

Evaluating and understanding combination therapy decision drivers for the treatment of overactive bladder in the United States

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Abstract

Objective: To understand factors guiding overactive bladder (OAB) therapy selection and experience with combination therapy (antimuscarinics and beta-3 agonists).

Methods: Cross-sectional surveys of OAB patients and OAB-treating physicians in the USA were conducted. Patients receiving monotherapy with antimuscarinics were categorized by OAB treatment history: monotherapy only; third-line procedures (e.g., onabotulinumtoxinA injections) and combination therapy; third-line therapy only; and combination therapy only. The patient survey assessed therapy choice drivers and barriers, treatment satisfaction and sociodemographic/clinical characteristics. The physician survey assessed drivers of and barriers to OAB treatment choices.

Results: Of 200 patients, 86.5% reported involvement in treatment decision-making; doctor's recommendation was the most frequently considered factor (84.4%). Most patients (71%) were unaware of combination therapy. The primary reason why those patients aware of combination therapy had not used it (N = 43/200; 21%) was physician recommendation of other treatments (69.8%). For physicians (N = 50), the most frequently considered factors when prescribing OAB treatment were effectiveness (92.0%) and side effects (84.0%); 70% prescribed combination therapy, primarily for symptom severity (82.9%). The main reasons for not prescribing combination therapy were cost/insurance coverage (80%) and lack of information (53.3%).

Conclusions: Shared decision-making guided treatment decisions; the main considerations were treatment safety and efficacy.

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Keywords

Overactive bladder, combination therapy, patient-reported outcome, decision-making, survey, cross-sectional

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Background

Overactive bladder (OAB) is a urinary symptom complex characterized by urgency, with or without urge urinary incontinence, and accompanied by frequency and nocturia.¹ Although prevalence estimates derived from longitudinal studies vary (16.5% to 23.3%), they indicate that OAB poses a substantial and growing burden to public health.² In terms of risk factors for OAB, women and minorities are particularly affected, as are older individuals.³

Upon diagnosis, patients with OAB are initially offered behavioral therapies; subsequent first-line pharmacotherapies include oral antimuscarinics or beta-3 adrenergic agonists. Dose modification or switching to a different agent is recommended when adverse events preclude continuation.⁴ Analyses of medical claims data indicate that switching among antimuscarinic agents is common, and is primarily owing to the adverse events associated with anticholinergic medications.⁵ Given that antimuscarinics have historically been the mainstay of OAB treatment, their low tolerability poses a general challenge in terms of adherence and persistence. Indeed, adherence and persistence regarding OAB therapies is comparatively poor compared with that associated with therapies for other chronic conditions.⁶ Several real-world studies of mirabegron, a beta-3 adrenergic agonist, have found that it is associated with substantially better adherence and persistence than antimuscarinics.^{5,7}

In 2018, combination therapy of mirabegron and solifenacin succinate was

approved for the treatment of OAB in the USA. An analysis of findings from randomized controlled trials indicated that although combination therapy (mirabegron 25 or 50 mg with solifenacin 5 mg) is more effective than monotherapy with mirabegron 50 mg, it is associated with more anticholinergic side effects.⁸ Current guidelines from the American Urological Association state that combination therapy can be considered when a patient is refractory to monotherapy with an antimuscarinic agent or beta-3 adrenergic agonist.⁴ Information is lacking on the factors that affect the use of combination therapy, including real-world data on treatment patterns, adherence and persistence, and the characteristics of patients who receive this treatment.

Third-line therapies are available to patients who are refractory to or cannot tolerate pharmacotherapy.⁴ These include intradetrusor onabotulinumtoxinA injections, peripheral tibial nerve stimulation (PTNS) and sacral neuromodulation. Data on patterns of use of third-line therapies are evolving. Recent data indicate that the use of these therapies among women is low (2.2%).⁹ Another study found that of the third-line therapies, sacral neuromodulation was most commonly used (48.8%), followed by onabotulinumtoxinA (38.3%) and PTNS (12.9%).¹⁰ Finally, several demographic factors have been found to be associated with use of third-line therapies, including age <65 years, education level below bachelor's degree and female sex.¹¹

Given the suboptimal adherence and persistence associated with monotherapies,

as well as the recent advent of combination therapy, it is important to understand patient and physician factors that guide OAB therapy selection and experience. In particular, the drivers and barriers to patient utilization and physician prescription of combination therapy should be examined. The objectives of this study were to understand 1) the sociodemographic and clinical characteristics of OAB patients who receive monotherapies, combination and/or third-line therapies, 2) patient-reported outcomes (PROs) associated with these therapies and 3) the decision-making processes for both patients and physicians that guide therapy selection, particularly regarding combination therapy.

Methods

Study design

This was a cross-sectional study with the following design:

- (1) Development and administration of an online patient survey questionnaire (Appendix 1) to understand the drivers of OAB combination treatment choices, the sociodemographic and clinical characteristics of patients on different OAB treatment modalities and PROs associated with the different treatment cohorts.
- (2) Development and administration of an online survey for OAB-treating physicians (Appendix 2) to understand the drivers of OAB treatment choices, particularly combination therapy, from physicians' perspectives.

Survey development and administration: patients

A targeted literature review was first conducted to obtain information on treatment decision processes and drivers of treatment choices for OAB patients, as well as key

patient characteristics and PROs associated with different treatments in the existing literature. Keywords included "overactive bladder," "treatment decision," "patient preference" and "physician preference." The search platforms used for the targeted literature review included PubMed (<http://www.ncbi.nlm.nih.gov/pubmed>) and Google Scholar (<https://scholar.google.com/>).

The questionnaire content was based on the findings from the targeted literature review and assessed the following variables: sociodemographic characteristics (e.g., age, sex, race/ethnicity, marital status, household income, education level, employment status and health insurance), clinical characteristics (comorbidities, time since the first OAB diagnosis/symptom onset), OAB treatment history (types of treatment, length of treatment) and drivers of treatment decisions (decision-making process, key considerations in choosing or discontinuing a treatment). PROs included assessments of OAB symptoms, symptom bother, health-related quality of life (HRQoL) and treatment satisfaction. Specific measures used were the OAB symptom score questionnaire (OABSS) and the OAB questionnaire (OAB-q). Higher scores on the OABSS (range: 0–15) indicate higher symptom severity; higher scores on the OAB-q (range: 0–100), which assesses both symptom bother and HRQoL, indicate greater symptom bother or better HRQoL.^{12,13} Treatment satisfaction was also assessed. The interview guides and informed consent forms for both the patient and physician surveys were approved by the New England Institutional Review Board (IRB) on 7 November 2019 (amendment 12 March 2020; IRB tracking number: 120190351). Data were collected via an online patient survey and an online physician survey. Consent was obtained digitally, and all data were stored in secure datasets. A control system prevented unauthorized access to survey questionnaires and

protected data on the internet via Secure Sockets Layer encryption technology. Duplicate records from the same patient were not allowed.

Participants were recruited from a proprietary, national panel of OAB patients (a convenience sample of $n > 10,000$ individuals) that is professionally managed by a research and marketing company (Dynata™). Recruitment occurs through a broad set of channels, including television, and online and offline methods. Notably, Dynata™ panels have recently been used as part of a federally funded effort to validate a PRO measure for bladder health.¹⁴

Subsequent to the satisfaction of inclusion and exclusion criteria (Appendix 3), upon enrollment, patients were assigned to one of four cohorts based on their treatment trajectory. The target sample size for each of the four cohorts was 50 patients, for a total of 200 patients. Cohort 1 included patients who had not received third-line therapies or combination therapy and who were currently on or had recently discontinued (within the past 12 months) monotherapy with mirabegron or an antimuscarinic. Cohort 2 included patients who had received combination therapy without ever

receiving any third-line therapy and had received pharmacological treatment in the last 12 months. Cohort 3 included patients who had received both combination and third-line therapies. Cohort 4 included patients who had received a third-line therapy but had never received combination therapy. A graphical depiction of the cohorts is presented in Figure 1.

Following the development of the questionnaire, pre-tests were conducted with two eligible patients in each cohort to identify any necessary revisions. Specifically, the content of the questionnaire was presented to the respondents by a moderator, who documented and addressed any questions and concerns. The data were subsequently reviewed to assess the consistency of responses, the range of responses and the need for any clarification changes to the questionnaire wording. Following this, a soft launch of the survey was initiated by administering the questionnaire to approximately 10% of the target number of patients; data were subsequently reviewed for quality purposes. The final survey, which took approximately 15 minutes to complete, was then administered to the full study sample. Participants were compensated through a point system (managed

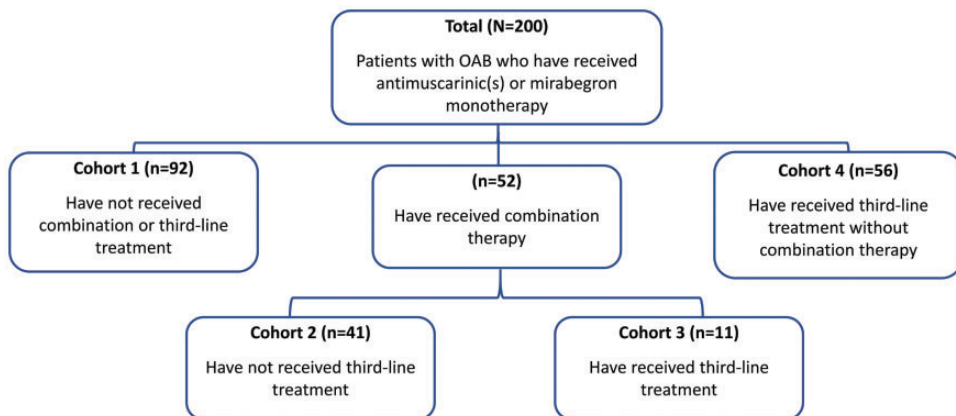


Figure 1. Schematic of study cohorts.

by Dynata™); the “panel points” awarded upon study completion had an equivalent value of USD 6.

Survey development and administration: physicians

Information regarding the OAB treatment decision processes and drivers of treatment choices from the physician perspective was obtained from the targeted literature review and subsequently used to develop a structured interview guide. Physicians were also recruited through Dynata™ using verified lists of physician-accrediting associations with validation against unique physician IDs. Physicians were required to meet inclusion and exclusion criteria (Appendix 4). Eligible physicians were stratified according to whether or not they prescribed combination therapy. One-on-one interviews (approximately 1 hour each) using the structured interview guide were conducted with five physicians to solicit input on the factors considered when choosing treatments for OAB and factors that affect patient treatment adherence. The information obtained from the interviews was summarized and used to guide the development of the online physician questionnaire. The questionnaire assessed the following variables: physician characteristics (e.g., age, sex, geographic region, specialty, years of practice, practice setting, number of OAB patients seen in the last year), past experience of prescribing combination therapy and drivers of treatment decisions (decision process, key factors considered when choosing OAB treatment in general and prescribing or not prescribing combination therapy, factors for discontinuing combination therapy, satisfaction with combination therapy).

Following the development of the questionnaire, pre-tests were conducted with two eligible physicians to identify any necessary revisions. In a process similar to that

followed for the patient questionnaire, the content of the physician questionnaire was presented to the respondents by a moderator. Subsequent review of the data was again conducted to assess the need for any changes to the questionnaire wording. A soft launch of the survey was then initiated by administering the questionnaire to 10 physicians; data were subsequently reviewed for quality purposes. The final survey, which took approximately 10 minutes to complete, was administered to the full study sample (50 physicians). For their participation, physicians received “panel points” that were equivalent in value to USD 60. The survey questionnaires for both physicians and patients can be found in the Supplementary Materials.

Informed consent was obtained from all individual participants included in the study and both the patient and physician interview guides and informed consent forms used for the interviews were approved by the New England IRB (IRB tracking number: 120190351). The study was conducted in accordance with the Health and Human Services Regulations on Research with Human Beings (45 CFR 46 Subparts A, B, C, and D)¹⁵ and the International Conference on Harmonization Guidance for Industry—E6 Good Clinical Practice: Consolidated Guideline.¹⁶ All patient information was de-identified. Details of the study design and results were reported in accordance with the Consensus-Based Checklist for Reporting of Survey Studies (CROSS).¹⁷

Statistical analyses

Descriptive statistics were used to summarize the results for both the patient and physician cohorts. Continuous outcome variables were summarized using means, medians and standard deviations (SD). Categorical outcome variables were summarized using frequencies and percentages.

Total scores were summarized for the OABSS and OAB-q. Data analysis was conducted using SAS Version 9.4 (SAS Institute Inc., Cary, NC, USA).¹⁸ No statistical testing was performed to compare the primary endpoints across cohorts. Only descriptive analyses were performed in this study.

The online surveys did not allow respondents to skip questions; however, respondents were allowed to select “unknown/not sure” for some questions (e.g., years of diagnosis, duration of each treatment). Responses were coded as missing if “unknown/not sure” was selected. Invalid responses (e.g., one patient selected third-line treatment but wrote “pills” when asked what type of third-line treatment was used) were also coded as missing.

Results

Patients

A total of 200 patients were eligible for the study: 92 were in cohort 1, 41 were in cohort 2, 11 were in cohort 3, and 56 were in cohort 4. The original target sample size of 50 patients per cohort was not feasible for two cohorts, particularly cohort 3, and reflects the relatively rare administration of third-line therapy. Patient demographics, clinical characteristics and OAB treatment history are shown in Table 1.

Demographics and clinical characteristics. Non-users of combination therapy: Cohort 1 (current or recent users of monotherapy only) contained the oldest patients of the four cohorts (mean = 60.1 [SD 14.7] years), the highest percentage of retirees (45.7%), patients with the lowest income (50.0% reported <50,000 USD annual income) and patients with the highest proportion of public insurance use (63.0%). Patients in this cohort had the longest OAB duration (7.2 [6.8] years) and the highest

HRQoL scores (60.7 [24.9]). Users of third-line therapies who had not used combination therapy (cohort 4) contained patients with the youngest mean age (41.9 [17.2]) and the highest income (64.3% ≥75,000 USD), and a high proportion of patients who had private insurance (73.2%). These patients had the highest OABSS and OAB-q symptom bother scale scores (9.3 [2.9] and 64.9 [21.0], respectively) and the lowest HRQoL scores (42.3 [24.2]).

Users of combination therapy: Cohorts 2 and 3 contained high proportions of patients from southern geographic regions (43.9% and 54.5%, respectively). Patients in these cohorts had higher education levels (65.9% and 81.8%, respectively, were college graduates or higher) than those who had not received combination therapy. Cohorts 2 and 3 were similar in terms of disease duration (5.5 [4.7] and 5.6 [6.2], respectively).

Treatment decision-making process. Most patients reported being involved in treatment decision-making (86.5%). Of these individuals, most (76.3%) were involved in the decisions to receive a treatment and which treatment to receive (67.1%). This was observed among all cohorts. Of all patients, 13.5% reported no discussion at any time, and most of these patients were in cohort 1. The factor most frequently considered among all cohorts when choosing a treatment was doctor’s recommendation (84.4%). Regarding other factors, users of third-line therapies placed more importance on severity of symptoms than treatment side effects; those who had never used third-line therapies placed more importance on side effects. The treatment decision-making is summarized in Table 2.

Interest in combination therapy. Among patients who had never used combination therapy (cohorts 1 and 4), more patients in cohort 4 were aware of combination

Table 1. Patient demographics, overall and by cohort.

	Total N = 200	Cohort 1 No combo, no third line N = 92	Cohort 2 Combo, no third line N = 41	Cohort 3 Combo, third line N = 11	Cohort 4 Third line, no combo N = 56
Age					
Mean (SD)	53.1 (17.3)	60.1 (14.7)	54.1 (15.4)	48.1 (15.4)	41.9 (17.2)
Median (range)	54 (19–88)	64 (23–88)	54 (20–80)	46 (32–79)	38 (19–79)
Men, n (%)	53 (26.5%)	18 (19.6%)	8 (19.5%)	1 (9.1%)	26 (46.4%)
Geographic region, n (%)¹					
Northeast	39 (19.5%)	20 (21.7%)	4 (9.8%)	1 (9.1%)	14 (25.0%)
Midwest	36 (18.0%)	17 (18.5%)	7 (17.1%)	2 (18.2%)	10 (17.9%)
South	70 (35.0%)	28 (30.4%)	18 (43.9%)	6 (54.5%)	18 (32.1%)
West	55 (27.5%)	27 (29.3%)	12 (29.3%)	2 (18.2%)	14 (25.0%)
Race, n (%)					
White or Caucasian	163 (81.5%)	78 (84.8%)	36 (87.8%)	8 (72.7%)	41 (73.2%)
Black or African American	22 (11.0%)	9 (9.8%)	2 (4.9%)	3 (27.3%)	8 (14.3%)
Asian or Pacific Islander	4 (2.0%)	3 (3.3%)	1 (2.4%)	0 (0.0%)	0 (0.0%)
American Indian or Alaska Native	1 (0.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.8%)
Mixed race	3 (1.5%)	0 (0.0%)	1 (2.4%)	0 (0.0%)	2 (3.6%)
Other	7 (3.5%)	2 (2.2%)	1 (2.4%)	0 (0.0%)	4 (7.1%)
Hispanic ethnicity, n (%)	22 (11.0%)	9 (9.8%)	4 (9.8%)	2 (18.2%)	7 (12.5%)
Level of education, n (%)					
Less than high school	1 (0.5%)	0 (0.0%)	1 (2.4%)	0 (0.0%)	0 (0.0%)
High school diploma or equivalent	25 (12.5%)	15 (16.3%)	4 (9.8%)	0 (0.0%)	6 (10.7%)
Some college or associate degree	62 (31.0%)	32 (34.8%)	9 (22.0%)	2 (18.2%)	19 (33.9%)
College graduate/bachelor's degree	76 (38.0%)	31 (33.7%)	18 (43.9%)	7 (63.6%)	20 (35.7%)
Advanced degree ²	36 (18.0%)	14 (15.2%)	9 (22.0%)	2 (18.2%)	11 (19.6%)
Current employment status, n (%)¹					
Full-time	87 (43.5%)	25 (27.2%)	19 (46.3%)	7 (63.6%)	36 (64.3%)
Retired	61 (30.5%)	42 (45.7%)	10 (24.4%)	3 (27.3%)	6 (10.7%)
Self-employed/homemaker	18 (9.0%)	6 (6.5%)	7 (17.1%)	0 (0.0%)	5 (8.9%)
Part-time	16 (8.0%)	6 (6.5%)	4 (9.8%)	1 (9.1%)	5 (8.9%)

(continued)

Table 1. Continued.

	Total N = 200	Cohort 1 No combo, no third line N = 92	Cohort 2 Combo, no third line N = 41	Cohort 3 Combo, third line N = 11	Cohort 4 Third line, no combo N = 56
Disabled	13 (6.5%)	9 (9.8%)	1 (2.4%)	1 (9.1%)	2 (3.6%)
Unemployed	7 (3.5%)	5 (5.4%)	0 (0.0%)	0 (0.0%)	2 (3.6%)
Student	3 (1.5%)	1 (1.1%)	1 (2.4%)	0 (0.0%)	1 (1.8%)
Current marital status, n (%)					
Married or domestic partnership	113 (56.5%)	49 (53.3%)	23 (56.1%)	5 (45.5%)	36 (64.3%)
Single, never married	47 (23.5%)	18 (19.6%)	12 (29.3%)	2 (18.2%)	15 (26.8%)
Widowed	20 (10.0%)	11 (12.0%)	3 (7.3%)	2 (18.2%)	4 (7.1%)
Divorced	20 (10.0%)	14 (15.2%)	3 (7.3%)	2 (18.2%)	1 (1.8%)
Total household income, n (%)					
Less than \$25,000	24 (12.0%)	17 (18.5%)	2 (4.9%)	1 (9.1%)	4 (7.1%)
\$25,000 to \$49,999	43 (21.5%)	29 (31.5%)	7 (17.1%)	1 (9.1%)	6 (10.7%)
\$50,000 to \$74,999	40 (20.0%)	16 (17.4%)	12 (29.3%)	3 (27.3%)	9 (16.1%)
\$75,000 to \$99,999	44 (22.0%)	12 (13.0%)	13 (31.7%)	3 (27.3%)	16 (28.6%)
\$100,000 to \$149,999	31 (15.5%)	11 (12.0%)	4 (9.8%)	1 (9.1%)	15 (26.8%)
\$150,000 and over	12 (6.0%)	2 (2.2%)	3 (7.3%)	2 (18.2%)	5 (8.9%)
Declined to answer	6 (3.0%)	5 (5.4%)	0 (0.0%)	0 (0.0%)	1 (1.8%)
Current health insurance, n (%) ¹					
Private/commercial insurance	119 (59.5%)	44 (47.8%)	25 (61.0%)	9 (81.8%)	41 (73.2%)
Public insurance	103 (51.5%)	58 (63.0%)	19 (46.3%)	2 (18.2%)	24 (42.9%)
No insurance	3 (1.5%)	2 (2.2%)	0 (0.0%)	0 (0.0%)	1 (1.8%)
Comorbidities, n (%) ^{1,3}					
Urinary tract infection	99 (49.5%)	44 (47.8%)	21 (51.2%)	9 (81.8%)	25 (44.6%)
Hypertension (high blood pressure)	73 (36.5%)	43 (46.7%)	13 (31.7%)	4 (36.4%)	13 (23.2%)
Depression	60 (30.0%)	28 (30.4%)	12 (29.3%)	4 (36.4%)	16 (28.6%)
Diabetes (Type 1 or 2)	52 (26.0%)	19 (20.7%)	10 (24.4%)	5 (45.5%)	18 (32.1%)
Asthma	43 (21.5%)	19 (20.7%)	6 (14.6%)	2 (18.2%)	16 (28.6%)
Obesity	41 (20.5%)	24 (26.1%)	8 (19.5%)	4 (36.4%)	5 (8.9%)
Cancer	24 (12.0%)	10 (10.9%)	7 (17.1%)	1 (9.1%)	6 (10.7%)

(continued)

Table 1. Continued.

		Cohort 1	Cohort 2	Cohort 3	Cohort 4
		No combo, no third line N = 92	Combo, no third line N = 41	Combo, third line N = 11	Third line, no combo N = 56
Total	N = 200				
Autoimmune disease	22 (11.0%)	10 (10.9%)	6 (14.6%)	2 (18.2%)	4 (7.1%)
Chronic obstructive pulmonary disease	19 (9.5%)	14 (15.2%)	3 (7.3%)	1 (9.1%)	1 (1.8%)
Stroke	14 (7.0%)	5 (5.4%)	4 (9.8%)	2 (18.2%)	3 (5.4%)
Inflammatory bowel disease	12 (6.0%)	5 (5.4%)	3 (7.3%)	1 (9.1%)	3 (5.4%)
Time since OAB diagnosis/ symptom onset (in years) ⁴	N = 169	N = 74	N = 36	N = 9	N = 50
Mean (SD)	6.2 (6.9)	7.2 (6.8)	5.5 (4.7)	5.6 (6.2)	5.4 (8.3)
Median (range)	4 (0–54)	5 (1–32)	5 (0–20)	2 (1–17)	3 (1–54)
OABSS (total score) ⁵	N = 200	N = 92	N = 41	N = 11	N = 56
Mean (SD)	8.7 (3.2)	8.8 (3.2)	7.6 (3.6)	9.1 (3.1)	9.3 (2.9)
Median (range)	9 (0–15)	9 (0–14)	7 (1–14)	9 (3–13)	9 (3–15)
OAB-q ⁶	N = 200	N = 92	N = 41	N = 11	N = 56
<i>Symptom bother scale</i>					
Mean (SD)	53.8 (24.8)	49.4 (23.1)	48.6 (29.3)	53.9 (24.2)	64.9 (21.0)
Median (range)	53 (0–100)	48 (0–100)	43 (7–100)	67 (20–83)	67 (13–100)
<i>Total HRQoL scale</i>					
Mean (SD)	54.4 (26.8)	60.7 (24.9)	55.8 (31.3)	58.5 (16.6)	42.3 (24.2)
Median (range)	57 (0–100)	63 (0–100)	62 (0–100)	54 (40–89)	38 (0–98)
First OAB treatment, n (%) ^{7,8}					
Antimuscarinic	133 (66.5%)	69 (75.0%)	18 (43.9%)	5 (45.5%)	41 (73.2%)
Mirabegron monotherapy	39 (19.5%)	21 (22.8%)	11 (26.8%)	4 (36.4%)	3 (5.4%)
Combination therapy	13 (6.5%)	0 (0.0%)	12 (29.3%)	1 (9.1%)	0 (0.0%)
Third-line treatment	15 (7.5%)	0 (0.0%)	0 (0.0%)	1 (9.1%)	14 (25.0%)
Other ⁹	2 (1.0%)	2 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Average time on treatment (in years) ¹⁰					
Antimuscarinic	N = 140	N = 58	N = 25	N = 6	N = 51
Mean (SD)	3.5 (4.4)	4.5 (5.5)	2.8 (3.3)	2.7 (5.3)	2.8 (2.9)
Median (range)	2.21 (0.04–30.00)	2.74 (0.17–30.00)	1.75 (0.04–15.00)	0.55 (0.04–13.50)	1.63 (0.04–13.29)

(continued)

Table 1. Continued.

	Cohort 1	Cohort 2	Cohort 3	Cohort 4
Total	No combo, no third line N = 92	Combo, no third line N = 41	Combo, third line N = 11	Third line, no combo N = 56
Mirabegron monotherapy	N = 64	N = 22	N = 6	N = 6
Mean (SD)	1.7 (1.7)	1.6 (1.8)	0.8 (1.0)	1.2 (1.3)
Median (range)	1.04 (0.04–5.67)	1.02 (0.04–5.17)	0.25 (0.04–2.04)	0.75 (0.04–3.33)
Combination therapy	N = 43	N = 34	N = 9	
Mean (SD)	1.7 (1.8)	1.7 (1.8)	1.7 (1.8)	–
Median (range)	1.08 (0.04–8.00)	1.08 (0.04–8.00)	1.08 (0.04–8.00)	–
Third-line treatment	N = 51		N = 9	N = 42
Mean (SD)	2.0 (2.6)	–	1.3 (1.8)	2.2 (2.7)
Median (range)	1.25 (0.04–13.21)	–	0.42 (0.04–5.67)	1.33 (0.04–13.21)

HRQL, health-related quality of life; OAB, overactive bladder; OAB-q, overactive bladder questionnaire; OABSS, overactive bladder symptom score; SD, standard deviation. Notes: [1] Patients could select multiple options. [2] Advanced degree included master's degree, professional degree beyond undergraduate, and doctoral degree. [3] Other comorbidity responses included irritable bowel syndrome, diverticulitis, myasthenia gravis, gastroesophageal reflux disease, sleep apnea, osteoporosis, hypothyroidism, traumatic brain injury, fibromyalgia, essential shakes, dry eye and hydrocephalus. [4] Patients were able to select "I don't remember the month or the year" or "I don't remember the month" to avoid collecting biased responses if patients could not accurately report time. [5] The OABSS quantifies OAB symptom severity as a single composite score ranging from 0 to 15, where a higher score represents more severe OAB. [6] The OAB-q takes into account both symptom bother and HRQL. Responses are transformed into a score ranging from 0 to 100. Higher scores represent either greater symptom bother or better HRQL, respectively. [7] A patient may be on multiple antimuscarinics or an antimuscarinic and third-line treatment concurrently, so the total sum across treatments may exceed the count of unique patients. If a patient selected both combination therapy and an antimuscarinic, they were not counted in the antimuscarinics category. [8] Two patients reported receiving antimuscarinics and peripheral tibial nerve stimulation concurrently as their first OAB treatments. [9] Other responses included desmopressin and amitriptyline (Elavil), a tricyclic antidepressant. [10] For antimuscarinics and third-line treatment, time on treatment was calculated as the average across all treatments the patient selected in that class. Patients could select "I don't remember how long I took the treatment" if they could not accurately report treatment duration. Durations were then summarized by treatment class among patients who reported at least one treatment duration in that class.

Table 2. Patient treatment decision drivers.

	Cohort 1 No combo, no third line N = 92	Cohort 2 Combo, no third line N = 41	Cohort 3 Combo, third line N = 11	Cohort 4 Third line, no combo N = 56
Total	N = 200			
Physician discussed treatment options with patient, n (%)	91 (45.5%)	16 (39.0%)	5 (45.5%)	27 (48.2%)
When starting treatment only	9 (4.5%)	0 (0.0%)	3 (27.3%)	2 (3.6%)
When switching treatment only	73 (36.5%)	23 (56.1%)	3 (27.3%)	25 (44.6%)
When starting and switching treatments	27 (13.5%)	2 (4.9%)	0 (0.0%)	2 (3.6%)
No discussion	N = 173	N = 34	N = 11	N = 53
<i>Patient involved in at least one OAB treatment decision¹</i>				
Type of OAB treatment decisions involved, n (%) ²				
Whether to receive a treatment	132 (76.3%)	26 (76.5%)	8 (72.7%)	39 (73.6%)
Which treatment to receive	116 (67.1%)	25 (73.5%)	7 (63.6%)	32 (60.4%)
Whether to change treatments	83 (48.0%)	19 (55.9%)	5 (45.5%)	24 (45.3%)
Whether to continue or stop receiving a treatment	71 (41.0%)	18 (52.9%)	5 (45.5%)	20 (37.7%)
Whether to add a treatment to the current ones	62 (35.8%)	21 (61.8%)	5 (45.5%)	20 (37.7%)
Key factors patient considered when choosing OAB treatments, n (%) ²				
Doctor's recommendation	146 (84.4%)	28 (82.4%)	10 (90.9%)	48 (90.6%)
Effectiveness of treatment	124 (71.7%)	28 (82.4%)	8 (72.7%)	31 (58.5%)
Side effects of treatment	114 (65.9%)	24 (70.6%)	7 (63.6%)	26 (49.1%)
Severity of symptoms	94 (54.3%)	19 (55.9%)	8 (72.7%)	34 (64.2%)
Cost / insurance coverage	87 (50.3%)	19 (55.9%)	6 (54.5%)	20 (37.7%)
Route of administration	75 (43.4%)	15 (44.1%)	6 (54.5%)	16 (30.2%)
Treatment frequency	72 (41.6%)	12 (35.3%)	7 (63.6%)	20 (37.7%)
Interactions with other medical treatments	68 (39.3%)	15 (44.1%)	5 (45.5%)	11 (20.8%)
Location of treatment	51 (29.5%)	12 (35.3%)	3 (27.3%)	15 (28.3%)
Interruption to daily life owing to treatment	47 (27.2%)	11 (32.4%)	4 (36.4%)	13 (24.5%)
Past treatment experience	45 (26.0%)	8 (23.5%)	4 (36.4%)	17 (32.1%)
Other patients' feedback on the treatment	18 (10.4%)	3 (8.8%)	1 (9.1%)	6 (11.3%)
Other	1 (0.6%)	0 (0.0%)	0 (0.0%)	1 (1.9%)

OAB, overactive bladder.

Notes: [1] The 27 patients who responded that they were not involved in their OAB treatment decisions were not asked about what treatment decisions they were involved in or what factors they considered when choosing an OAB treatment, as the questions were not applicable. [2] Patients could select multiple options.

therapy than patients in cohort 1 (57.1% versus 12.0%, respectively). More patients in cohort 4 reported that they would consider combination therapy (73.2% versus 46.7% for cohort 1). Among patients in cohort 1 who were aware of combination therapy but had not tried it, the primary reason was side effects (63.6%). In cohort 4, the primary reason was that their physician had recommended a different treatment (78.1%). Participants' interest in combination therapy is summarized in Table 3.

Patient satisfaction with combination therapy.

Among users of combination therapy (cohorts 2 and 3), most reported satisfaction with their regimen (63.5% were at least somewhat satisfied), and 71.4% planned to continue therapy. Among patients in cohort 3 who were not fully satisfied, the primary reason was lack of efficacy (66.7%). Among those in cohort 2 who were not fully satisfied, the primary reason was cost (34.6%).

Overall, most patients who had discontinued combination therapy reported that the reason for their decision was a doctor's recommendation (41.7%). A total of 45.8% of patients were unsure whether they would try it again. Satisfaction with combination therapy is summarized in Table 4.

Physicians

Demographics. Most physicians were in private practice (44.0%) and were men (96.0%); the mean years of practice was 15.0 (9.2) years. Physicians who reported that they did not prescribe combination therapy (n = 15, 30.0%) were slightly older than those who did (51.4 versus 47.4 years) and a larger proportion worked in academic settings (46.7% versus 25.7%). Physician demographics are shown in Table 5.

Treatment experience. In the year preceding the survey, physicians who prescribed combination therapy ("prescribers") saw a higher mean (SD) number of patients (351 [251]) than those who did not ("non-prescribers") (177 [134]). Overall, the factors most frequently considered when prescribing OAB treatments were effectiveness (92.0%) and side effects (84.0%). Compared with non-prescribers, more prescribers considered clinical guidelines, cost and patient feedback. Most stated that they always or often discussed treatment options with their patients when they started a new treatment (82.0% overall; 85.8% of prescribers; 73.3% of non-prescribers). More non-prescribers versus prescribers recommended switching when treatments caused side effects (93.3% versus 68.6%, respectively). Physicians' treatment experience is summarized in Table 6.

Decision drivers behind prescribing combination therapy. Among prescribers, the main reason for prescribing combination therapy was patients' symptom severity (82.9%). When the decision was made not to prescribe combination therapy, the main reason was cost/insurance coverage (77.1%). Among non-prescribers, the main reason for not prescribing was cost of therapy/insurance coverage (80.0%), followed by lack of information about combination therapy (53.3%). However, most physicians were willing to consider prescribing combination therapy in the future after failure of monotherapy (86.7%). Decision drivers are summarized in Tables 7 and 8.

Physician experience with combination therapy. Prescribers reported prescribing combination therapy to an average of 18.8% (SD 11.1%) of OAB patients (Table 7). Most indicated that they would consider prescribing it after monotherapy (88.6%). However, 82.8% reported having prescribed a third-line therapy before

Table 3. Patient interest in combination therapy.

	Total	Cohort 1 No combo, no third line	Cohort 4 Third line, no combo
Patient would consider trying combination therapy, n (%)	N = 148	N = 92	N = 56
Yes	84 (56.8%)	43 (46.7%)	41 (73.2%)
No	19 (12.8%)	11 (12.0%)	8 (14.3%)
Unsure	45 (30.4%)	38 (41.3%)	7 (12.5%)
Patients were previously aware of combination therapy, n (%)	N = 148	N = 92	N = 56
Yes	43 (29.1%)	11 (12.0%)	32 (57.1%)
No	105 (70.9%)	81 (88.0%)	24 (42.9%)
<i>Patients with prior awareness of combination therapy</i> ¹	N = 43	N = 11	N = 32
Key reasons for not having tried combination therapy in the past, n (%) ²			
Doctor recommended a different treatment	30 (69.8%)	5 (45.5%)	25 (78.1%)
Side effects	17 (39.5%)	7 (63.6%)	10 (31.3%)
Cost/insurance coverage	14 (32.6%)	2 (18.2%)	12 (37.5%)
Lack of information	13 (30.2%)	4 (36.4%)	9 (28.1%)
Number of pills	12 (27.9%)	3 (27.3%)	9 (28.1%)
Interactions with other medical treatments	11 (25.6%)	2 (18.2%)	9 (28.1%)
Having to receive treatment once a day	10 (23.3%)	0 (0.0%)	10 (31.3%)
Lack of efficacy	6 (14.0%)	0 (0.0%)	6 (18.8%)
Other patients' feedback on the treatment	6 (14.0%)	1 (9.1%)	5 (15.6%)
Interruption to daily life owing to treatment	5 (11.6%)	0 (0.0%)	5 (15.6%)
<i>Patients not willing to try combination therapy</i> ³	N = 12	N = 6	N = 6
Key reasons for unwillingness to try combination therapy, n (%) ²			
Side effects	6 (50.0%)	5 (83.3%)	1 (16.7%)
Doctor recommended a different treatment	5 (41.7%)	0 (0.0%)	5 (83.3%)
Lack of information	3 (25.0%)	1 (16.7%)	2 (33.3%)
Interactions with other medical treatments	2 (16.7%)	0 (0.0%)	2 (33.3%)
Lack of efficacy	2 (16.7%)	0 (0.0%)	2 (33.3%)
Interruption to daily life owing to treatment	2 (16.7%)	1 (16.7%)	1 (16.7%)
Other patients' feedback on the treatment	2 (16.7%)	1 (16.7%)	1 (16.7%)
Having to receive treatment once a day	1 (8.3%)	0 (0.0%)	1 (16.7%)
Number of pills	1 (8.3%)	0 (0.0%)	1 (16.7%)
Cost/insurance coverage	1 (8.3%)	1 (16.7%)	0 (0.0%)
Other	1 (8.3%)	1 (16.7%)	0 (0.0%)

Notes: [1] Forty-three patients who had not received combination therapy in the past (in cohorts 1 and 4) were aware of combination therapy prior to the survey. They were asked about their key reasons for not having tried combination therapy before. [2] Patients could select multiple options. [3] Of the 43 patients mentioned above, 12 patients were unwilling or unsure about trying combination therapy in the future. They were asked about their reasons for not being willing to try combination therapy.

combination therapy; 72.4% reported that this decision was driven by patient preference/input. Regarding satisfaction with combination therapy, 71.4% of prescribers

were very or somewhat satisfied. Among those who were not very satisfied, the primary reason was cost/insurance coverage (72.7%). However, most prescribers were

Table 4. Patient satisfaction with combination therapy.

	Total N = 52	Cohort 2 Combo, no third line N = 41	Cohort 3 Combo, third line N = 11
Antimuscarinic(s) taken in combination with Myrbetriq, n (%)¹			
Ditropan [®] /Ditropan [®] XL (oxybutynin)	18 (34.6%)	13 (31.7%)	5 (45.5%)
Detrol [®] /Detrol [®] LA (tolterodine)	13 (25.0%)	11 (26.8%)	2 (18.2%)
VESIcare [®] (solifenacin)	12 (23.1%)	10 (24.4%)	2 (18.2%)
Enblex [®] (darifenacin)	11 (21.2%)	9 (22.0%)	2 (18.2%)
Oxytrol [®] (oxybutynin topical)	8 (15.4%)	3 (7.3%)	5 (45.5%)
Toviaz [®] (fesoterodine)	4 (7.7%)	4 (9.8%)	0 (0.0%)
Sanctura [®] (trospium)	2 (3.8%)	1 (2.4%)	1 (9.1%)
Satisfaction with combination therapy, n (%)			
	N = 52	N = 41	N = 11
Very satisfied	20 (38.5%)	15 (36.6%)	5 (45.5%)
Somewhat satisfied	13 (25.0%)	13 (31.7%)	0 (0.0%)
Neither satisfied nor dissatisfied	10 (19.2%)	8 (19.5%)	2 (18.2%)
Somewhat dissatisfied	5 (9.6%)	5 (12.2%)	0 (0.0%)
Very dissatisfied	4 (7.7%)	0 (0.0%)	4 (36.4%)
Patients not fully satisfied with combination therapy²			
	N = 32	N = 26	N = 6
Reasons for dissatisfaction¹			
Lack of efficacy	10 (31.3%)	6 (23.1%)	4 (66.7%)
Cost / insurance coverage of combination therapy	9 (28.1%)	9 (34.6%)	0 (0.0%)
Side effects	6 (18.8%)	5 (19.2%)	1 (16.7%)
Interactions with other treatments	5 (15.6%)	4 (15.4%)	1 (16.7%)
Interruption to daily life owing to treatment	4 (12.5%)	4 (15.4%)	0 (0.0%)
Having to receive treatment once a day	2 (6.3%)	2 (7.7%)	0 (0.0%)
Number of pills	2 (6.3%)	2 (7.7%)	0 (0.0%)
Other	3 (9.4%)	3 (11.5%)	0 (0.0%)
Patients currently taking combination therapy³			
	N = 28	N = 24	N = 4
Patient plans to continue combination therapy			
Yes	20 (71.4%)	16 (66.7%)	4 (100.0%)
No	2 (7.1%)	2 (8.3%)	0 (0.0%)
Unsure	6 (21.4%)	6 (25.0%)	0 (0.0%)
Patients not currently taking combination therapy⁴			
	N = 24	N = 17	N = 7
Key reasons for discontinuing combination therapy, n (%)¹			
Doctor's recommendation	10 (41.7%)	7 (41.2%)	3 (42.9%)
Lack of efficacy	9 (37.5%)	7 (41.2%)	2 (28.6%)
Side effects	9 (37.5%)	6 (35.3%)	3 (42.9%)
Cost / insurance coverage of combination therapy	6 (25.0%)	6 (35.3%)	0 (0.0%)
Interactions with other treatments	5 (20.8%)	4 (23.5%)	1 (14.3%)
Other patients' feedback on combination therapy	3 (12.5%)	2 (11.8%)	1 (14.3%)
Interruption to daily life owing to treatment	2 (8.3%)	1 (5.9%)	1 (14.3%)
Improved OAB symptoms	2 (8.3%)	0 (0.0%)	2 (28.6%)
Number of pills	1 (4.2%)	1 (5.9%)	0 (0.0%)
Having to receive treatment once a day	2 (8.3%)	1 (5.9%)	1 (14.3%)
Other	2 (8.3%)	1 (5.9%)	1 (14.3%)

(continued)

Table 4. Continued.

	Total N = 52	Cohort 2 Combo, no third line N = 41	Cohort 3 Combo, third line N = 11
Patient would consider trying combination therapy again, n (%)	N = 24	N = 17	N = 7
Yes	5 (20.8%)	3 (17.6%)	2 (28.6%)
No	8 (33.3%)	6 (35.3%)	2 (28.6%)
Unsure	11 (45.8%)	8 (47.1%)	3 (42.9%)
Treatment used after discontinuing combination therapy, n (%) ¹	N = 24	N = 17	N = 7
Antimuscarinic	13 (54.2%)	8 (47.1%)	5 (71.4%)
Mirabegron monotherapy	11 (45.8%)	10 (58.8%)	1 (14.3%)
Third-line treatment	2 (8.3%)	–	2 (28.6%)
Did not switch to another treatment	0 (0.0%)	0 (0.0%)	0 (0.0%)

OAB, overactive bladder.

Notes: [1] Patients could select multiple options. [2] The 20 patients who responded that they were very satisfied with combination therapy were not asked about their reasons for dissatisfaction with combination therapy, as the question was not applicable. [3] Of the patients who had received or were currently receiving combination therapy (cohorts 2 and 3), 28 were currently receiving combination therapy. These patients were asked about whether or not they planned to discontinue combination therapy. [4] Of the patients who had received or were currently receiving combination therapy (cohorts 2 and 3), 24 were not currently receiving combination therapy. These patients were asked about their reasons for discontinuing combination therapy, whether or not they would consider trying combination therapy again, and about what treatment they used after discontinuing combination therapy.

willing to continue prescribing combination therapy (94.3%).

Prescribers reported that the average proportion of patients who discontinued combination therapy was 35.9% (18.7%), and that the primary reasons for discontinuation were lack of efficacy and cost/insurance coverage (each 79.4%). Prescribers reported that among patients who switched to another treatment (26.6%), most switched to a third-line therapy (94.1%). Physicians' experience with combination therapy is summarized in Table 9.

Discussion

Results for both patients and physicians indicated that treatment decisions were guided by shared decision-making, with most consideration given to treatment safety and efficacy. Physician recommendation

was of primary importance to patients. Most physicians prescribed combination therapy, primarily for severity of symptoms. Among those who did not prescribe combination therapy, the primary reasons were cost/insurance coverage and lack of information. Overall, these findings are congruent with research that has demonstrated the importance to OAB patients of treatment safety and tolerability. A previous discrete choice experiment found that although OAB patients valued symptom reduction, treatment preferences were heavily influenced by safety and tolerability.¹⁹ Likewise, in a survey of 5,392 OAB patients, 46% and 21% of those who discontinued treatment with antimuscarinics indicated that the primary reasons were treatment effectiveness and safety, respectively.²⁰

Patients in cohorts 1 and 4, who had never received combination therapy, had

Table 5. Physician demographics.

	All physicians N = 50	Prescribed combination therapy	
		Yes N = 35	No N = 15
Age, in years			
Mean (SD)	48.6 (12.6)	47.4 (11.6)	51.4 (14.9)
Median (range)	46 (30–88)	45 (30–75)	47 (37–88)
Men, n (%)	48 (96.0%)	34 (97.1%)	14 (93.3%)
Geographic region, n (%)			
Northeast	16 (32.0%)	12 (34.3%)	4 (26.7%)
Midwest	8 (16.0%)	6 (17.1%)	2 (13.3%)
South	12 (24.0%)	10 (28.6%)	2 (13.3%)
West	14 (28.0%)	7 (20.0%)	7 (46.7%)
Specialty, n (%)			
Urologist	48 (96.0%)	34 (97.1%)	14 (93.3%)
Urogynecologist	2 (4.0%)	1 (2.9%)	1 (6.7%)
Years of practice as a urologist or urogynecologist			
Mean (SD)	15.0 (9.2)	14.9 (8.8)	15.3 (10.5)
Median (range)	13 (4–40)	14 (4–30)	11 (4–40)
Practice setting, n (%)			
Academic institution	16 (32.0%)	9 (25.7%)	7 (46.7%)
Non-academic hospital or health system	11 (22.0%)	9 (25.7%)	2 (13.3%)
Public or government institution	1 (2.0%)	0 (0.0%)	1 (6.7%)
Private practice ¹	22 (44.0%)	17 (48.6%)	5 (33.3%)
Solo practice	1 (2.0%)	0 (0.0%)	1 (6.7%)
Small group	13 (26.0%)	12 (34.3%)	1 (6.7%)
Medium group	7 (14.0%)	5 (14.3%)	2 (13.3%)
Large group	1 (2.0%)	0 (0.0%)	1 (6.7%)

SD, standard deviation.

Notes: [1] Private practice group sizes are defined as follows: Small group: less than 10 physicians; Medium group: between 10 and 49 physicians; Large group: 50 or more physicians.

different characteristics. Cohort 1 contained patients with the highest mean age and the highest percentage of retired individuals. Priorities among this group when selecting an OAB treatment were minimizing side effects; most were not aware of combination therapy and unwilling to try it owing to concerns about side effects. Cohort 4 (users of third-line therapies) was primarily composed of younger individuals with full-time employment whose treatment selection was driven by symptom severity. Most were willing to try

combination therapy but had not because their doctors had recommended different treatments. As there is some evidence that use of certain third-line procedural therapies may be driven by provider incentives,¹⁰ future research should examine whether these incentives appreciably influence treatment decision-making and subsequent treatment patterns.

Most patients who did not receive combination therapy were unaware of it, and/or were interested in trying it. Similarly, most physicians who did not currently prescribe

Table 6. Physician treatment experience.

	All physicians N = 50	Prescribed combination therapy	
		Yes N = 35	No N = 15
OAB patients seen by physician in the past year			
Mean (SD)	299 (235)	351 (251)	177 (134)
Median (range)	220 (35–950)	250 (40–950)	150 (35–500)
Main factors physician considers when prescribing OAB treatments, n (%) ¹	N = 50	N = 35	N = 15
Effectiveness of treatment	46 (92.0%)	32 (91.4%)	14 (93.3%)
Side effects of treatment	42 (84.0%)	30 (85.7%)	12 (80.0%)
Prior experience treating other OAB patients	42 (84.0%)	30 (85.7%)	12 (80.0%)
Severity of patient OAB symptoms	40 (80.0%)	27 (77.1%)	13 (86.7%)
Patient treatment history	39 (78.0%)	27 (77.1%)	12 (80.0%)
Clinical guidelines	37 (74.0%)	29 (82.9%)	8 (53.3%)
Cost / insurance coverage	37 (74.0%)	27 (77.1%)	10 (66.7%)
Patient contraindications	36 (72.0%)	25 (71.4%)	11 (73.3%)
Patient comorbidities	35 (70.0%)	24 (68.6%)	11 (73.3%)
Route of administration	34 (68.0%)	22 (62.9%)	12 (80.0%)
Patient input / preference	30 (60.0%)	21 (60.0%)	9 (60.0%)
Feedback from other patients on the treatment	30 (60.0%)	24 (68.6%)	6 (40.0%)
Patient demographics	28 (56.0%)	21 (60.0%)	7 (46.7%)
Treatment frequency	28 (56.0%)	17 (48.6%)	11 (73.3%)
Patient disease history	27 (54.0%)	18 (51.4%)	9 (60.0%)
Recommendations from colleagues	21 (42.0%)	16 (45.7%)	5 (33.3%)
Location of treatment	17 (34.0%)	12 (34.3%)	5 (33.3%)
Physician discusses multiple treatment options and their benefits/risks with patients	N = 50	N = 35	N = 15
When patients start treatment, n (%)			
Always	27 (54.0%)	22 (62.9%)	5 (33.3%)
Often	14 (28.0%)	8 (22.9%)	6 (40.0%)
Sometimes	8 (16.0%)	4 (11.4%)	4 (26.7%)
Rarely	1 (2.0%)	1 (2.9%)	0 (0.0%)
Never	0 (0.0%)	0 (0.0%)	0 (0.0%)
When patients switch treatments, n (%)			
Always	30 (60.0%)	22 (62.9%)	8 (53.3%)
Often	16 (32.0%)	10 (28.6%)	6 (40.0%)
Sometimes	4 (8.0%)	3 (8.6%)	1 (6.7%)
Rarely	0 (0.0%)	0 (0.0%)	0 (0.0%)
Never	0 (0.0%)	0 (0.0%)	0 (0.0%)
Situations in which physician recommends a patient to switch treatments, n (%) ¹	N = 50	N = 35	N = 15
When current treatment(s) are not effective or not effective enough	43 (86.0%)	30 (85.7%)	13 (86.7%)

(continued)

Table 6. Continued.

	All physicians N = 50	Prescribed combination therapy	
		Yes	No
		N = 35	N = 15
When current treatment(s) cause side effects	38 (76.0%)	24 (68.6%)	14 (93.3%)
When patients express their preference for alternative treatments	36 (72.0%)	30 (85.7%)	6 (40.0%)
When patients' symptoms worsen	34 (68.0%)	24 (68.6%)	10 (66.7%)
When treatment(s) are no longer affordable/ there is a less costly alternative	31 (62.0%)	22 (62.9%)	9 (60.0%)
When test results show no underlying causes or complications	10 (20.0%)	7 (20.0%)	3 (20.0%)

OAB, overactive bladder; SD, standard deviation.

Notes: [1] Physicians could select multiple options.

combination therapy were willing to prescribe it in the future. Increasing awareness about combination therapy among both patients and physicians who prescribe for OAB may increase OAB treatment options for some patients, particularly those who have discontinued other treatments owing to safety and/or efficacy reasons. Notably, in the present study, the level of symptom bother was highest and the HRQoL was lowest among patients who had used third-line treatment but had never used combination therapy. Thus, the level of awareness of combination therapies among both patients and physicians should be further explored, particularly if increasing awareness could help to address unmet treatment needs.

There were some limitations regarding the study design, sample size and data availability. Regarding study design, participants were a convenience sample of patients and physicians, which may have introduced selection bias. This could potentially account for the observation that the mean duration of antimuscarinic therapy was higher across all four cohorts (3.5 years overall) than the average time

reported in the literature, which indicates that the study sample may be more persistent and adherent regarding their OAB therapies than patients in the general population.⁶ Therefore, the results may have limited generalizability to the general OAB population and/or practicing physicians. The small sample size (overall and particularly within some cohorts) may also reduce the generalizability of results; recruitment challenges precluded achievement of the target study sample size of equal patients per cohort, particularly in cohort 3. Furthermore, the relatively small number of physicians who were aware of combination therapy but did not prescribe it (n = 15, 30%) may not reflect the actual proportion. Finally, the potential presence of recall bias among patients who had discontinued their most recent OAB treatment may have affected the accuracy of the findings.

Regarding data availability, the number of variables of interest far exceeded what is measurable in a single study of this nature. Thus, this study did not capture all of the complexities related to treatment selection, including factors related to insurance coverage, access to care, adherence and quality

Table 7. Combination therapy decision drivers among physicians who prescribe combination therapy.

	Physicians who prescribe combination therapy
	N = 35
Proportion (%) of OAB patients prescribed combination therapy, reported by physicians	
Among their own OAB patients	
Mean (SD)	18.8% (11.1%)
Median (range)	20.0% (5%–70%)
Among patients managed by other urologists/urogynecologists	
Mean (SD)	19.3% (15.8%)
Median (range)	15.0% (2%–80%)
Antimuscarinic drug(s) typically prescribed with Myrbetriq [®] , n (%) ¹	N = 35
VESicare (solifenacin)	23 (65.7%)
Ditropan/Ditropan XL (oxybutynin)	21 (60.0%)
Detrol/Detrol LA (tolterodine)	12 (34.3%)
Sanctura (trospium)	12 (34.3%)
Toviaz (fesoterodine)	6 (17.1%)
Enablex (darifenacin)	5 (14.3%)
Main reasons physician prescribes combination therapy, n (%) ¹	N = 35
Severity of patient OAB symptoms	29 (82.9%)
Prior experience with combination therapy	27 (77.1%)
Patient comorbidities	26 (74.3%)
Improved efficacy	26 (74.3%)
Patient treatment history	24 (68.6%)
Feedback from other patients on combination therapy	23 (65.7%)
Cost of combination therapy/insurance coverage	22 (62.9%)
Clinical guidelines	21 (60.0%)
Safety profile of combination therapy	21 (60.0%)
Patient contraindications	20 (57.1%)
Patient input/preference	19 (54.3%)
Route of administration	17 (48.6%)
Patient disease history	16 (45.7%)
Patient demographics	16 (45.7%)
Availability of free Myrbetriq samples	14 (40.0%)
Recommendations from colleagues	12 (34.3%)
Location of treatment	8 (22.9%)
Main reasons for physician NOT to prescribe combination therapy to some patients, n (%) ¹	N = 35
Cost of combination therapy/insurance coverage	27 (77.1%)
Patient contraindications	23 (65.7%)
Side effects of combination therapy	23 (65.7%)
Patient comorbidities	19 (54.3%)
Patient input/preference	15 (42.9%)
Treatment burden	14 (40.0%)
Severity of patient OAB symptoms	14 (40.0%)
Prior experience with combination therapy	14 (40.0%)

(continued)

Table 7. Continued.

	Physicians who prescribe combination therapy
	N = 35
Patient treatment history	10 (28.6%)
Lack of efficacy	10 (28.6%)
Patient disease history	9 (25.7%)
Patient demographics	9 (25.7%)
Feedback from other patients on combination therapy	9 (25.7%)
Recommendations from colleagues	7 (20.0%)
Key characteristics of patients prescribed combination therapy, as reported by physicians, n (%) ¹	N = 35
More severe OAB symptoms	28 (80.0%)
Symptoms not under control after monotherapy treatment	27 (77.1%)
Had insurance covering combination therapy/can afford combination therapy	21 (60.0%)
Prefers pills over invasive procedures	19 (54.3%)
Younger age	10 (28.6%)
Active lifestyle	8 (22.9%)
Other ²	1 (2.9%)
No common key characteristics or treatment histories	1 (2.9%)

OAB, overactive bladder; SD, standard deviation.

Notes: [1] Physicians could select multiple options. [2] The other common key characteristic was patients being able to tolerate the side effects of anticholinergics.

Table 8. Combination therapy decision drivers among physicians who have never prescribed combination therapy.

Physicians who have never prescribed combination therapy	N = 15
Reasons for physician never prescribing combination therapy, n (%) ¹	
Cost of combination therapy/insurance coverage	12 (80.0%)
Lack of information about combination therapy	8 (53.3%)
Treatment burden	7 (46.7%)
Patient input/preference	6 (40.0%)
Patient contraindications	6 (40.0%)
Safety profile of combination therapy	5 (33.3%)
Patient comorbidities	5 (33.3%)
Patient demographics	5 (33.3%)
Severity of patient OAB symptoms	4 (26.7%)
Lack of efficacy	4 (26.7%)
Patient disease history	3 (20.0%)
Feedback from other patients on combination therapy	3 (20.0%)
Recommendations from colleagues	2 (13.3%)

(continued)

Table 8. Continued.

Willingness to consider prescribing combination therapy after the failure of pharmacological monotherapies, n (%)	N = 15
Yes	13 (86.7%)
No	0 (0.0%)
Not sure	2 (13.3%)
Willingness to consider prescribing combination therapy after the failure of both pharmacological monotherapies <u>and</u> third-line treatments, n (%)	N = 15
Yes	10 (66.7%)
No	0 (0.0%)
Not sure	5 (33.3%)

OAB, overactive bladder.

Notes: [1] Physicians could select multiple options.

Table 9. Physician experience with combination therapy.

	Physicians who prescribe combination therapy
	N = 35
Point at which physician considers prescribing combination therapy, n (%) ¹	
As first-line treatment	1 (2.9%)
Before pharmacologic monotherapy	1 (2.9%)
After pharmacologic monotherapy	31 (88.6%)
Before third-line treatment	24 (68.6%)
After third-line treatment	4 (11.4%)
Number of physicians prescribing third-line treatment before combination therapy ²	N = 35
Always	4 (11.4%)
Often	9 (25.7%)
Sometimes	13 (37.1%)
Rarely	3 (8.6%)
Never	6 (17.1%)
Among physicians who ever prescribed third-line treatment before combination therapy ³	N = 29 (82.8%)
Reasons for prescribing third-line treatment before combination therapy, n (%) ¹	
Patient preference/input	21 (72.4%)
Severity of patient OAB symptoms	19 (65.5%)
Adverse events associated with combination therapy	16 (55.2%)
Lack of efficacy of other therapies	16 (55.2%)
Prior experience using third-line treatments and combination therapy	15 (51.7%)
Patient contraindications	14 (48.3%)
Cost of combination therapy/insurance coverage	14 (48.3%)

(continued)

Table 9. Continued.

	Physicians who prescribe combination therapy
	N = 35
Patient comorbidities	13 (44.8%)
Patient treatment history	13 (44.8%)
Feedback from other patients on third-line treatments and combination therapy	11 (37.9%)
Recommendations from colleagues	9 (31.0%)
Treatment burden of combination therapy	8 (27.6%)
Patient disease history	7 (24.1%)
Location of treatment	5 (17.2%)
Patient demographics	5 (17.2%)
Physician satisfaction with combination therapy, n (%)	
Very satisfied	2 (5.7%)
Somewhat satisfied	23 (65.7%)
Neither satisfied nor dissatisfied	7 (20.0%)
Somewhat dissatisfied	3 (8.6%)
Very dissatisfied	0 (0.0%)
<i>Among physicians not very satisfied with combination therapy⁴</i>	N = 33
Reasons for physician not being very satisfied, n (%) ¹	
Cost of combination therapy/insurance coverage	24 (72.7%)
Lack of efficacy	19 (57.6%)
Adverse events	11 (33.3%)
Worse combination therapy adherence among patients	10 (30.3%)
Patient contraindications	10 (30.3%)
Patient feedback	6 (18.2%)
Worse behavioral modification adherence among patients	2 (6.1%)
Physician willingness to continue prescribing combination therapy in the future, n (%)	N = 35
Yes	33 (94.3%)
No	1 (2.9%)
Not sure	1 (2.9%)
Physician-reported proportion (%) of patients who discontinued combination therapy	N = 35
Mean (SD)	35.9% (18.7%)
Median (range)	35.0% (0%–90%)
<i>Among physicians with at least one patient who discontinued combination therapy⁵</i>	N = 34
Reasons for discontinuation of combination therapy, n (%) ¹	
Lack of efficacy	27 (79.4%)
Cost of combination therapy/insurance coverage	27 (79.4%)
Adverse events	17 (50.0%)
Treatment burden	12 (35.3%)
Patient comorbidities	7 (20.6%)
Patient contraindications	7 (20.6%)
Improved OAB symptoms	3 (8.8%)

(continued)

Table 9. Continued.

	Physicians who prescribe combination therapy
	N = 35
Physician-reported proportion (%) of patients who switched from combination therapy to another treatment	N = 35
Mean (SD)	26.6% (15.1%)
Median (range)	25.0% (0%–50%)
Treatments patients switched to after discontinuing combination therapy, n (%) ¹	
Third-line treatment	32 (94.1%)
More aggressive behavioral modification/pelvic floor rehabilitation	12 (35.3%)
Pharmacologic monotherapy	7 (20.6%)

OAB, overactive bladder; SD, standard deviation.

Notes: [1] Physicians could select multiple options. [2] Third-line treatments include treatments such as Botox, sacral neuromodulation and percutaneous tibial nerve stimulation. [3] The six physicians who had never prescribed a third-line treatment before combination therapy were not asked about reasons for prescribing a third-line treatment before combination therapy. [4] The two physicians who had responded that they were very satisfied with combination therapy were not asked about their reasons for not being very satisfied with combination therapy. [5] The one physician who reported that 0% of their patients discontinued combination therapy was not asked about reasons for discontinuation.

of care. Indeed, cohorts 3 and 4 contained the highest proportion of individuals with private insurance, as well as the highest income, which may be important determinants of the receipt of third-line therapy. Additionally, this study did not measure the effect of efforts to improve treatment adherence among some patients. Indeed, the emergence and uptake of tools to promote treatment behaviors among patients may result in a shift of current practice patterns.²¹ Finally, this study did not explore the effect of patient health, including comorbidities and concurrent medications, on reported treatment history and decisions. These factors are important considerations, particularly in light of studies such as that by Kilinc et al., who found that the incidence of severe coronary artery disease was substantially higher among older patients with OAB symptoms.²² Thus, future efforts should attempt to obtain more detailed information regarding the factors that affect treatment decision-making,

via qualitative interview methods and larger-scale survey administration within the clinic setting.

Conclusions

Findings from this study indicate that combination therapy (where it is indicated) may address some of the unmet needs related to the therapeutic management of OAB. However, the ability of combination therapy to address these needs is potentially hindered by a lack of awareness among both OAB-treating physicians and patients, which was identified in this study. As awareness of combination therapy increases and use becomes more widespread, real-world evidence will be needed to examine its associated adherence/persistence, as well as its effect on OAB-related outcomes and costs.

Availability of data and materials

The data that support the findings of this study are available from Analysis Group, Inc., but

restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. However, data are available from the authors upon reasonable request and with permission of Analysis Group, Inc.

Researchers may request access to anonymized participant level data, trial level data and protocols from Astellas sponsored clinical trials at www.clinicalstudydatarequest.com. For the Astellas criteria on data sharing see <https://clinicalstudydatarequest.com/Study-Sponsors/Study-Sponsors-Astellas.aspx>

Author contributions

JL, HY and MZ conducted and performed the analysis. All authors contributed to the drafting or revision of the manuscript and have read and approved the final version of this submitted manuscript, and all authors fulfill the ICMJE guidelines for authorship.

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Supplemental material

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