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One-Year Results for the ROBUST III Randomized Controlled Trial Evaluating the Optilume® Drug-Coated Balloon for Anterior Urethral Strictures

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Study Need and Importance: The gold standard treatment of urethral stricture is urethroplasty with 90% success, but the most common treatments by far are urethral dilation and/or direct vision internal urethrotomy (DVIU). Dilation/DVIU is successful in <50%, especially in recurrent disease. This creates a need for a therapy that is less invasive than urethroplasty but more successful than dilation/DVIU. The Optilume® paclitaxel-coated balloon combines urethral dilation with circumferential delivery of an antiproliferative agent that inhibits fibroblast growth and stricture recurrence.

What We Found: We randomized 127 men to Optilume vs dilation/DVIU. At 6 months, the rate of anatomic success (defined by the ability to pass a flexible cystoscope) was 75% for Optilume and 27% for dilation/DVIU. Several different 1-year outcomes were also superior for Optilume vs dilation/DVIU: freedom from repeat intervention was 83% vs 22% (see figure), urinary symptoms as measured by the International Prostate Symptom Score were 9 vs 20 and maximum urinary flow rate was 16 vs 8 ml per second, respectively. Most side effects were similar across treatments except hematuria and dysuria, which were more common after Optilume (11% vs 2% for both events).

Limitations: As this trial only compared Optilume with dilation/DVIU, we don't know how Optilume would compare with urethroplasty. It is possible that the early positive results are impacted by surgeons opening the urethra to a larger size with Optilume; however, immediately post-treatment the luminal diameter, measured by urethrogram, was the same (8 mm) in both groups.

Interpretation for Patient Care: Early findings indicate that Optilume offers superior outcomes to dilation/DVIU for men with recurrent bulbar urethral stricture. Men who have suffered stricture recurrence after dilation/DVIU may consider Optilume as an alternative to repeat dilation/DVIU.

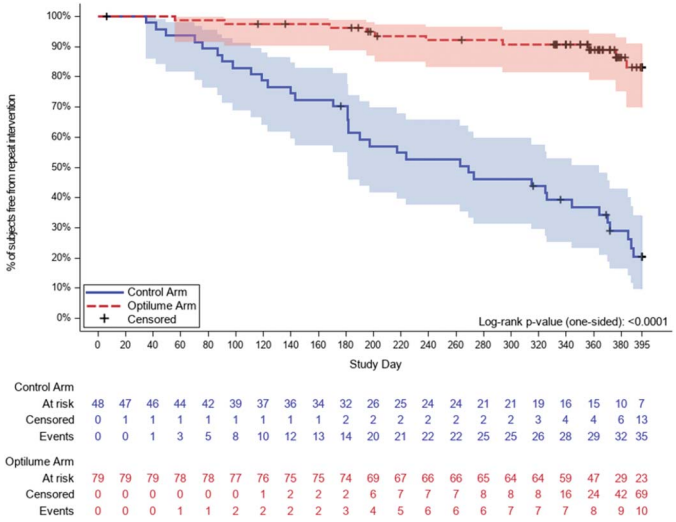

Figure. Kaplan-Meier curve of freedom from reintervention through 1 year.

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One-Year Results for the ROBUST III Randomized Controlled Trial Evaluating the Optilume® Drug-Coated Balloon for Anterior Urethral Strictures

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Purpose: The Optilume® drug-coated balloon (DCB) is a urethral dilation balloon with a paclitaxel coating that combines mechanical dilation for immediate symptomatic relief with local drug delivery to maintain urethral patency. The ROBUST III study is a randomized, single-blind trial evaluating the safety and efficacy of the Optilume DCB against endoscopic management of recurrent anterior urethral strictures.

Materials and Methods: Eligible patients were adult males with anterior strictures ≤12Fr in diameter and ≤3 cm in length, at least 2 prior endoscopic treatments, International Prostate Symptom Score ≥11 and maximum flow rate <15 ml per second. A total of 127 subjects were enrolled at 22 sites. The primary

Abbreviations and Acronyms

AE = adverse event
DCB = drug-coated balloon
DVIU = direct vision internal urethrotomy
IIEF = International Index of Erectile Function
IPSS = International Prostate Symptom Score
PK = pharmacokinetic
PROM = patient-reported outcomes measure
PVR = post-void residual
Qmax = maximum urinary flow rate
QoL = quality of life

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Ethics Statement: Institutional review board or research ethics board approval was obtained for all sites (IRB No. STUDY00005058).

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study end point was anatomical success (≥14Fr by cystoscopy or calibration) at 6 months. Key secondary end points included freedom from repeat treatment, International Prostatic Symptom Score and peak flow rate. The primary safety end point included freedom from serious device- or procedure-related complications.

Results: Baseline characteristics were similar between groups, with subjects having an average of 3.6 prior treatments and average length of 1.7 cm. Anatomical success for Optilume DCB was significantly higher than control at 6 months (75% vs 27%, p <0.001). Freedom from repeat intervention was significantly higher in the Optilume DCB arm. Immediate symptom and urinary flow rate improvement was significant in both groups, with the benefit being more durable in the Optilume DCB group. The most frequent adverse events included urinary tract infection, post-procedural hematuria and dysuria.

Conclusions: The results of this randomized controlled trial support that Optilume is safe and superior to standard direct vision internal urethrotomy/dilation for the treatment of recurrent anterior urethral strictures <3 cm in length. The Optilume DCB may serve as an important alternative for men who have had an unsuccessful direct vision internal urethrotomy/dilation but want to avoid or delay urethroplasty.

Key Words: urethral stricture, lower urinary tract symptoms, urinary bladder neck obstruction

URETHRAL stricture occurs at a rate of 0.2%–0.6% in the male population and accounts for hundreds of millions of dollars of health care costs yearly.[1] The gold standard treatment is urethroplasty, with success rates ranging from 80%–95%, depending on stricture characteristics.[2–4] Despite guidelines encouraging urethroplasty for longer or recurrent strictures, the vast majority are treated endoscopically.[5–8] Endoscopic treatments include direct vision internal urethrotomy (DVIU) and urethral dilation, with success rates of 50%–70% for short, treatment-naïve strictures and a lower success for recurrent strictures.[9–13]

One area of research aimed at improving endoscopic therapy has been the addition of adjunct medication such as mitomycin C into the stricture after DVIU/dilation.[14] The Optilume® urethral drug-coated balloon (DCB) builds on this success in that it combines mechanical dilation of the stricture with local, circumferential delivery of paclitaxel in a single balloon. Similar to mitomycin C, paclitaxel inhibits fibroblast growth and scar formation. Previous publications of phase I/II studies have shown that men treated with Optilume have a functional success rate of 70% at 2 years.[15] Results of a phase III, single-blind, randomized, controlled trial of Optilume vs standard endoscopic therapy are reported here.

MATERIALS AND METHODS

Study Design and Participants

ROBUST III is a multicenter, single-blind, randomized, controlled trial of the safety and efficacy of the Optilume DCB for treatment of anterior urethral strictures (clinicaltrials.gov NCT03499964). The study included a nonrandomized arm of 15 participants for paclitaxel pharmacokinetic (PK) assessments.

Eligible participants were adult males with anterior strictures ≤12Fr and ≤3 cm in length, ≥2 prior endoscopic treatments, International Prostate Symptom Score (IPSS) ≥11 and maximum urinary flow rate (Qmax) <15 ml per second. Participants with previous urethroplasty, hypospadias repair, lichen sclerosis or unresolved confounding etiologies (eg bladder neck contracture, neurogenic bladder, benign prostatic hyperplasia) were excluded. All participants provided written informed consent. An independent data monitoring committee oversaw the study and a clinical events committee adjudicated adverse events (AEs).

Randomization and Blinding

Eligible participants were randomized prior to the index procedure in a 2:1 allocation of treatment vs control, stratified by prior pelvic radiotherapy (yes/no) and number of prior endoscopic treatments (<5 vs ≥5).

Randomized participants were blinded to treatment through 6 months, which was the time point of the primary end point. Prior to 6 months, unblinding could occur only if medically necessary (eg recurrent stricture requiring intervention).

Interventions and Followup

For participants randomized to treatment, strictures were pretreated with an uncoated balloon or DVIU to ≥20Fr. Direct dilation with the DCB, though possible, was avoided to limit the chance that a subject would get 2 doses of paclitaxel if the stricture did not sufficiently dilate with the first dilation. Balloon sizes were selected based on lumen diameter and stricture length was measured via urethrogram with instructions to select a balloon length that allowed 0.5–1 cm overlap into normal tissue in both directions. Inflation to rated burst pressure occurred for ≥5 minutes to allow complete stricture dilation and paclitaxel delivery. The DCB was then removed and a 12Fr–14Fr Foley catheter inserted.

Control participants were treated by the endoscopic method that was considered standard of care for the site, which included serial dilation with urethral sounds, DVIU, balloon dilation or a combination; a lumen size goal was not prespecified. A 12Fr–14Fr Foley catheter was inserted. Participants randomized to the control arm were eligible to cross over to receive the DCB only if stricture recurrence was confirmed via recurrent symptoms, decreased flow and a stricture diameter <12Fr as measured by retrograde urethrogram before 12 months post-procedure.

Followup post-procedure occurred at Foley removal (2–5 days in both groups), 30 days, 3 months, 6 months and 1 year. DCB group participants will continue annual followups through 5 years.

Outcome Measures

The primary efficacy end point was anatomical success: the proportion of participants in whom we could atraumatically pass a 16Fr flexible cystoscope or a 14Fr catheter through the treated area at 6 months.[16] The primary safety end point was freedom from a composite of serious device- or procedure-related events including urethral fistula, unresolved *de novo* stress urinary incontinence or urethral rupture through 3 months. Additional outcomes included average Qmax, IPSS, IPSS quality of life (QoL) and International Index of Erectile Function (IIEF) over time. Freedom from repeat intervention (repeat dilation, DVIU or urethroplasty) was evaluated at 1 year. For the PK cohort, samples of plasma, semen and urine were taken at baseline and various time points post-procedure through 6 months.

Statistical Analysis

For the primary end point, a 2-sample continuity corrected chi-square test at the 2-sided 0.05 alpha level was implemented with multiple imputation to account for missing data. A sample size of 126 provided 90% power to show superiority of DCB to DVIU/dilation assuming a 32% between-group difference.[9,10,17]

A Kaplan-Meier curve was generated for freedom from repeat intervention, utilizing a log-rank test for comparison between arms. Subject characteristics were evaluated with Fisher's exact test for categorical measures and unpaired t-test for continuous measures. For all efficacy analyses, participants who underwent repeat intervention on the study stricture were considered failures for categorical end points or assigned the worst observed value for continuous end points for time points after the intervention. Descriptive statistics were used to summarize all outcome measures. Analyses were performed using SAS® 9.4.

RESULTS

Between October 2018 and December 2020, 127 participants were randomized and 15 participants were enrolled in the PK arm at 21 sites in the United States and 1 site in Canada (fig. 1). Demographics and stricture characteristics were similar between randomized groups (table 1). Strictures were mostly bulbar (92.1%) and averaged 1.7 cm in length. Participants had an average of 3.6 prior dilations with 18.1% (23/127) having ≥5 prior treatments.

Control group strictures were treated with an uncoated balloon (58.3%; 24Fr in 16, 28Fr in 1 and 30Fr in 11), DVIU (25.0%) or urethral sounds (16.7%). DCB group strictures were predilated with an uncoated balloon (92.4%), DVIU (5.1%) or both (2.5%). The most used DCB size was 30Fr and either 30 mm (28.2%) or 50 mm (60.8%) length. Average time between insertion and removal of the DCB was 8 minutes and 42 seconds. Posttreatment lumen diameter was estimated by urethrography; the mean was 24Fr in both groups.

Efficacy Results

At 6 months, anatomical success was 74.6% in the DCB group and 26.8% in the control group, resulting in an estimated difference of 44.4% using multiple imputation and meeting the primary efficacy end point of the study ($p < 0.0001$; table 2). The treatment effect was consistent across some prespecified clinical subgroups, including participants with ≥5 vs <5 prior endoscopic treatments and stricture length ≥2 vs <2 cm. There were too few participants in some etiology categories and too few with penile strictures or radiation to comment on the impact of these subgroups on success (fig. 2). A subset analysis of 11 control participants dilated with a 30Fr balloon compared to 70 participants dilated with a 30Fr DCB showed results similar to the overall findings: 22% vs 75% success at 6 months ($p < 0.01$).

Kaplan-Meier estimates of freedom from repeat intervention through 1 year were significantly higher for the DCB group as compared to the control group (83.2% vs 21.7%, $p < 0.0001$; fig. 3). Both groups showed a significant increase in Qmax from baseline to 30 days, with control participants exhibiting a marked deterioration beginning at the 3-month visit. By 1 year, the average Qmax in the DCB group was nearly double that of the control group (table 3). The post-void residual (PVR) urine volume in the control group was higher than baseline at 6 months and 1 year.

Trends in IPSS and IPSS QoL were similar to Qmax. Both groups showed improvements in scores through 30 days; however, average scores for the control group deteriorated sharply at the 3-month visit and returned to near baseline levels by 1 year, while the DCB group remained significantly improved (table 3).

Safety Results

No subject experienced a primary safety end point event through 3 months. AE types and rates were well matched between groups, except that the DCB group had higher rates of post-procedure hematuria and dysuria compared to controls (11.4% vs 2.1% for both event types). These events were judged as mild in nature and resolved within 30 days in 10 of 11 men. Serious AEs occurred in 16.7% of controls and 10.1% of the DCB group. One serious event of urinary tract infection was judged as possibly related to the device/procedure in each group. There was no change in sexual function as measured by the IIEF in either group (table 3).

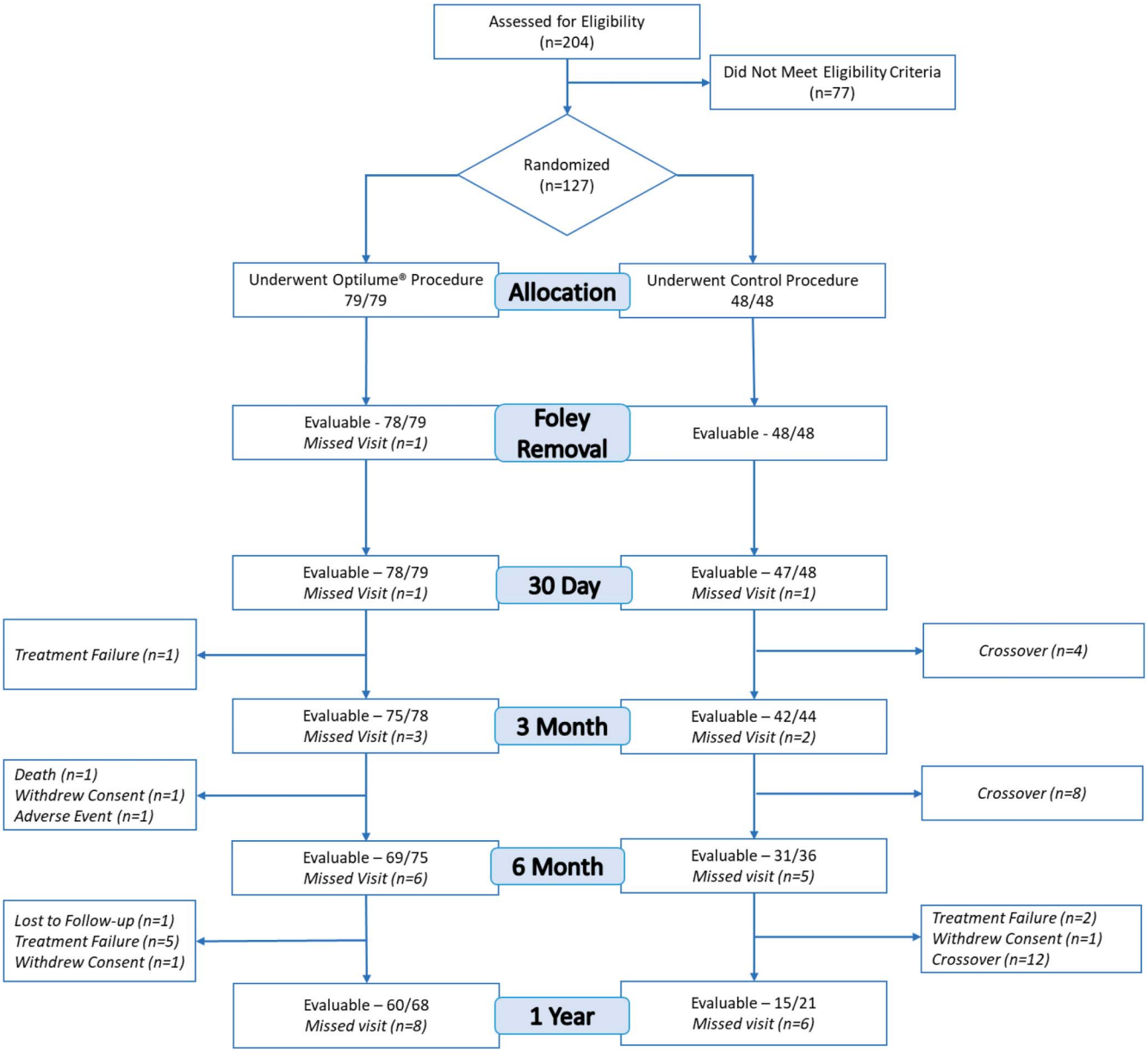

Figure 1. Subject accountability in randomized cohort. Note that discontinuations (eg treatment failure) are discrete values at each time point.

Systemic exposure to paclitaxel was minimal, with average plasma concentration rising above the limit of quantitation at 1 hour (0.12 ng/ml) and 3 hours (0.11 ng/ml) post-procedure. Average paclitaxel concentration in the urine was highest immediately post-procedure (414.4 ng/ml), and decreased to 13.8 ng/ml at Foley removal and to below the limit of quantitation by 30 days post-procedure. Drug concentration in semen was 2.99 ng/ml at 30 days, 0.48 ng/ml at 3 months and 0.12 ng/ml at 6 months; paclitaxel was detected in measurable quantities in 60% (9/15), 39% (5/13) and 8.3% (1/12) of participants, respectively.

DISCUSSION

The Optilume DCB is safe and has superior success rates compared to standard endoscopic management with DVIU/dilation in men with recurrent urethral stricture <3 cm in length. These results were consistent across stricture lengths and number of prior interventions. Success by several different measures (anatomical success, freedom from repeat intervention, Qmax and IPSS) were consistently higher with DCB. Definitive assessments of subgroups such as some stricture etiologies, penile strictures and participants with prior pelvic radiation were not possible due to small sample size.

Table 1. *Subject demographics and stricture characteristics*

Characteristic	Standard of Care*	Optilume DCB*	p Value†
No. pts	48	79	
Demographics:			
Mean±SD age (yrs)	60.6±16.0	58.7±15.5	0.500
No. race (%):			0.838
Black or African American	6/48 (12.5)	9/78 (11.5)	
White	39/48 (81.3)	65/78 (83.3)	
Other‡	3/48 (6.3)	4/78 (5.1)	
No. ethnicity (%):			0.673
Hispanic or Latino	3/48 (6.3)	3/78 (3.8)	
Not Hispanic or Latino	45/48 (93.8)	75/78 (96.2)	
Mean±SD BMI (No. pts)	28.9±6.9 (48)	30.5±6.7 (77)	0.206
Baseline stricture characteristics:			
Stricture etiology:			0.566
Iatrogenic	16/47 (34.0)	21/78 (26.9)	
Idiopathic	22/47 (46.8)	42/78 (53.8)	
Inflammatory	2/47 (4.3)	1/78 (1.3)	
Traumatic	7/47 (14.9)	14/78 (17.9)	
Prior pelvic radiation	6/48 (12.5)	9/79 (11.4)	>0.999
Anatomical location:			0.319
Bulbar	45/47 (95.7)	71/79 (89.9)	
Penile	2/47 (4.3)	8/79 (10.1)	
Mean±SD stricture measurements:			
Length (cm)	1.72±0.73	1.63±0.76	0.528
Diameter (mm)	2.33±0.88	2.46±0.96	0.470
Prior dilations:			
Mean§	4.3±7.5	3.2±1.73	0.321
Median	3.0	3.0	
No. ≥5 overall (%)	10/48 (20.8)	13/79 (16.5)	0.636

* Some rows contain fewer than 48 or 79 participants due to missing demographic or clinical data.
† P values based on unpaired t-test for continuous variables and Fisher's exact test for categorical variables.
‡ Pacific Islander, Asian or Native American
§ Single subject with 53 prior dilations, average is 3.3 when excluding this subject.

The anatomical success rates of DIVU and urethral dilation have been shown to be similar to each other in a randomized trial.[9] One-year success may be as high as 70% for treatment-naïve, short, bulbar strictures. However, recurrent strictures, penile strictures or strictures undergoing repeat endoscopic treatment all represent high-risk strictures with 1-year success rates far less than 50%.[10,11] Despite low success rates, endoscopic therapies remain the most common procedures for urethral stricture, likely owing to their minimally invasive nature.[5,6] Urethroplasty is the gold standard urethral stricture treatment, with anatomical success rates of 80%–95% depending on stricture characteristics. However, urethroplasty is more invasive than endoscopic treatment and can be associated with complications of pain, neuropathy and sexual dysfunction.[18]

The choice between urethroplasty and endoscopic therapy is a function of surgeon skill set, success rates, side effects and cost. Previous cost-benefit analyses and subsequent guideline statements suggest that 1 endoscopic treatment be pursued for treatment-naïve, short, bulbar strictures; any high-risk stricture should be managed with urethroplasty, including any recurrent stricture, owing to low success rates with endoscopic therapy in these scenarios.[8,19] Still, nearly twice as many men undergo another endoscopic treatment rather than urethroplasty even when they have failed 2 prior endoscopic treatments.[20] This discrepancy between the science-based recommendations and utilization rates of endoscopic therapy may represent problems with access to urethroplasty experts, reluctance to refer patients to urethroplasty experts or patient preference, perhaps related to out-of-pocket expense, recovery time or side effects.

There are many ways to measure success of urethral stricture treatment, but these can generally be categorized as freedom from repeat treatment, anatomical success and functional success.[21] Freedom from repeat treatment is important in that it measures the consumption of important health resources; this tends to be the measure with the highest success rates because not all men with anatomical narrowing or symptoms pursue repeat treatment.[22] The most commonly used anatomical measure is the ability to atraumatically pass a flexible adult cystoscope through the treated area. Functional success includes measures such as Qmax, patient-reported outcomes measures (PROMs) and PVR. Although PROMs better represent what is important to the patient, anatomical success has the advantage of not being influenced by comorbid conditions like prostatic obstruction or cystopathy, which can impact PROMs and Qmax. Because each of these outcome measures has its own advantages and disadvantages, we included all of them in our assessment. In the current study,

Table 2. *Primary efficacy end point results*

End Point	Standard of Care	Optilume DCB	Difference* (95% CI)	p Value*
No. pts	48	79		
% Stricture-free (No./total No.)	26.8 (11/41)	74.6 (50/67)	44.4 (27.6–61.1)	<0.0001
No. subject accountability:				
Pass urethral lumen test at 6 mos	11	50		
Failed urethral lumen test at 6 mos†	12	15		
Repeat intervention prior to 6 mos‡	18	2		
Missing cystoscopy at 6 mos	7	12		

* Estimates of the difference (Optilume vs control), 95% CI and 1-sided p value are based on the model-based estimates resulting from multiple-imputation of missing data.
† Urethral lumen test included 105 subjects assessed with 16Fr flexible cystoscope and 3 with 14Fr Foley catheter.
‡ Repeat intervention includes participants receiving additional DVIU, dilation or urethroplasty, including those in control arm with confirmed stricture recurrence (lumen <12Fr by urethrography with recurrent symptoms) who opted to cross over to receive treatment with the Optilume DCB.

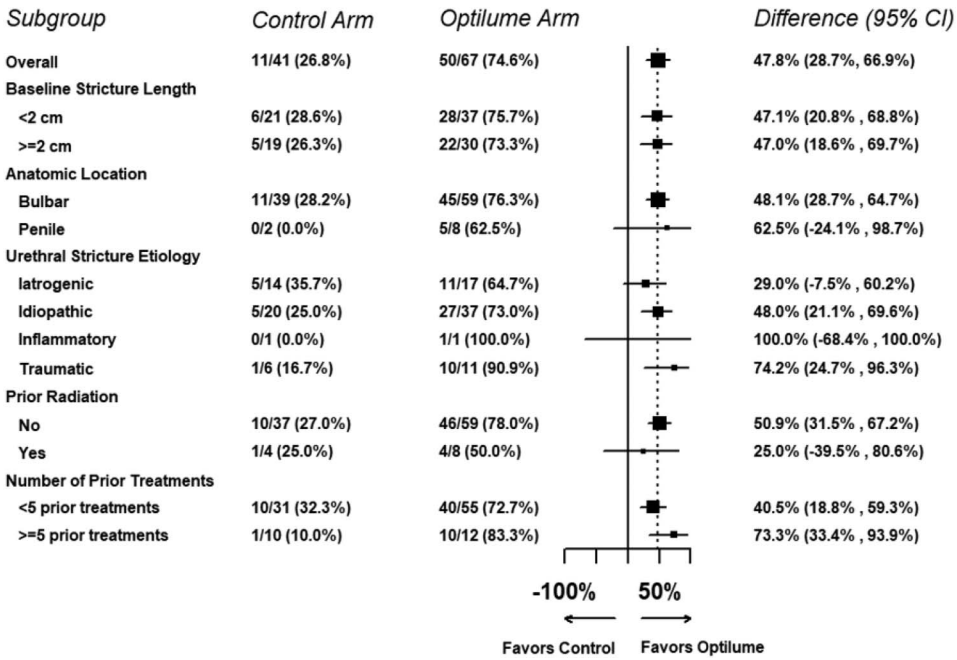

Figure 2. Subgroup analysis of anatomical success for specified subgroups.

each outcome measure showed superiority of the DCB over standard endoscopic management.

A Forest plot demonstrates that 6-month anatomical success favored DCB in all subgroups, although some subgroups were too small for definitive comparison, including etiology, stricture location and previous radiation (fig. 2). Still, these findings demonstrate the robustness of the results with DCB across several subgroups.

Minor AEs that were more common with DCB were hematuria and dysuria. This may represent delayed wound healing as would be expected with

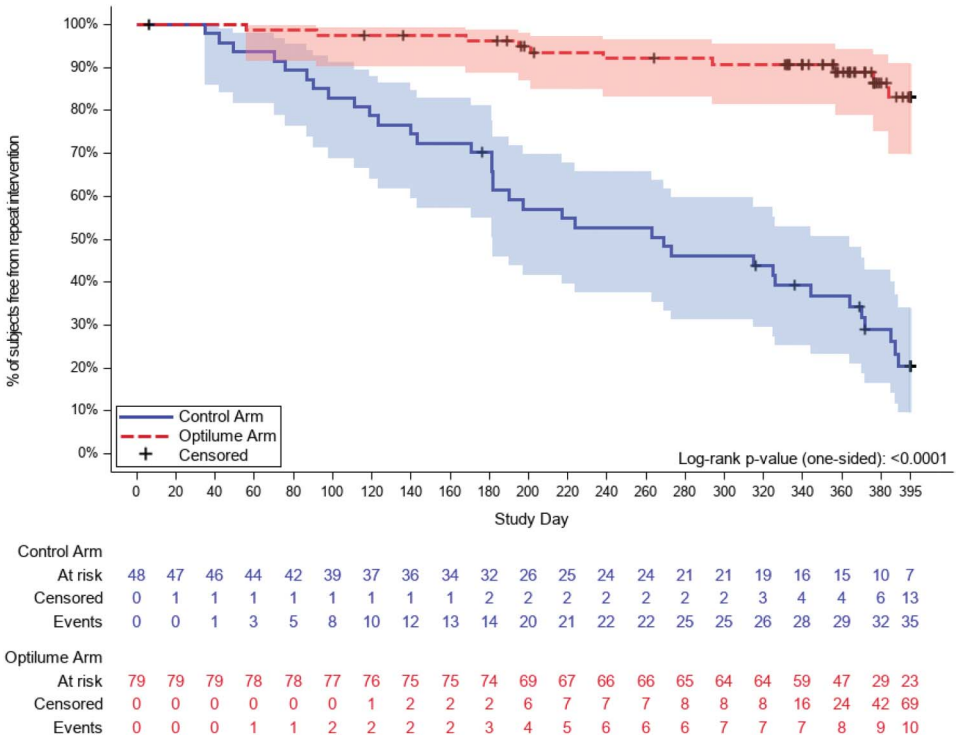

Figure 3. Kaplan-Meier curve of freedom from repeat intervention through 1 year.

Table 3. *Additional outcome measures*

Measure	Baseline		30 Days		3 Mos		6 Mos		1 Yr	
Mean±SD IPSS (No. pts):										
Optilume	22.0±6.8	(79)	7.6±5.7	(78)	7.4±5.8	(74)	8.3±6.2	(71)	9.0±7.1	(67)
Standard of care	22.8±7.0	(47)	9.5±7.4	(47)	12.4±9.2	(45)	15.4±9.6	(43)	19.9±7.5	(42)
Mean±SD IPSS—QoL (No. pts):										
Optilume	4.5±1.3	(79)	1.7±1.4	(78)	1.6±1.4	(74)	1.7±1.3	(71)	1.9±1.5	(67)
Standard of care	4.7±1.2	(47)	2.0±1.6	(47)	2.7±1.8	(45)	3.4±1.8	(43)	4.0±1.3	(42)
Mean±SD ml/sec Qmax (No. pts):										
Optilume	7.6±3.4	(78)	18.3±9.1	(75)	18.6±10.9	(71)	16.6±8.9	(67)	15.5±9.0	(65)
Standard of care	7.4±3.5	(47)	15.8±8.5	(44)	13.3±9.3	(39)	11.1±7.6	(44)	7.6±4.0	(41)
Mean±SD ml PVR urine (No. pts):										
Optilume	109.8±116.9	(77)	75.6±86.2	(75)	103.4±134.4	(70)	73.1±117.7	(67)	94.6±121.8	(66)
Standard of care	133.8±155.1	(47)	79.1±87.3	(45)	113.4±124.2	(41)	141.4±194.1	(44)	181.5±201.7	(42)
Mean±SD IIEF (No. pts):										
Optilume	5.8±2.9	(72)	5.9±2.8	(75)	6.6±2.7	(71)	6.5±2.8	(68)	6.9±3.0	(59)
Standard of care	6.0±3.2	(46)	5.7±3.0	(45)	6.1±3.0	(40)	6.6±3.2	(30)	5.8±2.7	(13)

the mechanism of action for paclitaxel. These events were judged as being mild and typically resolved within 30 days. Likewise, erectile function as measured by IIEF did not change from baseline in either the DCB or DVIU/dilation group. Finally, in a subgroup of men who had their urine and seminal level of paclitaxel followed after treatment, we show that urine levels drop below the level of quantification by 30 days and seminal levels by 6 months. Given the presence of paclitaxel in semen for up to 6 months, it is recommended that men receiving this treatment utilize contraception through 6 months posttreatment if their partner has child-bearing potential.

Limitations of our study include 1) surgeons were not blinded to the type of treatment; this might bias their interpretation of cystoscopic findings or the decision to proceed with repeat treatment. However, other outcomes that would not be biased by the surgeon (ie IPSS, Qmax and PVR) also supported the superiority of Optilume. 2) Patients were unblinded after 6 months; unblinding could have biased some secondary outcomes. For instance, the chance to cross over to the active arm may have impacted the control participants' desire to undergo repeat treatment. However, outcomes that would not be impacted by unblinding (Qmax and PVR) were superior with DCB, both before and after the unblinding. 3) The primary outcome was missing for 7 control and 12 DCB participants; however, even assuming worst-case scenario, wherein all 7 controls were successes and all 12 DCBs were failures, DCB was still superior at 63% vs 38% for controls. 4) It is possible that the better results seen with DCB were due to dilation to a larger lumen size than in controls; however, post-treatment urethrogram estimated the lumen diameters were not different between groups, and a subset analysis of just patients treated with 30Fr balloons showed similar findings to the overall analysis. 5) Repeated endoscopic treatments have been shown to make eventual urethroplasty more complex.[23] We do not know how DCB might impact the complexity or success of reconstruction in men who progress to urethroplasty.

CONCLUSIONS

The results of this randomized controlled trial support that Optilume DCB is safe and superior to standard DVIU/dilation for the treatment of recurrent anterior urethral strictures <3 cm in length. Superior outcomes were observed for freedom from repeat treatment at 1 year, anatomical success at 6 months and functional success at 1 year. We will continue to follow these men for 5 years. The Optilume DCB may serve as an important alternative for men who have had an unsuccessful DVIU/dilation but who want to avoid or delay urethroplasty.

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EDITORIAL COMMENTS

Despite recommendations that recurrent urethral strictures be managed with urethroplasty due to superior efficacy, patients are much more likely to undergo repeat endoscopic treatments (references 5, 6 and 8 in article). Reasons for this are often obvious. From a provider perspective, endoscopic procedures are quick and simple and do not require extensive experience or training. From a patient perspective, procedures are low risk and can often be performed close to home by community urologists.

The Optilume® drug-coated balloon, however, has the potential to result in a significant change to these management recommendations. As presented here, this procedure resulted in a repeat intervention-free survival of 83.2% at 1 year vs just 21.7% for controls. While these data are still in their infancy, the potential to provide a quick and simple endoscopic procedure that rivals open reconstruction techniques in terms of success will be very appealing and may alter our stance on what defines the standard of care for these patients. Furthermore, as this procedure would be able to be performed by most, if not all, community urologists, the need for patients to travel long distances to tertiary referral centers may become much less common.

However, while we should be optimistic about its potential, we must be cautious about where the data currently stand. Long-term success and head-to-head comparisons to urethroplasty will need to be evaluated to better know how these procedures compare. The impact that paclitaxel has on surrounding tissues, and thus future procedures, also remains unclear. Lastly, we have to consider the price and how this impacts cost-effective care. In short, while it is too early to know where the Optilume will fit into existing treatment algorithms, the potential for benefit is clear, and I am eager to see how the future data guide us.

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This manuscript reports the results of a multi-institutional, industry-sponsored, randomized, controlled trial examining use of a drug-coated balloon dilator in patients with recurrent bulbar urethral stricture. This novel technology looks to fill the clinical niche between repeat temporizing endoscopic treatments and high-efficacy open urethroplasty techniques.

This study fulfills the majority of the criteria for a well-performed randomized controlled trial.[1] However, some questions exist with respect to whether

or not the 2 study groups were treated equally and if these results are applicable to a typical patient population with recurrent bulbar urethral stricture.

In this study, the treatment arm underwent predilation to a minimum caliber of 20Fr prior to the application of the drug-coated balloon dilator. While in the control arm, the type and degree of endoscopic treatment was left to the discretion of the surgeon. This difference potentially creates a confounding factor in the treatment arm. In particular, it is unclear if the treatment effect at 6 months is primarily related to the superiority of the balloon dilator or to paclitaxel, or both.

Additionally, mean stricture length in the study population was 1.7 cm, which is likely shorter than the typical patient population presenting for bulbar urethroplasty after failed endoscopic treatment.[2] This is in part related to the device design. Surgeons were instructed to select a balloon length that allowed for 0.5−1 cm overlap into normal urethra on either side of the stricture. Thus, patients with a 3 cm bulbar urethral stricture required the maximal length 5 cm balloon, which potentially limits device application to patients with bulbar strictures 3 cm or less in length.

On balance, these early results are encouraging. With further followup, time will tell if this novel technology results in sustainable stricture cure or simply delays the onset of stricture recurrence.

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REPLY BY AUTHORS

Drs. Johnsen and Rourke correctly identify that direct comparative data are lacking for the drug-coated balloons vs urethroplasty, and the population studied may not directly correspond to typical urethroplasty patients. However, it is important to reiterate that the randomized trial reported herein compared the device against standard of care endoscopic management; urethroplasty remains the gold standard for complex urethral strictures. These data support Optilume® as an option for men with a short bulbar urethral stricture that has failed primary endoscopic management. In the United States, even after ≥2 prior failed endoscopic procedures, 2 out of 3 men still opt for another endoscopic procedure instead of urethroplasty (reference 20 in article). For these men determined to give endoscopic procedures another try, Optilume presents an alternative to a third or fourth dilation/direct vision internal urethrotomy.

With regard to the use of predilation potentially confounding study results, this aspect of the treatment algorithm was driven primarily by regulatory considerations. As described, the post-procedure urethral lumen size was similar between arms, indicating a similar degree of dilation between study arms regardless of treatment received. Thus, the improved outcomes appear to be driven primarily by the novel paclitaxel coating. In a prior study, anatomical success was similar between those receiving predilation and those being directly dilated with the drug-coated balloon.[1]

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