

# CUA 2023 Annual Meeting Abstracts – Podium Session 2: Functional Urology

## Saturday, June 24, 2023 • 8:10–9:10

Cite as: *Can Urol Assoc J* 2023;17(6Suppl2):S19-21. <http://dx.doi.org/10.5489/cuaj.8405>

### POD 2.1

**MVI40 sublingual vaccine reduces risk of recurrent urinary tract infection (rUTI) in women with and without bladder pain syndrome: Results from the first North American clinical experience study**  
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**Introduction:** Recurrent urinary tract infection (rUTI) in women is associated with widespread morbidity, massive antibiotic use, increasing antibiotic resistance, significant costs and is believed to be implicated in the etiology of infection phenotype of bladder pain syndrome (BPS). This is the first North American real-world, clinical experience evaluation of MVI40, a novel bacterial sublingual vaccine developed for prevention of rUTI.

**Methods:** Female participants with  $\geq 3$  documented UTI/year ( $\geq 3$  one culture proven) underwent a three-month vaccination treatment period, nine-month efficacy period, and subsequent three-month followup (total 15 months). Primary outcome was no clinically diagnosed UTI (defined as symptoms requiring antibiotic therapy) following vaccination. Secondary outcomes included reduction in UTI compared to pre-vaccination, quality of life (QoL), global response assessment (GRA), microbiology, and safety. A sub-study evaluated subjects with rUTI and concurrent BPS.

**Results:** Sixty-seven subjects (mean age 55.6 years, range 18–80), including 16 with BPS, were enrolled; 64 completed the three-month vaccination period and at least one post-vaccination assessment. Prior to vaccination, subjects reported  $6.8 \pm 4.6$  UTI/year. The UTI-free rate for the nine-month post-vaccination efficacy period was 40.6%. Compared to the UTI rate in the year prior to vaccination (0.56 UTI/subject/month), the reduction in UTI rate was 74.8% for the nine-month efficacy period (0.14 UTI/subject/month) post-vaccination. The total number of UTI and the number of patients reporting UTI decreased substantially for each three-month followup period, while the percentage of UTI-free subjects increased following vaccination. At the 12-month efficacy visit, 82% reported (GRA) that they were moderately/markedly improved; 59% were mostly satisfied, pleased, or delighted, while mean SF-12 improved by 1.5 points on QoL assessment. In the BPS sub-study, 6/16 subjects were UTI-free, while all 16 subjects had a reduction (overall 80%) in UTI compared to the year pre-vaccination (0.5 to 0.1 UTI/subject/month). At 12 months, 13 subjects (81.3%) reported moderate or marked improvement, with eight reporting significant or almost complete resolution of their specific long-term bladder discomfort/pain and bothersome urinary frequency or urgency. In the entire group, 11 adverse events in nine subjects were potentially related to the vaccine; all were mild and resolved by three months. None of the 13 serious adverse events were related to the vaccine.

**Conclusions:** This first Health Canada-approved North American experience with the sublingual vaccine, MVI40, demonstrates its safety and potential effectiveness in real-world clinical practice in reducing UTI risk and rendering a significant number of women suffering from rUTI, including those with IC/BPS, completely UTI-free (and offering amelioration of BPS symptoms for those with BPS).

*Acknowledgements:* Investigator-initiated study was partially supported by Immunotek and Redleaf Medical.

### POD 2.2

**The Optilume BPH catheter system: 12-month outcomes from the randomized PINNACLE study**

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**Introduction:** The PINNACLE study is a prospective, randomized, double-blind, sham-controlled study evaluating the Optilume BPH system. Optilume BPH is a novel minimally invasive surgical therapy (MIST) that combines mechanical dilation with the delivery of paclitaxel for the treatment of lower urinary tract symptoms (LUTS) secondary to BPH.

**Methods:** A total of 148 subjects were randomized in a 2:1 fashion at 18 centers in the U.S. and Canada. Subjects and evaluating personnel were blinded to the treatment received through 12 months. Twelve-month followup is complete. Symptom improvement was measured using the International Prostate Symptom Score (IPSS) and BPH Impact Index (BPH-II), and functional improvement was measured by peak urinary flow rate (Q<sub>max</sub>) and postvoid residual volume (PVR). Erectile and ejaculatory functions were evaluated using validated questionnaires. Adverse events were prospectively collected and relatedness to treatment was adjudicated by a clinical events committee.

**Results:** Subjects treated with Optilume BPH showed a significant reduction in IPSS from baseline to 12 months (23.4 vs. 10.9,  $p < 0.001$ ). Improvement in IPSS at 12 months was significantly greater for Optilume BPH compared to sham in the intent-to-treat population (11.5 vs. 4.8,  $p < 0.001$ ). Q<sub>max</sub> more than doubled, from 8.9 mL/sec at baseline to 19.0 mL/sec after treatment with Optilume BPH, while average PVR decreased from 84 mL to 58 mL ( $p = 0.004$ ). There were no changes in perceived sexual or ejaculatory function. The most reported treatment-related adverse events after treatment with Optilume BPH included hematuria (39/98 [39.8%]), urinary tract infection (11/98 [11.2%]), and dysuria (8/98 [8.2%]).

**Conclusions:** Treatment with Optilume BPH resulted in significant, immediate symptomatic and functional improvements and to date the highest Q<sub>max</sub> reported in BPH MIST trials. Durability of these outcomes was shown through 12 months. Long-term outcomes will be verified with five-year followup for Optilume BPH. *Acknowledgements:* The authors wish to thank all the clinical investigators contributing to the PINNACLE study. Primary results from this study were previously presented. This study was funded by Urotronic, Inc.

### POD 2.3

**Aquablation therapy<sup>®</sup> vs. transurethral resection of the prostate: 5-year outcomes of the WATER randomized clinical trial for medium-sized prostates**

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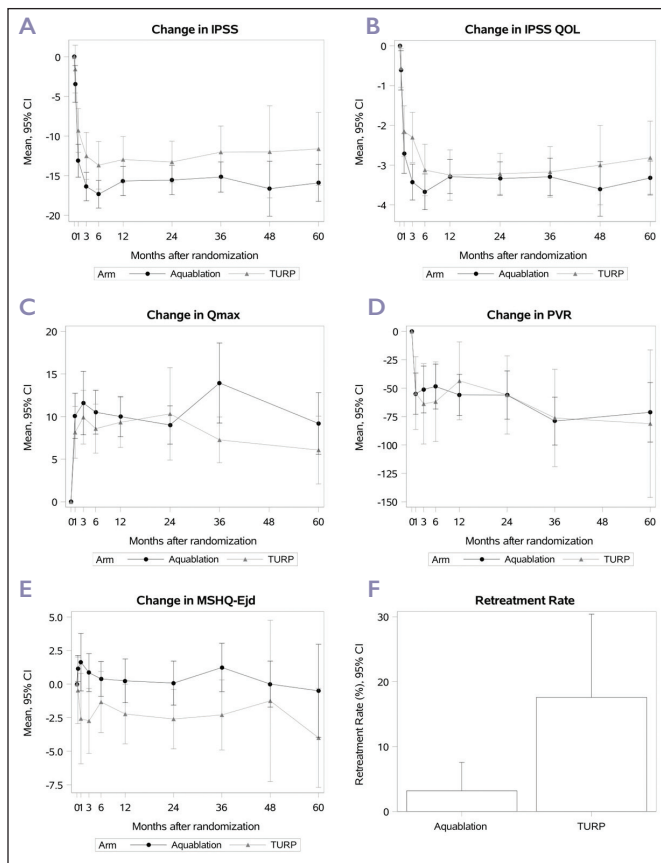
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**Introduction:** The WATER trial previously introduced Aquablation® as a safe and effective TURP alternative in the management of lower urinary tract symptoms (LUTS) related to benign prostatic hyperplasia (BPH) for prostates <80 mL. To date, no long-term superiority endpoints have been reported for medium-sized prostates. In this subset analysis of the WATER cohort, we aim to compare the five-year efficacy and safety of Aquablation® vs. TURP for the management of 50–80 mL prostates.

**Methods:** WATER is a double-blinded, multicenter, prospective, randomized, controlled clinical trial for prostates 30–80 mL. The trial received ethical committee approval. Ninety-six men with prostates 50–80 mL randomized to either Aquablation® therapy or TURP from the initial cohort were retained for the subset analysis. Men received followup at one, three, six, and 12 months, then annually up to five years. The primary efficacy endpoint was reduction of IPSS at five-year followup. The primary safety endpoint was the occurrence of Clavien-Dindo postoperative complications grade 1 persistent (CD1P) and grade 2 (CD2) or higher at six months. Other measures included QoL, Qmax, PVR, and MSHQ-EJd.

**Results:** Both groups had comparable baseline voiding parameters and clinical demographics. Study endpoints are shown in Figure 1. Overall reduction in IPSS score was significantly higher in the Aquablation group across five years of followup (-14.1 vs. -10.8, p=0.02). Changes in QoL, Qmax, and PVR were similar across groups (p>0.05). The Aquablation® group displayed no changes in MSHQ-EJd score, while TURP yielded poorer questionnaire scores across all followups (0.6 vs. -2.1, p=0.01). The Aquablation® group achieved a significantly lower rate of CD1P and CD2 or higher events at six months (RD -23.1%, 95% CI -29.9, -15.5, p=0.018). Among complications, postoperative ejaculatory dysfunction was notably lower in Aquablation® (RD -21.9%, 95% CI -32.5, -10.7, p=0.0005), while



**POD 2.3. Figure 1.** Change in (A) IPSS total score; (B) IPSS QoL; (C) Qmax; (D) PVR; (E) MSHQ-EJd; (F) retreatment rate over 5 years of followup for men undergoing Aquablation therapy vs. TURP for LUTS related to BPH.

risk of bleeding was similar. The surgical and medical retreatment rate was also lower in Aquablation® (RD -14.4%, 95% CI -2.29, -30.4, p=0.015).

**Conclusions:** Aquablation® yields better long-term efficacy and safety outcomes than TURP in the management of LUTS for prostate volumes of 50–80 mL within the WATER trial. This further supports the adoption of Aquablation® therapy over TURP for men with medium-sized prostates.

**POD 2.4**

**Predicting response to mirabegron treatment in patients with overactive bladder: A post-hoc analysis of clinical trial data**

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**Introduction:** Many patients discontinue overactive bladder (OAB) treatment due to unmet expectations and/or tolerability issues. We aimed to develop a predictive model of individual mirabegron treatment response using patient characteristics.

**Methods:** This was a post-hoc data analysis of eight global phase 2 and 3 double-blind, randomized, placebo/active-controlled trials in adults with OAB receiving mirabegron monotherapy 50 mg once daily for ≥12 weeks. Primary efficacy outcomes were change at week 12 in mean number of micturitions and incontinence episodes/24 h. Secondary efficacy outcomes were change at week 12 in mean number of urgency episodes/24 h and Symptom Bother score. Baseline demographics, OAB-related characteristics, and intrinsic/extrinsic factors were used to create multivariable linear regression models to predict treatment response.

**Results:** Of 3627 patients, 74% were female; mean age was 58.4 years. Overall, the predicted effects for mirabegron 50 mg were an average of 2.5 fewer micturition episodes/24 h (95% CI -2.85, -2.14 episodes) and 0.81 fewer incontinence episodes/24 h (-1.15, -0.46) from baseline to week 12. A higher baseline number of urgency episodes was predictive of a larger reduction in micturition and incontinence episodes. Body mass index ≥30 kg/m<sup>2</sup>, OAB symptoms lasting ≥12 months, and presence of incontinence predicted a smaller reduction in micturition episodes. Mixed stress/urgency incontinence and >5 urgency episodes/day predicted a larger reduction in incontinence episodes. Reductions in urgency episodes and Symptom Bother score were also predicted with mirabegron treatment.

**Conclusions:** Data from this predictive model provide new insights into the effects of modifiable and non-modifiable factors on treatment outcomes with mirabegron 50 mg once daily and will allow construction of a nomogram to predict individual patient response. This is the first model to predict the response of mirabegron on urgency, frequency, and incontinence episodes.

**Acknowledgements:** Astellas Pharma, Inc provided funding for this study. Medical writing support was provided by Sue Cooper, CMPP, from Envision Pharma, Inc., and funded by Astellas Pharma, Inc.

**POD 2.5**

**Refining bacteriuria as a risk factor for complications after urethroplasty: Finding the culprit**

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**Introduction:** Preoperative bacteriuria is independently associated with 90-day complications after urethroplasty; however, it remains unclear which specific micro-organisms are the primary drivers of this morbidity. The objective of this study was to characterize which specific bacteria are associated with an increased risk of 90-day complications after urethroplasty.

**Methods:** A single-institution, two-surgeon, retrospective review was performed on patients undergoing urethroplasty from August 2003 to June 2020. Variables included the incidence, type, and Clavien-Dindo grade of complications, patient age, comorbidities, Charlson Comorbidity Index (CCI), smoking status, obesity, type of urethroplasty, stricture etiology, length, location, prior endoscopic procedures, previous urethroplasty, preoperative suprapubic catheterization, and bacteriuria. The latter was considered significant when the patient had either

a mixed culture with  $\geq 108$  CFU/l or an identifiable microorganism with  $\geq 106$  CFU/l. The primary outcome was the incidence of 90-day complications, defined as Clavien grade  $\geq 2$ . Descriptive statistics were used to summarize the results and Chi-squared was used to determine if the presence of a specific bacterium was associated with 90-day complications.

**Results:** Of the 1611 patients included in the analysis, 23.2% (373/1611) had clinically significant preoperative bacteriuria. The most common pathogens on urine culture included coagulase-negative staphylococcus (18.5%, n=69), mixed growth (15.8%, n=59), E. coli (10.7%, n=40), and enterococcus (14.2%, n=53). Overall, 7.9% (128/1611) experienced a significant 90-day complication (Clavien  $\geq 2$ ), with a higher rate of complications for those with preoperative bacteriuria (10.5% vs. 7.2%, p=0.04). Gram-negative bacilli, including E. Coli, Pseudomonas sp., Klebsiella sp., Serratia sp., Citrobacter sp., Achromobacter sp., Stenotrophomonas sp., and Morganella sp. were associated with higher rates of postoperative complications (14.2%, p=0.01) as were Enterococcus sp. (15.1%, p=0.03); however, gram-positive cocci (10.4%, p=0.23), gram-positive bacilli (11.8%, p=0.47), mixed growth (5.1%, p=0.54), and Candida (20.0%, p=0.27) were not. Neither escalating concentrations of bacteria on culture (p=0.44) nor number of bacterial strains (p=0.08) were associated with a higher rate of complications.

**Conclusions:** While preoperative bacteriuria is associated with higher rates of 90-day complications, the main driver of these complications is gram-negative bacilli and Enterococcus sp. Patients with preoperative bacteriuria related to gram-positive cocci, gram-positive bacilli, and mixed growth can likely proceed with urethroplasty with appropriate infection prophylaxis without increased risk of postoperative complications.

## POD 2.6

### Surgical management of rectourethral fistula: Methods of repair and identifying adverse features

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**Introduction:** Rectourethral fistula (RUF) is an uncommon complication with variable etiologies. There are multiple approaches available for surgical management. The aim of this study is to review our experience and to identify factors that contribute to failure of repair.

**Methods:** This was a retrospective evaluation of 52 male patients with a RUF that received surgical management at one institution using different surgical methods from October 1986 to July 2022. Ethics approval was obtained. Success was defined as effective fistula closure, with or without the need for permanent urinary  $\pm$  bowel diversion. The following variables were reviewed: demographics, previous treatments, etiology of fistula, bowel diversion, and surgical approach.

POD 2.6 Table 1. Primary procedures per group

Procedure	Group 1 (n=30)	Group2 (n=22)
York Mason	16	2
Transanal	4	-
Transabdominal (+/- radical prostatectomy or vesicourethral takedown)	8	12
Transperineal	2	1
Cystectomy and rectal repair	-	7

**Results:** The average age at repair was 66.9 (IQR 10.85, range 46–85). Patients were divided into two groups based on etiology: surgery only (G1, n=30) and radiation with or without surgery (G2, n=22). Prostate cancer treatment was the predominant etiology (n=42). Overall success rate of repair was 88.4% (n=46). Median followup from time of surgery was 4.65 years (IQR 5.08, range 0.07–27.85). Table 1 shows the primary procedures. The RUF repair was successful in all 30 patients in G1 and no one required secondary surgery. In G2, seven of the 15 patients who did not have upfront cystectomies required secondary surgery, of which five were successful (p=0.0013). A total of 45 patients achieved success after one surgical procedure while seven required more than one procedure and of which all were from G2. Of the seven who required more than one procedure, five underwent a permanent secondary urinary diversion. Patients from G1 were more likely to undergo less complex approaches (n=22, 73%) as compared to patients from G2 (n=3, 13.6%) (p=0.0001). Patients from G2 were more likely to get an upfront permanent urinary diversion (n=7) compared to G1 (n=0) (p=0.0013).

**Conclusions:** Patients with radiation-associated therapies are more likely to have a complex RUF and require a more complex surgical repair via an abdominoperineal approach with or without an interposition flap or a permanent urinary diversion. Recognizing and understanding the etiology and the possible need for upfront diversion will help with treatment choice and assist in setting expectations for patients.