


Vesomni improves the quality of life in men with lower urinary tract symptoms in routine clinical practice in Europe

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Abstract

Aim: To evaluate the impact of Vesomni/Urizia/Volutsa, a fixed-dose combination tablet containing 6 mg solifenacin (antimuscarinic) and 0.4 mg tamsulosin (α -blocker), on health-related quality of life (HRQoL) and treatment satisfaction in men with lower urinary tract symptoms (LUTS) associated with benign prostatic hyperplasia (BPH) in routine clinical practice.

Methods: EUROPA was a noninterventional study of men with LUTS/BPH not responding to monotherapy who were prescribed Vesomni in routine clinical practice. Data were collected retrospectively (1 year) and prospectively (1 year). Assessments were performed at baseline, weeks 4 to 8, weeks 9 to 18 (optional), weeks 19 to 39 (optional), and Weeks 40 to 52. The primary endpoint was change from baseline in HRQoL, as assessed by the Overactive Bladder Questionnaire (OAB-q) symptom bother subscale score. Change from baseline in OAB-q total and coping, sleep, and social interaction subscale scores, treatment satisfaction-visual analog scale (TS-VAS), International Prostate Symptom Score (IPSS), and European Quality of Life 5-Dimension-5-Level (EQ-5D-5L) questionnaire were also evaluated.

Results: Five hundred and eighty-nine patients were enrolled. The mean changes in adjusted mean (95% confidence interval [CI]) OAB-q symptom bother subscale scores were -16.40 ($-24.31, -8.49$) at weeks 4 to 8 and -19.59 ($-28.26, -10.92$) at weeks 40 to 52; at weeks 40 to 52, changes were clinically meaningful in 84.6% of patients. Adjusted mean (95% CI) change from baseline to weeks 40 to 52 were 15.02 (7.35, 22.69), 19.37 (10.86, 27.89), 18.65 (7.44, 29.86), 9.85 (3.90, 15.81), and 16.09 (9.07, 23.11) for concern, coping, sleep, social interaction, and total, respectively. TS-VAS, IPSS, and EQ-5D-5L all improved, and treatment persistence at weeks 40 to 52 was 77.1%. Urinary retention was reported in four (0.7%) patients.

Conclusions: Vesomni was well-tolerated and improved HRQoL and treatment satisfaction in patients with LUTS/BPH.

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KEYWORDS

benign prostatic hyperplasia, Europe, lower urinary tract symptoms, male, quality of life, treatment satisfaction, Vesomni

1 | INTRODUCTION

Lower urinary tract symptoms (LUTS) is a term describing storage, voiding, and postmicturition symptoms associated with urination.¹ The global prevalence of LUTS has been estimated to range from 14.8% among men aged 40 to 49 years to 38.4% among men aged ≥ 80 years.² Notably, nearly half of the men with LUTS report both storage and voiding symptoms.³ Although the underlying pathophysiology of LUTS has not been fully elucidated, changes in both prostate and bladder physiology have been implicated. For instance, benign prostatic hyperplasia (BPH) may lead to benign prostatic obstruction (BPO) and compensatory changes in bladder detrusor muscle.⁴

Although not generally life-threatening, LUTS are associated with reduced health-related quality of life (HRQoL), as well as anxiety, depression, insomnia, and sexual dysfunction and dissatisfaction.⁴ Despite the bother associated with LUTS and the availability of medications, this condition is often underdiagnosed and undertreated, and treatment adherence is often low.^{5,6} In Europe, 19% of men with LUTS seek treatment and 10.2% receive medications.⁷ Men with voiding or mixed voiding/storage LUTS typically receive α -blocker monotherapy as first-line pharmacological treatment (and/or 5 α -reductase inhibitors in those with an enlarged prostate).^{8,9} However, many patients with LUTS do not achieve sufficient symptom relief with monotherapy. Approximately two-thirds of men with mixed voiding/storage LUTS do not adequately respond to α -blocker monotherapy and may require combination therapy with an antimuscarinic to treat residual storage symptoms.^{8,10} Despite this, the use of antimuscarinics in men with mixed symptoms is less than 15% and many remain suboptimally treated.⁶

Vesomni/Urizia/Volutsa is a fixed-dose combination (FDC) tablet containing 6 mg solifenacin (antimuscarinic) and 0.4 mg tamsulosin (α -blocker) indicated for the treatment of moderate-to-severe storage and voiding symptoms associated with BPH in patients not adequately responding to monotherapy.¹¹ The efficacy of Vesomni (FDC of solifenacin 6 mg+tamsulosin 0.4 mg or FDC of solifenacin 9 mg+tamsulosin 0.4 mg) has been demonstrated in the NEPTUNE study, where men with storage and voiding LUTS had a significant reduction in total International Prostate Symptom Score (IPSS) and total urgency and frequency scores compared with tamsulosin

monotherapy and placebo¹²; the improvements were maintained for up to 52 weeks in the NEPTUNE II open-label extension.¹³ Furthermore, a retrospective study conducted in the Netherlands revealed that among men with LUTS/BPH, treatment persistence was significantly higher among those who received FDC compared with those receiving an α -blocker plus an antimuscarinic.¹⁴ However, because NEPTUNE was a randomized controlled trial and therefore restricted in patient population, intervention, and timing of assessments, the results may not represent the true impact of combination treatment in real-world clinical practice. The real-world evaluation of combination therapy with an α -blocker and an antimuscarinic in men with LUTS is not well documented in Europe. EUROPA was a 1-year real-world study of men with LUTS/BPH who were not adequately responding to monotherapy and had been prescribed Vesomni as part of routine clinical practice in Europe.

2 | MATERIALS AND METHODS

2.1 | Study design, patients, and setting

EUROPA was a prospective, noninterventional study conducted at 48 sites in Belgium, Czech Republic, Portugal, Slovenia, Spain, and the United Kingdom. Men with LUTS/BPH who were not responding to monotherapy with an α -blocker and/or 5 α -reductase inhibitor (5-ARI) and who were prescribed Vesomni once daily as part of routine clinical practice were invited to participate. Patients with hypersensitivity to the excipients in Vesomni were excluded. For patients who had received a LUTS/BPH diagnosis ≥ 1 year before informed consent was signed, medical and surgical history, physical examinations, previous medications, and any medical history relevant to LUTS/BPH were collected retrospectively for 1 year before informed consent was signed; for patients who had received a LUTS/BPH diagnosis < 1 year before informed consent was signed, retrospective data were collected from the date of diagnosis. Patients who were prescribed Vesomni once daily were followed for 1 year; assessments were performed during routine clinic visits at baseline (visit 1), weeks 4 to 8 (visit 2), weeks 9 to 18 (visit 3, optional), weeks 19 to 39 (visit 4, optional), and weeks 40 to 52 (visit 5, end of study visit). Because this was a noninterventional and noncontrolled study designed to collect real-life patient data during their routine visits to

TABLE 1 Derivation of symptom bother subscale score, HRQoL subscale, and total Scores

Subscale	Sum item values	Lowest, highest possible raw scores	Possible raw score range
Symptom bother	1 to 8	8, 48	40
HRQoL - coping	9 + 11 + 16 + 21 + 22 + 26 + 32 + 33	8, 48	40
HRQoL - concern	12 + 13 + 14 + 19 + 23 + 25 + 29	7, 42	35
HRQoL - sleep	10 + 15 + 17 + 24 + 30	5, 30	25
HRQoL - social	18 + 20 + 27 + 28 + 31	5, 30	25
HRQoL - total	Sum of HRQoL subscales	25, 150	125
Subscale	Transformed score formula	Interpretation of the transformed Score	
Symptom bother*	$\frac{(Actual\ raw\ score - lowest\ possible\ raw\ score)}{Possible\ raw\ score\ range} \times 100$	100 is the worst severity. A negative change from baseline indicates an improvement.	
HRQoL - coping	$\frac{(Highest\ possible\ score - Actual\ raw\ score)}{Possible\ raw\ score\ range} \times 100$	A higher HRQoL score indicates a better quality of life. A positive change from baseline indicates improvement	
HRQoL - concern			
HRQoL - sleep			
HRQoL - social			
HRQoL - total			

Abbreviation: HRQoL, health-related quality of life.

*Symptom bother subscale score was used to assess HRQoL.

the clinic, prespecified scheduling of clinic visits was not mandated. The time points of primary interest were weeks 4 to 8 (visit 2) and weeks 40 to 52 (visit 5).

2.2 | Endpoints

The primary endpoint was the change from baseline in HRQoL as assessed by the Overactive Bladder Questionnaire (OAB-q)¹⁵ symptom bother subscale score. Secondary outcomes included change from baseline in OAB-q HRQoL total score and the HRQoL subscales of concern, coping, sleep, and social interaction; change from baseline in treatment satisfaction-visual analog scale (TS-VAS), symptom severity as measured by IPSS,¹⁶ and health status via the visual analog scale (EQ-VAS) component of the European Quality of Life 5-Dimension-5-Level (EQ-5D-5L) questionnaire¹⁷; changes in treatment patterns including adherence (number of Vesomni tablets taken during the previous 5 days), persistence (proportion of patients who had not permanently discontinued treatment of reasons other than study completion), discontinuation, and switching patterns; summary of healthcare resource utilization for LUTS/BPH management; and incidence of treatment-emergent adverse events (TEAEs).

2.3 | Assessments

Patients completed electronic patient-reported outcome (ePRO) questionnaires on-site at baseline and either on-site or remotely within each visit window for visits 2 to 5. Medical and surgical history, previous medications related to LUTS, and retrospective data for LUTS/BPH

symptoms (IPSS total, storage, and voiding) were collected at baseline. Physical examination and urology assessment results were obtained retrospectively and performed at each visit as part of the site's routine clinical practice. Healthcare resource utilization was recorded at baseline and at each after the visit. The symptom bother subscale of the OAB-q included questions 1 to 8 with scores ranging from 1 to 6 (1, "not at all" to 6, "a very great deal"), whereas the concern, coping, sleep, and social interaction subscales included questions 9 to 33 with scores ranging from 1 to 6 (1, "none of the time" to 6, "all of the time"). All OAB-q scores were transcribed to a scale of 0 to 100 as described in Table 1. The EQ-5D-5L was used to evaluate health status using the EQ-VAS component on a scale of 0 to 100 (0, "the worst health you can imagine" to 100, "the best health you can imagine"). The TS-VAS was rated on a scale ranging from 0 to 100 (0, "no, not at all" to 100, "yes, completely"). The IPSS questionnaire was used to evaluate symptoms, with total scores ranging from 0 to 35 (0, "none" to 35, "severe"), and one question related to HRQoL (IPSS-QoL; 0, "delighted" to 6, "terrible").

2.4 | Statistical analyses

Based on a confidence interval (CI) approach, we calculated that 590 patients would be required to describe HRQoL (OAB-q symptom bother subscale score) with sufficient precision. This was determined to assume a standard deviation (SD) of 15.66, based on a previous study of tamsulosin/solifenacin (0.4 mg/6 mg),^{12,13} and choosing a precision of 2 for the HRQoL observed mean. Based on these assumptions, a minimum of 236 patients

was calculated. Considering a rate of persistence up to 12 months of 40%, enrollment of 590 patients was required to guarantee at least 236 patients at the end of the study.

Demographic and baseline characteristics were reported using descriptive statistics. The full analysis set (FAS) comprised all patients who had an OAB-q symptom bother subscale score at baseline and at least one postbaseline visit and was used for all analyses except for safety. Safety analysis was conducted using the safety analysis set (SAF), comprising all patients who received at least one dose of Vesomni. Safety was analyzed by monitoring TEAEs, which were coded according to the MedDRA Version 17.1. Descriptive statistics were used to report OAB-q symptom bother subscale scores at each study visits, as well as changes from baseline (95% CI). An analysis of covariance (ANCOVA) model was used as the primary method to assess changes from baseline for the OAB-q symptom bother subscale score. Baseline OAB-q symptom bother subscale score was included as a covariate, and baseline incontinence and baseline prescription status were included as fixed factors in the ANCOVA model. Descriptive statistics were used for all secondary HRQoL endpoints, and 95% CI were calculated for changes from baseline. Treatment adherence was reported in the ePRO and was reported using descriptive statistics. A 10-point improvement in any OAB-q subscale score and a 3-point improvement in total IPSS score were considered clinically meaningful; a 0.5-point improvement in IPSS-QoL was considered the minimal clinically important difference.^{18,19}

3 | RESULTS

3.1 | Patients disposition

Of 589 patients enrolled in the study, 575 (97.6%) and 493 (83.7%) were included in the SAF and FAS populations, respectively; 91 patients (15.8%) discontinued due to withdrawal by patient ($n = 23$ [4.0%]), lost to follow-up ($n = 21$ [3.7%]), adverse event ($n = 16$ [2.8%]), other ($n = 16$ [2.8%]), lack of efficacy ($n = 9$ [1.6%]), death ($n = 4$ [0.7%]), and protocol deviation ($n = 2$ [0.3%]). Demographics and baseline characteristics are summarized in Table 2.

3.2 | Efficacy results

Improvements in mean (SD) OAB-q symptom bother subscale scores were observed at weeks 4 to 8 (-17.4 [17.7]), weeks 9 to 18 (-17.2 [18.1]), and weeks 40 to 52 (-20.4 [19.1]; Figure 1A). At weeks 40 to 52, this difference was clinically meaningful (≥ 10 points) in 84.6% of patients. Adjusted least squares mean (95% CI) changes (ANCOVA analysis) from baseline in OAB-q symptom bother subscale scores were -16.40 (-24.31 , -8.49) at

weeks 4 to 8 and -19.59 (-28.26 , -10.92) at weeks 40 to 52. Improvements in concern, coping, and sleep subscales were also achieved (Figure 1B). Adjusted least squares mean (95% CI) change from baseline to weeks 40 to 52 was 15.02 (7.35, 22.69) for concern, 19.37 (10.86, 27.89) for coping, 18.65 (7.44, 29.86) for sleep, 9.85 (3.90, 15.81) for social interaction, and 16.09 (9.07, 23.11) for OAB-q HRQoL total score. At weeks 40 to 52, clinically meaningful improvements (≥ 10 point) in OAB-q HRQoL total score and in the concern, coping, sleep, and social interaction subscale scores were observed in 65.7%, 60.8%, 67.3%, 68.9%, and 40.3% of patients, respectively.

Treatment satisfaction improved by weeks 4 to 8 and continued improving throughout the study (Table 3); adjusted least squares mean (95% CI) change (ANCOVA analysis) from baseline was 12.85 (-3.06 , 28.77) at weeks 4 to 8 and 37.76 (22.31, 53.20) at weeks 40 to 52. Health status (EQ-VAS) also improved from baseline (Table 3) and continued improving to the end of the study; adjusted least squares mean (95% CI) change (ANCOVA analysis) from baseline was 4.96 (-4.19 , 14.11) at weeks 4 to 8 and 7.24 (-1.24 , 15.72) at weeks 40 to 52. Improvements on all dimensions of the EQ-5D-5L were observed. The proportion of patients reporting “no problems” increased from baseline to Weeks 40 to 52.

Improvements in IPSS were observed throughout the study. Adjusted mean (95% CI) change (ANCOVA analysis) from baseline to weeks 40 to 52 occurred in the total IPSS (-5.40 [-8.77 , -2.02]), IPSS voiding (-2.19 [-4.40 , 0.01]), IPSS storage (-3.10 [-4.75 , -1.46]), and IPSS-QoL (-1.46 [-2.22 , -0.69]). Clinically meaningful improvements occurred in total IPSS (≥ 3 -point), IPSS storage (≥ 3 -point), and IPSS-QoL (≥ 0.5 -point) scores (Figure 2).

Furthermore, at baseline, 29.1%, 17.0%, 5.5%, and 54.0% of patients with available data reported daytime micturition frequency of < 8 , fewer than two nocturia episodes per night, no urgency episodes, and no urgency incontinence episodes, respectively, whereas by weeks 40 to 52, these proportions increased to 73.2%, 58.1%, 44.6%, and 75.6%, respectively.

Treatment persistence was high throughout the study; 380 (77.1%) patients continued Vesomni to the end of study visit (weeks 40 to 52). Treatment adherence did not substantially vary throughout the study. Healthcare resource use was low across all categories; one patient had an additional hospital visit due to storage symptoms. The mean (SD) number of incontinence pads used in the 7 days preceding each visit were 0.9 (3.5) at baseline, 0.5 (2.8) at weeks 19 to 39 and 0.5 (2.2) at weeks 40 to 52.

3.3 | Safety results

A total of 195/575 (33.9%) patients reported 383 adverse events during the study; 373 were TEAEs. Among them,

TABLE 2 Demographics and baseline characteristics

Parameter	Full analysis set (n = 493)
Age, y	
n	493
Mean (SD)	65.0 (10.4)
Range	29-89
Age group, y, n (%)	
< 65	216 (43.8)
≥ 65 to < 75	195 (39.6)
≥ 75	82 (16.6)
Race, n (%)	
Caucasian	453 (91.9)
Asian	3 (0.6)
Not collected	37 (7.5)
Weight, kg	
n	415
Mean (SD)	87.39 (14.29)
Median	85.00
Range	58.0-150.0
Height, cm	
n	415
Mean (SD)	175.36 (6.98)
Median	176.00
Range	149.0-198.0
BMI, kg/m ²	
n	415
Mean (SD)	28.39 (4.08)
Median	27.70
Range	19.5-41.8
Postvoid residual volume, mL	
n	184
Mean (SD)	36.4 (50.3)
Median	20.0
Range	0-350
Prostate size, mL	
n	367
Mean (SD)	36.3 (16.8)
Median	35.0
Range	0-100
Prostate size group, mL, n (%)	
< 40	200 (54.5)
≥ 40	167 (45.5)
Not done	126 (25.5)
Baseline IPSS total	
n	485
Mean (SD)	15.7 (6.3)
Median	15.0
Range	1-35
Baseline IPSS total group, n (%)	
0-7	41 (8.4)
8-19	316 (64.8)
20-35	128 (26.2)
Not done	3 (0.6)
Lost to follow-up	5 (1.0)

(Continues)

TABLE 2 (Continued)

Parameter	Full analysis set (n = 493)
Baseline IPSS storage	
n	485
Mean (SD)	8.0 (3.1)
Median	8.0
Range	1-15
Baseline IPSS voiding	
n	485
Mean (SD)	7.7 (4.6)
Median	7.0
Range	0-20
Baseline OAB-q symptom bother score	
n	493
Mean (SD)	42.3 (17.6)
Median	40.0
Range	3-100
Baseline prescription status, n (%)	
Add-on to monotherapy ¹	74 (16.9)
Switched ²	363 (82.7)
Add-on to combination therapy ³	2 (0.5)
Not done	54 (10.9)
Baseline incontinence status, n (%)	
Incontinent	138 (31.7)
Continent	297 (68.3)
Not done	58 (11.8)

Abbreviations: BMI, body mass index; IPSS, International Prostate Symptom Score; OAB-q, Overactive Bladder Questionnaire; SD, standard deviation.

¹Patients who had Vesomni added to their original monotherapy with an α -blocker or 5-ARI.

²Patients who were switched to Vesomni from their original monotherapy with an α -blocker or 5-ARI.

³Patients who had Vesomni added to their original treatment with an α -blocker and 5-ARI monotherapy.

133 (23.1%) experienced 219 Vesomni-related TEAEs. The most common Vesomni-related TEAEs were dry mouth (n = 41, 7.1%), constipation (n = 27, 4.7%), dyspepsia (n = 13, 2.3%), and blurred vision (n = 9, 1.6%). Lack of efficacy of Vesomni was reported in 18 (3.1%) patients. Overall, the proportion of patients who reported mild, moderate, and severe Vesomni-related TEAEs was 16.0%, 5.9%, and 1.2%, respectively. A total of 25 (4.3%) patients experienced 34 serious TEAEs. Among them, 21 (3.7%) experienced 29 serious TEAEs that were emergent to Vesomni. Three patients experienced serious TEAEs (dysuria, n = 1; tachycardia, n = 1; blurred vision, n = 1) that were possibly or probably related to Vesomni. None of the serious TEAEs required corrective treatment and all resolved upon discontinuation of Vesomni. Of 100 (17.4%) patients who reported TEAEs leading to permanent discontinuation of

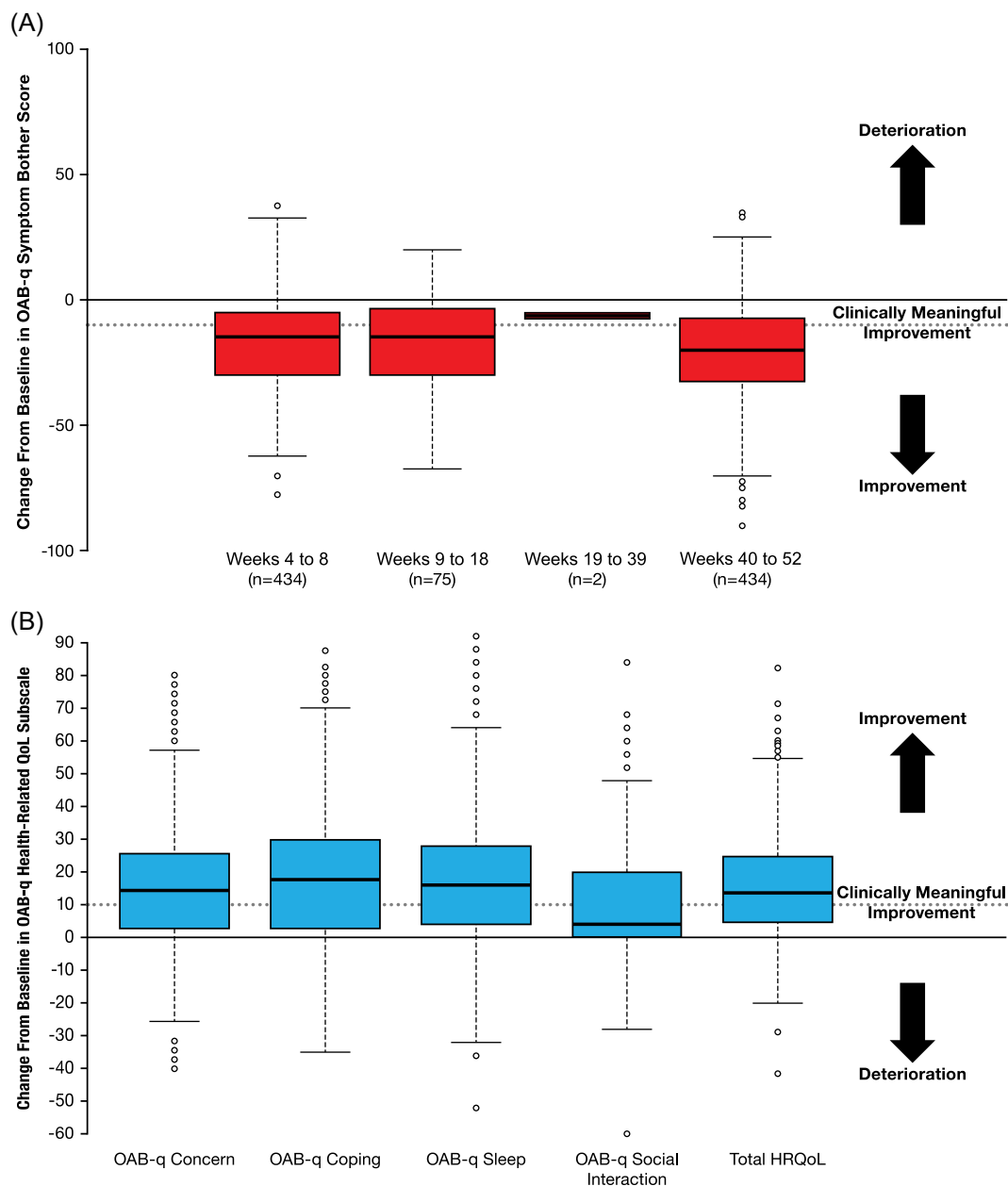


FIGURE 1 OAB-q symptom bother subscale scores (A) and OAB-q HRQoL total and subscale scores at end of study (B). Boxplots depict the median and interquartile range (box), range (whiskers), and outliers (circles). HRQoL, health-related quality of life; OAB-q, Overactive Bladder Questionnaire [Color figure can be viewed at wileyonlinelibrary.com]

TABLE 3 Treatment satisfaction and EQ-VAS scores

Treatment satisfaction				EQ-VAS		
Time point	N	Mean (SD)	Mean (SD) change from baseline	N	Mean (SD)	Mean (SD) change from baseline
Baseline	484	42.0 (28.0)	...	483	66.3 (17.5)	...
Weeks 4 to 8	415	64.9 (24.9)	22.8 (34.9)	414	72.7 (15.6)	6.0 (17.4)
Weeks 40 to 52	425	72.0 (24.0)	30.5 (34.3)	422	75.9 (14.1)	9.5 (17.9)

Abbreviations: EQ-VAS, health status via the visual analog scale; SD, standard deviation.

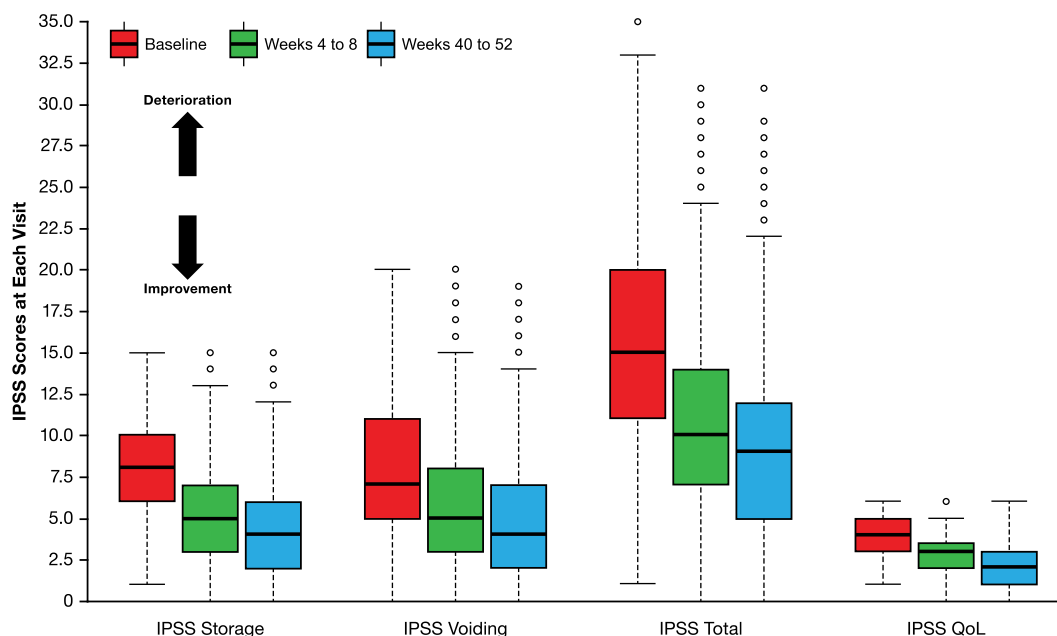


FIGURE 2 IPSS scores at each visit. Boxplots depict the median and interquartile range (box), range (whiskers), and outliers (circles). IPSS, International Prostate Symptom Score; QoL, quality of life [Color figure can be viewed at wileyonlinelibrary.com]

Vesomni, 82 (14.3%) experienced 109 Vesomni-related TEAEs. Urinary retention (UR) was considered a TEAE of special interest and was reported in four (0.7%) patients. All of these cases of UR were considered to be related to Vesomni. Two UR cases were reported as moderate incomplete bladder emptying and did not result in catheterization or permanent discontinuation of Vesomni. The other two UR cases resulted in catheterization and discontinuation of Vesomni. One of these was reported as mild chronic UR after the patient had been on Vesomni for 121 days. On the day the event was reported, Vesomni was discontinued due to UR and the patient was catheterized (for 30 days). The patient was switched to dutasteride/tamsulosin combination therapy and treated for a urinary tract infection (UTI) with ciprofloxacin. The second case of catheterization was reported as moderate UR after the patient had been on Vesomni for 29 days. On the day the event was reported, the patient was treated for a UTI with trimethoprim/sulfamethoxazole. Four days later, the patient discontinued Vesomni due to the UR event, switched to tamsulosin monotherapy, and was catheterized for 10 days. The UR lasted for 62 days, during which the patient was treated further for UTI using cefuroxime followed by ciprofloxacin. Four deaths were reported during the study, none of which were related to Vesomni; three patients died while on Vesomni due to unknown reasons ($n = 2$) or respiratory failure ($n = 1$), and one died of an unknown cause 28 days after Vesomni treatment had ended.

4 | DISCUSSION

LUTS/BPH represent a significant health issue in aging men and can negatively impact the HRQoL of patients and their families.⁴ Nevertheless, LUTS/BPH is largely underdiagnosed and undertreated. Monotherapy with α -blockers and 5-ARIs are among the currently available medications that can improve HRQoL by relieving urinary symptoms; 5-ARIs are also effective in reducing the risk of complications associated with BPH.²⁰ However, since α -blockers and 5-ARIs predominantly improve voiding symptoms, add-on therapy with an antimuscarinic is often required to relieve residual storage symptoms.²¹ The efficacy of α -blockers in combination with antimuscarinics has been demonstrated in numerous clinical trials conducted in different countries, including some European countries.^{14,22} The current European guidelines on the management of LUTS recommend the combination of an α -blocker and antimuscarinics in patients with moderate-to-severe LUTS whose storage symptoms do not improve with monotherapy.⁸ EUROPA is the first large-scale report of a treatment benefit of Vesomni in routine clinical practice. These real-world data demonstrate that, in most patients (> 80%), once daily Vesomni yields clinically meaningful improvements in HRQoL and symptom severity as early as 1 to 2 months after initiation. Furthermore, treatment satisfaction and patient-reported health status were also improved. These results are consistent with those observed in clinical trial settings that demonstrated improvements in clinical outcomes and HRQoL with Vesomni.^{12,21,23}

An important finding from EUROPA was the high persistence rate. At the end of the study (weeks 40 to 52), 77.1% of men were still taking Vesomni, and treatment adherence was consistently high throughout the study. The persistence rate observed in this study is higher than that observed in previous studies where patients received monotherapy with α -blockers and antimuscarinics.^{5,6,24} Although specific reasons for discontinuation of treatment were not captured in EUROPA, it is possible that the lower number of daily pills prescribed to patients treated with Vesomni may have contributed to the higher persistence rate observed in this study compared with previous studies. This notion was based on a study of Dutch men aged ≥ 45 years that reported a longer median time to treatment discontinuation (414 vs 112 days; adjusted hazard ratio, 2.04; $P < 0.0001$) and a higher persistence at 12 months (51.3% vs 29.9%) with an FDC of an α -blocker and an antimuscarinic than with free combination therapy.¹⁴

Another important finding from EUROPA is the safety profile of Vesomni. The addition of an antimuscarinic to α -blocker therapy in patients with BPO has historically raised concerns of acute UR.⁹ In an analysis of men participating in the NEPTUNE I and II studies, UR was reported in 13 (1.1%) patients and AUR was reported in 8 (0.7%) patients when treated with FDC solifenacin/tamsulosin for up to 52 weeks.²⁵ In EUROPA, despite nearly half of the patients having an enlarged prostate (≥ 40 mL), the rate of UR was low. Even though postvoid residual (PVR) volume assessments were not mandated and were conducted in 184 out of 493 patients (37%), only four cases of UR (0.7%) were reported. This finding, the first report of the incidence of UR associated with Vesomni in routine clinical practice, demonstrates that Vesomni is associated with a low risk of UR in men with LUTS/BPH. This provides support for the conclusion that primary care physicians may prescribe an α -blocker and an antimuscarinic to men with LUTS even when PVR assessments are not available, provided that patients are not suffering significant untreated voiding or postmicturition symptoms, in which case prior assessment of PVR may be necessary. The adverse event profile in EUROPA is consistent with previous findings.^{12,13} Importantly, the rate of serious drug-related TEAEs after 1 year of treatment with Vesomni was slightly lower in EUROPA (0.5%) than in patients who completed NEPTUNE I and entered NEPTUNE II (1.1%).¹³

EUROPA provides important real-world data on routine clinical situations for patients with LUTS/BPH. However, the noncontrolled design of EUROPA has some limitations. EUROPA enrolled patients with LUTS/BPH who were prescribed Vesomni because of inadequate response to monotherapy. However, specific criteria for

LUTS/BPH diagnosis and symptom severity were not applied; therefore, patients were not stratified by symptom severity. Since the number of tablets taken was patient-reported, an overestimation of treatment adherence cannot be completely ruled out. Another possible limitation is that EUROPA was conducted in multiple countries, and therefore the results may not be generalizable to other regions with different treatment patterns. Despite these limitations, the data reported herein confirm the results of previous randomized controlled studies showing that Vesomni is effective in the treatment of LUTS/BPH, and demonstrate a comparable safety profile.


5 | CONCLUSION

Treatment with Vesomni yielded clinically meaningful improvements in OAB-q symptom bother in $> 80\%$ of patients with LUTS/BPH, a high treatment persistence (77% at weeks 40 to 52), and a low risk of UR. These results support the use of Vesomni in men with LUTS/BPH who are not adequately responding to monotherapy in Europe.

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