

Management of Lower Urinary Tract Symptoms Attributed to Benign Prostatic Hyperplasia: AUA Guideline (2026) Part II: Medical Management

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Abbreviations and Acronyms

5ARI = 5-alpha reductase inhibitor

AB = Alpha blocker

AUA = American Urological Association

AUA-SI = American Urological Association Symptom Index

AUA-SS = American Urological Association Symptom Score

AUR = Acute urinary retention

BOO = Bladder outlet obstruction

BPH = Benign prostatic hyperplasia

DHT = Dihydrotestosterone

ED = Erectile dysfunction

EPD = Ejaculatory dysfunction

FDA = U.S. Food and Drug Administration

IEF-EF = International Index of Erectile Function-Erectile Function

IFS = Intraoperative floppy iris syndrome

IPSS = International Prostate Symptom Score

LUTS = Lower urinary tract symptoms

MD = Mean difference

OAB = Overactive bladder

PCPT = The Prostate Cancer Prevention Trial

PDE-5i = Phosphodiesterase-type 5 inhibitor

PFS = Post-Finasteride Syndrome

PCDTs = Populations, interventions, comparators, outcomes, timing, settings

PSA = Prostate-specific antigen

Q_{max} = Maximum urinary flow rate

RCT = Randomized controlled trial

SUFU = Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction

TURP = Transurethral resection of the prostate

WAE = Withdrawal due to adverse event

WMD = Weighted mean difference

Purpose: This Guideline covers the treatment of lower urinary tract symptoms/benign prostatic hyperplasia (LUTS/BPH). The summary presented herein

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represents Part II of the three-part series dedicated to Management of LUTS attributed to BPH. Please refer to Parts I and III for additional information on this topic.

Materials and Methods: The systematic review that informs this Guideline was based on searches in Ovid MEDLINE, the Cochrane Central Register of Controlled Trials, and the Cochrane Database of Systematic Reviews through January 2025. Update searches were conducted on December 15, 2025. Literature searches were limited to studies of medical therapies published since 2009 and surgical studies published since 2014. The searches were supplemented by reviewing electronic database reference lists of relevant articles. Criteria for inclusion and exclusion of studies were based on the Key Questions and the populations, interventions, comparators, outcomes, timing, types of studies and settings (PICOTS) of interest developed by the Panel.

Results: The medical management of LUTS/BPH is considered a part of non-procedural management, and the Guideline statements herein address this topic in addition to behavioral/lifestyle interventions for patients with LUTS/BPH. Specific risks are further elucidated for unique patient populations such as those undergoing ophthalmologic surgery.

Conclusions: Non-procedural interventions should be provided within the shared decision-making context and take into account efficacy as well as durability and adverse events. It is also important to disclose unique actions of medication to relevant patient populations such as patients on active surveillance for prostate cancer.

Key Words: benign prostatic hyperplasia, BPH, lower urinary tract symptoms, benign prostatic enlargement, LUTS, prostate-specific antigen, 5-alpha reductase inhibitor, alpha blocker, bladder outlet obstruction, erectile dysfunction, international prostate symptom score, overactive bladder, maximum urinary flow rate, acute urinary retention, ejaculatory dysfunction, intraoperative floppy iris syndrome, phosphodiesterase-type 5 inhibitor, post-finasteride syndrome, transurethral resection of the prostate

BACKGROUND

Non-procedural interventions for BPH include individual pharmacologic agents, combinations of these agents, as well as behavioral/lifestyle interventions. Efficacy and adverse event profiles are important considerations when discussing these within the shared-decision model. The addition of behavioral/lifestyle interventions when pharmacologic agents alone do not provide adequate benefit is also an important consideration.

NON-PROCEDURAL INTERVENTIONS

Alpha Blocker (AB) Monotherapy

Clinicians should offer one of the following uroselective ABs as a treatment option for patients with LUTS/BPH: alfuzosin, silodosin, or tamsulosin (Strong Recommendation; Evidence Level: Grade A)

In patients with LUTS/BPH, uroselective ABs, tamsulosin, alfuzosin, and silodosin result in improved symptom scores and therefore should be recommended as a treatment option. These agents typically reduce International Prostate Symptom Score (IPSS) by 30 to 40% and increase maximum urinary flow rate (Q_{max}) by 20 to 25%.¹ A systematic review² and multiple RCTs³⁻⁵ reported an improvement in IPSS of 2 to 4 points over placebo regardless of the uroselective agent used. Therefore, ABs are usually considered the first-line treatment for LUTS/BPH because of their rapid onset, good efficacy, and low incidence of severe adverse events.

Older ABs, doxazosin and terazosin, have been used for the management of LUTS/BPH, but due to higher rates of orthostatic hypotension and dizziness,⁶ these are not considered ideal because of the readily available uroselective drugs. However, if patients have been managed well with non-uroselective ABs without side effects, the Panel found no reason to discontinue treatment and start uroselective agents. It is not advisable to add uroselective ABs for patients who are on ABs for other reasons (eg, hypertension).

Comparative studies between the uroselective ABs were sparse but did not show a consistent comparative difference in terms of IPSS improvement. There were, however, relatively consistent differences in side effects between agents in the comparative trials. Ultimately, the use of specific uroselective ABs is not guided by differences in efficacy but more so by differences in side-effect profiles.

When selecting ABs to treat patients with LUTS/BPH, clinicians should educate patients that symptomatic improvements are similar among all ABs. (Clinical Principle)

Clinicians can choose from multiple ABs when selecting appropriate medical therapy for their patients. A large meta-analysis shows an absolute effect, or mean change from baseline symptoms to study end, ranging from -3.69 to -7.06 points with most uroselective ABs (also known as subtype [alpha-1a]-selective) demonstrating a > 5-point IPSS improvement.⁷ Clinicians should not change between different ABs if patients fail to have sufficient

improvement with the initiation of drug therapy; however, they may consider a change when patients respond to medications but have intolerable side effects that may be ameliorated with a different AB.

Silodosin vs alfuzosin was compared in 2 randomized controlled trials (RCTs); one showed greater symptom improvement with silodosin and the other with alfuzosin. The quality of life and withdrawal due to adverse events were not different between the 2 drugs.^{8,9} Silodosin vs tamsulosin was studied and showed similar improvement in LUTS; however, quality of life improvement favored silodosin while it simultaneously had a higher rate of withdrawal due to adverse effects.¹⁰ Finally, there was no change in LUTS or withdrawal of the medication for adverse events when comparing alfuzosin with tamsulosin; however, quality of life favored alfuzosin at 12 weeks.^{8,9}

When prescribing ABs, clinicians should counsel patients with LUTS/BPH regarding the different side effect profiles and make a selection based on patient preference and comorbidities. (Clinical Principle)

ABs are clinically effective and well-tolerated by patients with LUTS/BPH.¹¹ However, there are differences in side effects between agents which may lead to worsening in quality of life or withdrawal of the agent. Therefore, it is important to engage in shared decision-making, taking into account patient preference and comorbidities when selecting an AB. Specifically, younger men concerned about sexual function or fertility should be counseled regarding the possibility of ejaculatory dysfunction (EjD) and that alfuzosin is likely the first choice for these men. In older men or those with cardiac risk factors, silodosin would likely be the first choice because they are probably less concerned about ejaculation, and silodosin has a decreased risk of orthostatic hypotension.

The most common reported side effects were dizziness/orthostatic hypotension, and the most common sexual side effect was EjD.^{8-10,12,13} Abnormal ejaculation was reported to be 3 to 10% for patients on tamsulosin and silodosin compared to 0% for those on alfuzosin, suggesting that alfuzosin is the agent of choice for patients concerned about EjD.⁹ Abnormal ejaculation may be due to classic retrograde ejaculation, or a decrease or absence in seminal fluid.¹⁴ Prior studies have shown that alfuzosin had lower rates of EjD compared to tamsulosin and silodosin.¹⁴ In addition, the known higher selectivity towards the alpha-1A receptor likely plays a role in lower hypotensive effects of silodosin and tamsulosin compared to alfuzosin.¹⁵ The non-uroselective ABs, doxazosin and terazosin, also have higher rates of orthostatic hypotension compared to the uroselective agents due to decreased selectivity towards the alpha-1A receptors. Finally, ABs should be used with caution in patients with severe renal or

hepatic impairment due to the metabolism and clearance pathway of these agents, and interactions with other pre-existing medications should be considered.

Clinicians should counsel patients with LUTS/BPH planning for cataract surgery about the associated risks of intraoperative floppy iris syndrome (IFIS) with ABs and advise patients to discuss these risks with their ophthalmologist. (Clinical Principle)

Updated literature continues to show an increased risk of IFIS with AB therapy. The risk persists even after discontinuation of the medication for as long as a year. This was initially described for tamsulosin, however, other ABs were also implicated along with other classes of medications and systemic risk factors. Tamsulosin continues to carry the highest risk as does terazosin and doxazosin. Alfuzosin also has some risks but to a lesser extent, and the incidence of silodosin has not been studied. It is imperative that patients, urologists, and ophthalmologists work to identify risk factors preoperatively and take intraoperative measures to avoid this complication during cataract surgery.¹⁶ In patients with symptomatic LUTS/BPH and a cataract, it should be recommended to undergo cataract surgery before starting ABs.

Phosphodiesterase-5 Inhibitors

In patients with LUTS/BPH, with or without erectile dysfunction (ED), clinicians should offer daily 5 mg tadalafil. (Moderate Recommendation; Evidence Level: Grade B)

Phosphodiesterase-5 inhibitors (PDE-5Is) have beneficial effects on LUTS with or without comorbid ED and therefore should be offered to men with LUTS/BPH. The mechanism of action of this PDE-5I effect is only partially understood, but there is emerging clinical evidence of their effect on LUTS/BPH (alone or in combination with other agents) as summarized below.

PDE-5Is vs Placebo

A meta-analysis by Gacci et al demonstrated that PDE-5Is, in addition to significant improvement in International Index of Erectile Function (IIEF) score, reduce IPSS, storage and voiding LUTS, and improve quality of life with no significant difference in Q_{max} compared to placebo.¹⁷

A systematic review by Brasure et al identified 9 RCTs comparing tadalafil to placebo.² At three-month follow-up, tadalafil treatment was associated with a small improvement in symptom scores and quality of life. There was an increase in withdrawal due to adverse events in the treatment group. Short-term, serious adverse effects were rare and reported in similar proportions with tadalafil and placebo.

5-Alpha Reductase Inhibitors

In patients with LUTS/BPH and an estimated prostate volume >30 cc and/or prostate-specific antigen (PSA) > 1.5 ng/mL, clinicians should offer 5-alpha reductase inhibitor (5-ARI) therapy for symptom relief. (Moderate Recommendation; Evidence Level: Grade A)

In patients with LUTS/BPH and an estimated prostate volume >30 cc and/or PSA > 1.5 ng/mL, clinicians may offer 5-ARI therapy to reduce the risk of clinical BPH progression (e.g., worsening symptoms, acute urinary retention [AUR], need for BPH surgery). (Clinical Principle)

In symptomatic LUTS/BPH patients with large prostates, 5-ARI monotherapy can provide significant symptom relief and prevent progression to AUR and the need for surgery when compared to placebo. A measure of effectiveness of intended treatment “50% rule” applies to the PSA reduction after 3 to 6 months of 5-ARI treatment.¹⁸

5-ARIs lead to a mean prostate volume reduction ranging from 17.9 to 21% after 12 and 24 months of medication use, respectively.^{19,20} Lower doses of 5-ARIs used for hair loss (typically 1 mg) will also cause PSA reductions of 40% after 48 weeks of using the medication.²¹

Although dutasteride has a pronounced dihydrotestosterone (DHT) reduction when compared to placebo, both dutasteride and finasteride showed significant symptom improvements in patients with BPH.^{4,22} Studies show no differences in prostate volume reduction, American Urological Association Symptom Index (AUA-SI), and Q_{max} between finasteride and dutasteride. Both medications are an option for monotherapy to treat BPH.

When considering monotherapy treatment of BPH with 5-ARIs, clinicians and patients should discuss the relationship of prostate volume and PSA levels. Studies have shown that the prostate volume reduction is greater with larger prostates.²³ Several large studies used a 30 cc prostate volume cut-off with significant results, making it a reasonable lower limit when using 5-ARIs.²⁴ Populational studies have shown strong association between PSA and prostate volume.²⁵ A PSA threshold > 1.6 ng/mL has a specificity of 70% for detecting men (without evidence of prostate cancer) with prostates > 40 cc.²⁵ Even though 5-ARIs are usually used for patients with PSA > 1.5 ng/mL, clinicians do not need to order a PSA if the goal is only to determine eligibility for 5-ARIs.

In a large prospective, double-blinded, placebo-controlled trial, men treated with 5-ARIs had a 55% reduced risk of needing surgery, and a 57% reduced risk in developing AUR compared to placebo.²⁶ The findings of this trial suggest that in patients with large prostates and LUTS/BPH, the

use of 5-ARIs could alter the natural course of the disease and reduce complications of BPH progression such as AUR and surgery.

When prescribing 5-ARIs, clinicians should counsel patients with LUTS/BPH about the risks of side effects and the impact on prostate cancer diagnosis. (Moderate Recommendation; Evidence Level: Grade C)

Sexual Function. The MTOPS trial⁴ observed a gradual worsening of libido, erectile function, and ejaculatory function in all treatment groups including placebo with time. The investigators also observed a small but significant worsening of ejaculatory function in the finasteride group and worsening of both ejaculatory and erectile function in the combination group.

The 4-year results of the CombAT trial similarly noted a small worsening of ejaculatory and erectile function in the combination group, but did not comment on statistical significance.²⁷

Gynecomastia. The REDUCE trial found a small but statistically significant increase in gynecomastia in the dutasteride group (1.9% vs 1.0%).²⁸ This rate did not appear to increase during the two-year observational extension study where no new cases of gynecomastia were reported.²⁹

Dementia. One observational study has reported a higher incidence of dementia in men taking 5-ARIs during the first 2 years of administration.³⁰ However, it is thought these findings may represent coexistent cognitive impairment identified at the time of initial LUTS assessment, rather than a direct effect of the medication.

Depression. One large observational study found an increased risk of depression, but not suicide risk, in men taking 5-ARIs.³¹ Another large retrospective cohort study showed no increase in medically treated depression in men taking 5-ARIs when compared to ABs only, although there was an increase in treated depression with longer duration of BPH treatment, independent of drug exposure.³²

Post-Finasteride Syndrome. Current data on post-finasteride syndrome (PFS) draw primarily from anecdotal patient-reported outcomes mostly related to the use of finasteride to treat baldness in younger men. The adverse event reporting of available RCTs have not substantiated the clinical entity of PFS. Nevertheless, these concerns regarding PFS have prompted the U.S. Food and Drug Administration (FDA) to amend the labels for 5-ARIs with a warning of its risks.

Prostate Cancer Diagnosis. The Prostate Cancer Prevention Trial (PCPT) noted a 24.8% reduction in the overall number of prostate cancers identified in the

finasteride group, but there was an increased rate of high-grade ($\geq$ Gleason Score 8) cancers (2.1% vs 1.1%).³³

The REDUCE trial showed similar findings with a 23% reduction in overall prostate cancer but also an increased risk of high-grade cancer (0.9% vs 0.6%).²⁸

While these findings of an increased rate of high-grade prostate cancer raised concerns about the long-term impact of 5-ARI use, the 18 year follow-up of the PCPT showed no difference in overall survival between groups.³⁴ Nevertheless, these findings prompted an FDA black box warning in 2011 stating that “healthcare professionals should be aware of this safety information and weigh the known benefits against the potential risks when deciding to start or continue treatment with 5-ARIs in men.”³⁵

In patients with persistent prostate-related hematuria due to LUTS/BPH, clinicians may offer 5-ARI treatment. (Expert Opinion)

Administration of 5-ARIs has been demonstrated to reduce the microvascular density in prostatic stroma and, in RCTs, has shown to reduce the amount of perioperative blood loss at transurethral resection of the prostate (TURP).³⁶ This same mechanism is thought to be clinically useful to treat hematuria from a prostatic source, although its efficacy has only been substantiated in small case series.³⁷

Combination Therapy

In patients with LUTS/BPH and an estimated prostate volume >30 cc and/or PSA >1.5 ng/mL, clinicians should offer a 5-ARI in combination with an AB as a treatment option. (Moderate Recommendation; Evidence Level: Grade B)

Several large, well-known studies found statistically significant improvements with combination therapy in overall IPSS as well as quality of life. More significantly, however, is the risk reduction patients experience in terms of reduced rates of urinary retention and progression to surgical intervention as cited in the MTOPS trial.³⁸

CombAT randomized participants to dutasteride in combination with tamsulosin or either drug alone. Combination therapy provided better relief than tamsulosin alone in terms of both LUTS and quality of life as evidenced by reduced IPSS and better urinary flow rates, as well as better clinical outcomes (decreased need for surgery and urinary retention). CombAT did not show clinically important differences in symptoms or quality of life between combination therapy and dutasteride alone, and there was some limited evidence of better clinical outcomes with combination therapy. Combination therapy was well-tolerated with a safety profile consistent with the individual medications.²⁷

The REDUCE trial noted men on dutasteride had a lower incidence of low-grade prostate cancer by approximately 23% but found an increase in cases of

high-grade prostate cancer. The exact mechanism is unknown and remains debated.²⁸

The MTOPS trial evaluated the effectiveness of finasteride, doxazosin, and their combination in managing BPH symptoms. The combination group was found to have significantly improved symptoms (7-point improved American Urological Association Symptom Score [AUA-SS] score vs baseline), reduced risk of urinary retention (81% risk reduction vs placebo; 0.1 vs 0.6 cases/100 person-years), and decreased need for surgical intervention (near 67% risk reduction vs placebo). Symptom improvement with combination therapy was similar to that with doxazosin (-7 points vs -6 points at year 4), and slightly better than that with finasteride (-7 points vs -5 points). Clinical outcomes were better with combination therapy than with doxazosin alone, but similar between combination therapy and finasteride.

The CONDUCT trial found improved IPSS, quality of life, and rates of clinical progression associated with immediate combination therapy of dutasteride plus tamsulosin compared with watchful waiting and delayed tamsulosin therapy. However, the study also noted increased withdrawal rates in the combination group for ED, EjD, and rarely cardiovascular adverse events.^{39,40}

There continues to be a paucity of large studies regarding the initiation of combination therapy with the intention of later withdrawal or discontinuation of the AB medication. This has been referred to as “Withdrawal Therapy” in the previous Guideline.⁴¹ While the strategy of withdrawal seems reasonable in theory, the concept has not been studied sufficiently to determine the utility of this approach or the optimal durations of combination therapy before the cessation of the AB.

In patients with LUTS/BPH, with or without ED, clinicians may offer the combination of daily 5 mg tadalafil with uroselective ABs. (Conditional Recommendation; Evidence Level: Grade C)

There was a high degree of heterogeneity with results among the different trials looking at AB therapy with 5 mg tadalafil. One systematic review evaluated tadalafil combined with any AB vs an AB alone. This demonstrated a small improvement in IPSS; however, clinical significance was borderline (mean difference [MD]: 2 points).² Two additional RCTs looked at tadalafil with silodosin or tamsulosin; one demonstrated a small statistically significant improvement in IPSS that was not clinically significant,⁴² while the other found no significant difference in symptoms.^{42,43} Overall, the body of literature shows a small improvement in symptom scores with combination therapy, but the benefits are small when looking at individual trials. Combination therapy is

generally considered safe but there is a risk for potentiated hypotension and requires monitoring.

PDE-5Is + ABs versus PDE-5Is. Five RCTs compared a PDE-5I combined with an AB to a PDE-5I alone, including combinations of tadalafil, vardenafil, or sildenafil with silodosin, tamsulosin, or doxazosin.⁴²⁻⁴⁶ These studies showed a small improvement in LUTS associated with combination therapy, as well as better quality of life and erectile function. Most studies reported no differences in adverse events.

In patients with LUTS/BPH and an estimated prostate volume >30 cc and/or PSA >1.5 ng/mL, with or without ED, clinicians may offer the combination of daily 5 mg tadalafil with a 5-ARI. (Conditional Recommendation; Evidence Level: Grade C)

Combination therapy utilizing 5 mg tadalafil with finasteride demonstrates a small, but statistically significant improvement in IPSS compared to finasteride alone for prostates > 30 cc. Furthermore, patient satisfaction was greater with combination therapy as were IIEF-Erectile Function (EF) scores.

One RCT evaluated combination therapy using 5 mg tadalafil combined with 5 mg finasteride vs finasteride alone. Companion analyses that add additional outcomes to the same patient cohort were included in the meta-analysis conducted for this Guideline.^{2,47,48} Combination therapy improved IPSS more than finasteride alone; however, quality of life improvement was similar in both groups. Furthermore, combination treatment resulted in improved erectile function for patients with or without baseline ED compared to monotherapy.

In patients with moderate to severe predominant storage LUTS, clinicians may offer anticholinergic agents alone or in combination with an AB as a treatment option. (Conditional Recommendation; Evidence Level: Grade C)

Storage LUTS in men are often left untreated, even though these symptoms can be highly bothersome, often more so than voiding LUTS. In the EPIC study, of all men identified with LUTS, > 80% had storage LUTS.⁴⁹ In the EpiLUTS study,⁵⁰ storage symptoms were experienced by around two-thirds of men, with approximately 50% of men reporting mixed storage and voiding symptoms. In men who present with overactive bladder (OAB), predominant LUTS should be evaluated to assess for the relative contribution of bladder outlet obstruction (BOO) secondary to BPH. In studies for anticholinergics with ABs or an AB alone, there is evidence to support symptomatic, quality of life improvement with combination therapy with low risk of retention. Two meta-analyses and 4 RCTs have evaluated cohorts of patients with storage LUTS and concomitant BPH. The studies compared combination therapy with ABs and either antimuscarinic

medications or beta-3 agonists to monotherapy with an alpha-adrenergic antagonist.^{51,52} Combined use of tamsulosin and solifenacin showed significant improvement in storage symptoms compared to tamsulosin monotherapy. The American Urological Association/Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction (AUA/SUFU) OAB Guideline further addresses the use of anticholinergics in men with storage symptoms.⁵³

At 3 to 6 months follow-up, treatment with an AB plus tolterodine vs placebo was associated with improved total IPSS and quality of life score in 2 trials, though the smaller trial showed a larger benefit.^{2,5} Three RCTs of solifenacin plus an AB (n = 1023) showed a decrease in total IPSS associated with combination therapy vs placebo that was statistically significant but may not have been clinically significant (weighted mean difference [WMD]: -1.50 points; 95% CI: -1.80 to -1.20). The IPSS quality of life scores also improved (1 RCT; n = 629). The 3 trials suggested a large increase in withdrawal due to adverse events (WAEs) associated with treatment, but the estimate was imprecise.²

In patients with moderate to severe predominant storage LUTS, clinicians may offer beta-3 agonists alone or in combination with an AB as a treatment option. (Conditional Recommendation; Evidence Level: Grade C)

The use of beta-3 agonists in combination with ABs has emerging evidence of safety and symptomatic improvement. Vibegron, randomized to placebo, in men with LUTS/BPH with predominant storage LUTS on ABs or 5-ARIs, showed a significant improvement in urgency, frequency, and nocturia.⁵⁴ Mirabegron used alone in patients with BOO did not adversely affect Q_{max} and detrusor pressure at Q_{max} compared with placebo after 12 weeks of treatment.⁵⁵

One RCT (n = 706), the PLUS trial, compared a beta-3 agonist combined with an AB to AB monotherapy.⁵⁶ The trial enrolled men who had been taking tamsulosin for at least 2 months for LUTS/BPH; almost all had moderate or severe symptoms at baseline. Patients were randomized to add-on mirabegron or continued tamsulosin monotherapy. Adverse event rates were similar between groups. The AUA/SUFU OAB Guideline supports the use of monotherapy with beta-3 agonists in patients with predominant storage LUTS and BPH.⁵³

For patients with LUTS/BPH and persistent storage LUTS despite pharmacologic treatment, clinicians should add behavioral/lifestyle interventions. (Expert Opinion)

Persistent storage LUTS despite effective medical or surgical treatment of BOO is common. Although comparative effectiveness trials of behavioral and/or lifestyle interventions vs an active drug comparator group were not included in the literature search criteria for this Guideline, multiple high-quality

clinical trials have demonstrated that behavioral and/or lifestyle interventions are superior to antimuscarinic drug monotherapy for persistent storage LUTS after AB monotherapy for BPH. For example, the MOTIVE trial demonstrated that the effect of 8-week behavioral intervention on mean voids per day was non-inferior to oxybutynin extended release among 143 men with persistent storage LUTS after 4 weeks of AB monotherapy.⁵⁷ In a planned subgroup analysis of MOTIVE participants with nocturia, the behavioral intervention was superior to oxybutynin.⁵⁸ A subsequent trial (COBALT) further demonstrated superiority of 6-weeks of behavioral therapy compared to oxybutynin plus tamsulosin as first-line treatment for men with storage LUTS with or without BPH.⁵⁹ After men in both intervention groups were escalated to combination therapy with behavioral therapy plus oxybutynin and tamsulosin, combination therapy was superior to drug therapy alone but was not superior to behavioral therapy alone. No adverse events were reported by 86% of participants in the behavioral therapy alone group vs 32% in the drug therapy alone group and 34% in the combination therapy group. Overall, there is a clear net benefit for behavioral therapy alone vs pharmacologic treatment for storage LUTS in patients with BPH.

SPECIAL CASES

Concurrent LUTS/BPH and Prostate Cancer Active Surveillance

Clinicians should counsel patients with LUTS/BPH on active surveillance for prostate

cancer that 5-ARI treatment is unlikely to increase the risk of prostate cancer progression. (Expert Opinion)

The FDA has issued a warning about the higher risk of high-grade prostate cancer in men treated with 5-ARIs.³⁵ This is based on studies which tried to establish a chemopreventive effect of 5-ARIs on prostate cancer.^{28,34} These trials showed a lower rate of prostate cancer, but this effect was entirely confined to low-grade cancer and in fact showed a higher rate of high-grade prostate cancer in patients treated with 5-ARIs. This effect may be due to detection bias (ie, same number of samples in a smaller prostate because of the decrease in prostate volume by a 5-ARI that may lead to higher detection of cancer which may not decrease in volume) and has not been replicated in active surveillance cohorts.

Patients on active surveillance for prostate cancer with LUTS are generally treated the same as those with LUTS/BPH. A study which did not specifically evaluate the effect of 5-ARIs on LUTS, but did follow progression of prostate cancer, reported no increase in the rate of high-risk prostate cancer in the group of patients treated with finasteride on active surveillance for prostate cancer.⁶⁰ While this is not direct evidence, it did provide enough information for the Panel to discuss and come to a consensus that 5-ARIs are unlikely to increase the rate of high-risk prostate cancer in patients on active surveillance. It should be noted that 5-ARIs change PSA kinetics and this should be taken into consideration while monitoring these patients.

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