delivery Handle with Scope Seal and the UroLift Implant Cartridge.

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Primary Objective	To evaluate the efficacy of iTind compared to UroLift at 3 months post-procedure
Primary Endpoint	Difference in change of IPSS from baseline between iTind and UroLift groups at 3 months
Powered Secondary Objectives	**Powered Secondary Efficacy Objective:** To evaluate the efficacy of iTind compared to UroLift at 12 months post-procedure. **Powered Secondary Safety Objective:** To evaluate the safety of iTind compared to UroLift through 3 months post-procedure.
Powered Secondary Endpoints	**Powered Secondary Efficacy Endpoint:** Difference in change of IPSS from baseline between iTind and UroLift groups at 12 months **Powered Secondary Safety Endpoint:** Incidence of all intraoperative and post-operative adverse events (AEs) (i.e., related to procedure and/or device) through 3 months post-procedure.
Secondary Objectives	**Secondary Efficacy Objective** To evaluate the short to long-term efficacy of iTind compared to UroLift **Secondary Safety Objective** To evaluate the short to long-term safety of iTind compared to UroLift **Exploratory Objectives:** To evaluate the health economics of iTind compared to UroLift
Secondary Endpoints	**Secondary Efficacy Endpoint** 1) Difference in change of IPSS from baseline between iTind and UroLift groups at 1, 6, 24, and 36 months 2) Difference in change of QoL scores from baseline between iTind and UroLift at 1, 3, 6, 12, 24, and 36 months • SHIM • MSHQ-EjD • SF-6D v2

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	3) Difference in rate of re-intervention between iTind and UroLift groups at 1, 3, 6, 12, 18, 24, and 36 months **<u>Secondary Safety Endpoint</u>** Difference in reporting between iTind and UroLift groups at 1, 6, 12, 18, 24, and 36, months • Overall incidence of procedure and/or device related adverse events **<u>Exploratory Endpoints</u>** Difference between iTind and UroLift groups for the following parameters: • Concomitant medication usage • Anesthesia type • Procedure time • Hospital length of stay • Post-operative foley catheterization • Number of UroLift implants (UroLift arm only) • iTind retrieval time (iTind arm only) • iTind post-retrieval foley catheterization (iTind arm only)
Planned Study Population	Males with symptomatic BPH who meet all inclusion criteria and none of the exclusion criteria.
Planned Study Sites/Countries	Up to 25 sites located in the United States and the United Kingdom.
Key Inclusion Criteria	**Inclusion Criteria:** Subjects must meet all of the inclusion criteria listed below to be eligible for the study: 1. Diagnosis of lower urinary tract symptoms presumed to be secondary to benign prostatic enlargement causing bladder outlet obstruction for which treatment is recommended 2. Willing and able to provide informed consent 3. Males ≥ 50 years of age or older

	4. PSA < 4 ng/ml or if the PSA is 4 – 10 ng/ml, prostate cancer must be ruled out to the satisfaction of the Principal Investigator (PI) by local standard of care methods within prior 6 months 5. Prostate volume up to 75 cc (inclusive) documented by cross-sectional imaging (TRUS, MRI, etc.). Results from standard of care imaging may be accepted up to 6 months prior to Screening 6. International Prostate Symptom Score (IPSS) for urinary symptoms ≥ 13 7. Maximum urinary flow rate (Qmax) of ≤ 15 mL/sec and ≥ 5 mL/sec (voided volume must be ≥ 125 mL) 8. Willing and able to complete all study visits including questionnaires at baseline and at follow-up visits
Key Exclusion Criteria	**Exclusion Criteria:** Subjects with any one of the exclusion criteria listed below will not be eligible for randomization into the study: 1. History of prostate cancer or if suspected, should be ruled out to the satisfaction of the PI by local standard of care methods within prior 6 months 2. Confirmed bladder cancer within the last 2 years or currently suspected bladder cancer 3. History of acute bacterial prostatitis within the last 2 years 4. Median lobe obstruction of the prostate as confirmed by cross-sectional imaging 5. PSA value > 10 ng/ml 6. Contraindicated for iTind or UroLift as determined by the PI 7. Neurogenic bladder and/or sphincter abnormalities due to Parkinson's disease, multiple sclerosis, cerebral vascular accident, diabetes or other neurological disorders that affect bladder function 8. Clinically significant bladder diverticulum 9. Diagnosed with urethral stricture, meatal stenosis, bladder neck contracture, rectal disease, artificial urinary sphincter, incompetent sphincter, urinary incontinence due to incompetent sphincter 10. Prior rectal surgery (other than hemorrhoidectomy) or history of rectal disease treatment if the therapy may potentially cause injury to site (e.g., if a transrectal probe is used), pelvic radiotherapy or radical pelvic surgery, urinary diversion surgery, prostate surgery, balloon dilation, urethral stent implantation, laser prostatectomy, or any other invasive treatment to the

	prostate, or penile prosthesis if it may prevent insertion of the iTind or UroLift device 11. An active urinary tract infection during randomization 12. Clinically significant hematuria within the last 3 months or ongoing cystolithiasis 13. Prostate volume > 75 cc 14. Post-void residual volume (PVR) > 250 mL 15. Actively using catheterization or unable to void naturally 16. Unable to complete a 2-week washout period for alpha blockers prior to procedure or unable to discontinue 5ARIs or daily use of PDE5 inhibitors by the time of procedure 17. Taking anti-platelet or anticoagulants (except low dose aspirin – 81 mg – 100 mg) within the last 7 days prior to procedure 18. Known or suspected allergy to nickel, titanium or polyester/polypropylene
Statistical Considerations	Two hundred fifty-six (256) subjects will be randomized and treated with either iTind or UroLift. Continuous variables will be summarized using the mean, standard deviation, median, minimum, maximum, and sample size. Categorical variables will be summarized with frequencies, sample sizes, and percentages.
Sample Size	The study was sized using the powered secondary safety endpoint of difference in overall incidence of procedure and/or device related adverse events between UroLift and iTind since the sample sizes needed to show non-inferiority in the change in IPSS were smaller than the sample size needed to demonstrate the powered secondary safety endpoint. See section 9.2 for details. The sample size required to demonstrate non-inferiority for powered secondary safety endpoint of difference in overall incidence of procedure and/or device related adverse events at 3 months is 230 subjects to obtain 90% power. This calculation takes into account the AE rates observed during an interim analysis with the first 81 subjects treated with 32.6% for iTind and 47.1% for Urolift arm, a non-inferiority margin of 5% and a one-sided test setting alpha to 0.04019 for the final analysis. To this sample size we will add an additional 10% for dropout for a total enrollment of 230/0.9= 256 subjects.