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Efficacy and Safety of Vibegron for the Treatment of Overactive Bladder in Women: A Subgroup Analysis From the Double-Blind, Randomized, Controlled EMPOWUR Trial

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Author affiliations, Conflicts of Interest, and article information are provided at the end of this article.

Importance The international phase 3 EMPOWUR trial demonstrated efficacy and safety of vibegron, a newer β_3-adrenergic receptor agonist, in adults with overactive bladder (OAB). Women are disproportionately affected by OAB, especially those with bothersome symptoms, such as urge urinary incontinence (UUI).

Objective This subgroup analysis from EMPOWUR assessed efficacy and safety of vibegron in women.

Study Design In EMPOWUR, patients with OAB were randomized 5:5:4 to 12 weeks of treatment with once-daily vibegron 75 mg, placebo, or tolterodine 4-mg extended release. Efficacy end points included change from baseline at week 12 in mean daily number of micturitions, UUI episodes, and urgency episodes. Safety was assessed through adverse events (AEs).

Results Of the patients included in the analysis, 1286 (84.9%) were women (vibegron, n = 463; placebo, n = 459; tolterodine, n = 364). At week 12, women receiving vibegron showed significant reductions (95% confidence intervals of least squares mean differences does not include 0) from baseline versus placebo in mean daily micturitions, UUI episodes, and urgency episodes, with least squares mean differences (95% confidence intervals) of −0.5 (−0.8 to −0.2), −0.7 (−1.0 to −0.4), and −0.8 (−1.3 to −0.4), respectively. Treatment-emergent AE incidence was similar with vibegron (39%) and placebo (35%); the most common AE with incidence higher with vibegron (4.3%) than placebo (2.6%) was headache.

Conclusions In this subgroup analysis, women receiving vibegron showed significant reductions in key efficacy end points versus placebo and favorable safety profile, consistent with the overall results from EMPOWUR, suggesting that vibegron is efficacious and safe for the treatment of OAB in this patient population.

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WHY THIS MATTERS

Anticholinergics are commonly used and can be effective in the treatment of overactive bladder (OAB); however, long-term use is of concern because of the associated elevated risk of dementia and falls or fractures. The prevalence of anticholinergic burden is greater in women compared with men, as is the rate of falls among older women (≥65 years) with urge urinary incontinence (UUI). In the EMPOWUR trial, treatment with the β_3-adrenergic receptor agonist vibegron for 12 weeks was shown to be safe and efficacious in the treatment of OAB. In this prespecified subgroup analysis of women with OAB, patients receiving vibegron showed significant reductions from baseline versus placebo in mean daily micturitions, UUI episodes, and urgency episodes. In addition, significant improvements in quality-of-life measures, the OAB questionnaire and Patient Global Impression, scores were seen. Results were consistent with the overall EMPOWUR trial. The frequency of treatment-emergent adverse events with vibegron was similar to placebo (39% and 35%, respectively), including hypertension (1.9% and 1.7%, respectively), and to the overall EMPOWUR trial. The significant improvements in OAB symptoms observed in this analysis suggest that vibegron may be a beneficial and safe treatment option among women with OAB.

Overactive bladder (OAB) is a chronic disorder characterized by the sudden, intense urge to urinate, with or without urge urinary incontinence (UUI), usually accompanied by frequency and nocturia.[1] While the overall prevalence of OAB in the United States is similar between women and men (17% and 16%, respectively), women are

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disproportionately affected by one of the most bothersome symptoms, namely UUI, compared with men.[2,3] Moreover, the prevalence of OAB with UUI increases with age at a greater rate in women compared with men (P<0.0001).[3] As such, a higher percentage of women than men with OAB report experiencing symptoms of UUI and/or urinary urgency at least sometimes (43.1% vs 27.2%, respectively) or often (32.6% vs 15.8%).[4] In addition, women with OAB with or without UUI have significantly decreased scores in measures of quality of life (QoL), depression, sexual function, and quality of sleep compared with individuals without OAB.[3,5]

Behavioral therapies (eg, pelvic floor muscle exercises and bladder training), alone or in combination with pharmacotherapy, are recommended as first-line treatment in managing symptoms of OAB.[1] Recommended second-line treatments include anticholinergics and β_3-adrenergic receptor agonists. Anticholinergics are commonly prescribed for the treatment of OAB and are more likely to be prescribed for women than for men.[6,7] However, their use is associated with persistence-limiting side effects.[1,8] Accumulating evidence suggests that long-term use of anticholinergics increases the risk of developing cognitive impairment and dementia.[9–12] For this reason, the American Urogynecologic Society recommends consideration of alternative medications such as β_3-adrenergic receptor agonists for all patients as well as avoidance of anticholinergics to treat OAB in women older than 70 years.[13]

Vibegron is a selective β_3-adrenergic receptor agonist approved in 2020 in the United States for the treatment of adult patients with OAB.[14,15] In the international, randomized, double-blind, placebo- and active-controlled, phase 3 EMPOWUR trial, vibegron for 12 weeks showed efficacy and was safe and well tolerated among adults with OAB.[16] Patients who received vibegron demonstrated significant improvements from baseline in micturitions, UUI episodes, and urgency episodes versus placebo (P<0.01 each).[16] Furthermore, vibegron showed significantly greater improvements versus placebo at week 12 in OAB questionnaire (OAB-q) scores and Patient Global Impression (PGI) scores (P<0.001 each).[17] Given the disproportionate bother and prevalence of symptoms of OAB experienced by women, as well as the greater impact on QoL, we performed these subgroup analyses of the EMPOWUR trial to assess the efficacy, QoL outcomes, and safety of 12 weeks of treatment with vibegron in women from the EMPOWUR trial.

METHODS

Study Design

EMPOWUR (NCT03492281) was a phase 3, 12-week, double-blind, placebo- and active (tolterodine)-controlled trial of vibegron in adults with OAB. Detailed methods have been previously reported.[16] Briefly, the trial enrolled adults 18 years or older with a history of OAB for ≥3 months before the screening visit who met prespecified criteria for OAB wet or dry (ie, with or without UUI, respectively). Patients completed a 24-hour voiding diary for 7 days before baseline and the weeks 2, 4, 8, and 12 study visits. Patients completed the OAB-q at baseline and at week 12 and the PGI subscales at baseline and at weeks 4, 8, and 12. Criteria for OAB wet included an average of ≥8 micturitions and ≥1 UUI episode per day based on the 7-day patient voiding diary at baseline; criteria for OAB dry included an average of ≥8 micturitions, ≥3 urgency episodes, and <1 UUI episode per day based on the 7-day patient voiding diary at baseline. After a 2-week, single-blind (patient), placebo run-in period, participants were randomly assigned 5:5:4 to receive once-daily vibegron 75 mg, placebo, or tolterodine 4 mg extended release (active control), respectively, for 12 weeks. Randomization occurred via stratification by sex (male, female) and by OAB type (wet, dry).

The EMPOWUR trial was performed in accordance with International Conference on Harmonisation of Technical Requirements for Pharmaceuticals for Human Use Good Clinical Practice. Investigators received institutional review board, research ethics board, or independent ethics committee approval. All patients provided written informed consent.

Outcomes

The coprimary efficacy end points were change from baseline at week 12 in mean daily number of micturitions and UUI episodes (prespecified subgroup analysis in women). A key secondary efficacy end point was change from baseline at week 12 in mean daily number of urgency episodes (post hoc subgroup analysis in women). Exploratory outcomes included change from baseline at weeks 2, 4, and 8 in mean daily number of micturitions, UUI episodes, and urgency episodes. The QoL outcomes included changes from baseline at week 12 in OAB-q and PGI subscales (severity, control, frequency, leakage, and change; post hoc subgroup analysis). Details regarding the QoL outcomes have

been previously reported.[17] Safety (post hoc subgroup analysis) was assessed through adverse events (AEs), clinical laboratory assessments, and postvoid residual urine volume.

Statistical Analyses

The full analysis set (FAS), which included all randomized women who received ≥1 dose of the double-blind study drug and had ≥1 evaluable change from baseline measurement for micturitions, was used for analysis of micturitions, urgency episodes, and QoL outcomes not related to incontinence. The FAS for incontinence included all randomized women with OAB wet at baseline (based on randomized stratification into OAB wet) who received ≥1 dose of the double-blind study drug and had ≥1 evaluable change from baseline measurement for UUI episodes and was used for analysis of UUI episodes and QoL outcomes related to incontinence. Safety was assessed in the safety set, which included all randomized women who received ≥1 dose of the double-blind study drug.

In analyzing the subgroup of women, the statistical methods used in the original EMPOWUR trial were used for these analyses to maintain consistency. A mixed model for repeated measures (MMRM) with restricted maximum likelihood estimation was used to analyze changes from baseline at weeks 2, 4, 8, and 12 in efficacy outcomes and PGI scores (week 12 only); covariates included in the MMRM were study visit, OAB type (for analysis of micturitions and urgency episodes), region (U.S. vs non-U.S.), baseline efficacy by outcome, and visit-by-treatment interaction. The model corrects for missing data and accounts for the fact that measurements were taken on the same patient over time and that these measurements tend to be correlated.

Statistical significance was determined if the 95% confidence interval (CI) of least squares mean difference (LSMD) at the time point did not include zero. If significance at the 0.05 α level for the coprimary end points was achieved, then the key secondary end points were tested sequentially in a predefined order. The MMRM accounts for partial missingness in longitudinal outcomes by estimating a random within-subject effect. This results in unbiased estimates under the assumption that data are missing at random. An unstructured correlation structure was specified because the visit variables are included in the model as classification variables. An analysis of covariance was used to analyze changes from baseline in the OAB-q; covariates included OAB type, region, and baseline score. Individual OAB-q scores were imputed as the mean of the remaining items if <50% of the items were missing, with no further imputation for the OAB-q analysis of covariance. The primary comparison of interest in these subgroup analyses was vibegron with placebo; all other outcomes, including comparisons between tolterodine and placebo, were considered descriptive. Safety outcomes were analyzed using descriptive statistics.

The overall trial planned to enroll 1400 patients (500 to vibegron, 500 to placebo, 400 to tolterodine). Assuming a 10% dropout, this would provide 98% power to detect a between-group difference of 0.6 in mean daily micturitions and 98% power to detect a between-group difference of 0.51 in mean daily UUI episodes, each using a 2-sided α level of 0.05.

RESULTS

Study Participants

Of the 1515 patients included in the safety set, 1286 (84.9%) were women (vibegron, n = 463; placebo, n = 459; tolterodine, n = 364; Fig. 1). The mean age of the women was 59.5 years; 40.8% were ≥65 years old, and 10.9% were ≥75 years old (Table 1). Overall, 78.9% of women were White, and 18.7% were of child-bearing potential. Most women (80.9%) were randomized to OAB wet (ie, incontinence at baseline). At baseline, the mean daily number of micturitions, UUI episodes, and urgency episodes were comparable between treatment groups, as were OAB-q and PGI scores (Table 1).

Efficacy Outcomes

Among women, vibegron was associated with statistically significantly greater reductions (95% CI of LSMD does not include 0) from baseline at week 12 versus placebo in the mean daily number of micturitions (LS mean, −1.9 vs −1.4, respectively; Fig. 2A; Supplementary Table 1, http://links.lww.com/FPMRS/A346); a statistically significant reduction was seen as early as week 2 and was maintained at weeks 4 and 8 with vibegron versus placebo (Fig. 2A). Vibegron was associated with statistically significantly greater reductions (95% CI of LSMD does not include 0) from baseline at week 12 versus placebo in mean daily number of UUI episodes among women (LS mean, −2.1 vs −1.4, respectively; Fig. 2B; Supplementary Table 1, http://links.lww.com/FPMRS/A346); the reduction from baseline

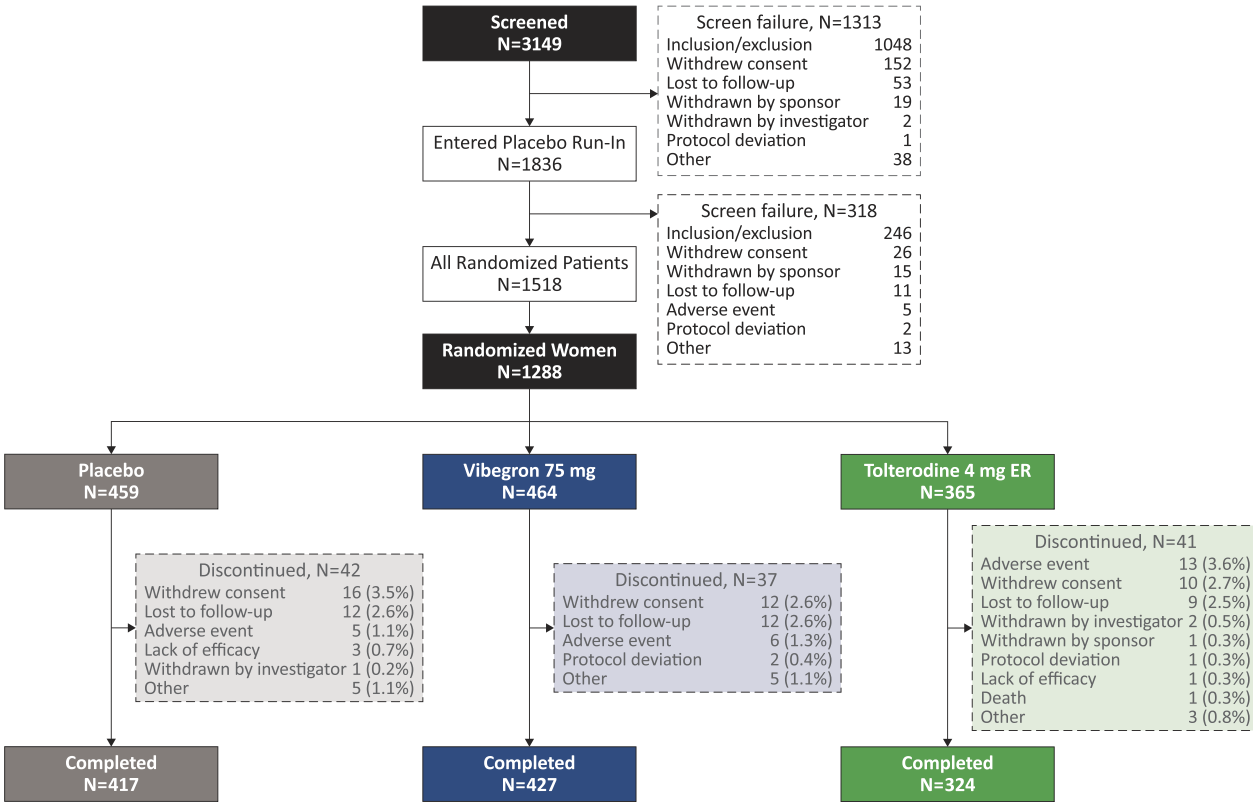


FIGURE 1. Patient disposition. ER, extended release.

was significant beginning at week 2 and was maintained at weeks 4 and 8 with vibegron versus placebo (Fig. 2B). Among women, vibegron was associated with statistically significantly greater reductions (95% CI of LSMD does not include 0) from baseline at week 12 versus placebo in mean daily number of urgency episodes (LS mean, –2.8 vs –1.9, respectively; Fig. 2C; Supplementary Table 1, http://links.lww.com/FPMRS/A346); a statistically significant reduction was also seen at weeks 2, 4, and 8 with vibegron versus placebo (Fig. 2C).

Quality of Life Outcomes

Women receiving vibegron had significantly greater improvement from baseline to week 12 in OAB-q health-related QoL (HRQL) total, coping, concern, sleep, and symptom bother subscale scores compared with placebo (P<0.01 each; Fig. 3A; Supplementary Table 2, http://links.lww.com/FPMRS/A346). Similarly, women receiving vibegron had significantly greater improvement in all PGI end points (severity, control, frequency, leakage, and change) versus placebo (P<0.01 each; Supplementary Table 2, http://links.lww.com/FPMRS/A346); at week 12, greater percentages of women receiving vibegron compared with placebo reported the most favorable responses on each PGI scale (Fig. 3B).

Safety

The incidence of treatment-emergent AEs (TEAEs) was 39.3% with vibegron, 34.9% with placebo, and 39.6% with tolterodine (Table 2). Overall, 1.5%, 1.1%, and 3.8% of women, respectively, discontinued treatment because of TEAEs. The most common TEAE in women receiving vibegron reported at a higher rate than placebo was headache (4.3% vs 2.6%, respectively). In addition, the rate of TEAE of hypertension with vibegron, placebo, and tolterodine was 1.9%, 1.7%, and 2.7%, respectively. No clinically meaningful changes were seen in laboratory parameters (eg, hematologic tests, urinalysis) or in postvoid residual urine volume (Supplementary Table 3, http://links.lww.com/FPMRS/A346).

DISCUSSION

In this prespecified subgroup analysis of women with OAB in the EMPOWUR trial, treatment with vibegron

TABLE 1. Demographics and Baseline Clinical Characteristics of Women From the EMPOWUR Trial

Characteristic*	Placebo (n = 459)	Vibegron 75 mg (n = 463)	Tolterodine 4 mg ER (n = 364)	Overall (N = 1286)
Mean (SD) age, y	59.1 (13.3)	59.9 (13.3)	59.4 (13.2)	59.5 (13.2)
Age subgroup, n (%)				
≥65 y	183 (39.9)	205 (44.3)	137 (37.6)	525 (40.8)
≥75 y	45 (9.8)	59 (12.7)	36 (9.9)	140 (10.9)
Race, n (%)				
White	362 (78.9)	375 (81.0)	278 (76.4)	1015 (78.9)
Black or African American	70 (15.3)	67 (14.5)	61 (16.8)	198 (15.4)
Asian	22 (4.8)	19 (4.1)	21 (5.8)	62 (4.8)
Other	5 (1.1)	2 (0.4)	4 (1.1)	11 (0.9)
Diabetes mellitus, n (%)	67 (14.6)	80 (17.3)	61 (16.8)	208 (16.2)
Preexisting hypertension, n (%)†	43 (9.4)	36 (7.8)	36 (9.9)	115 (8.9)
Child-bearing potential, n (%)	88 (19.2)	84 (18.1)	68 (18.7)	240 (18.7)
HRT, n (%)				
Receiving any HRT	25 (5.4)	17 (3.7)	20 (5.5)	62 (4.8)
Receiving transvaginal HRT	5 (1.1)	1 (0.2)	1 (0.3)	7 (0.5)
OAB type, n (%)‡				
Wet	374 (81.5)	372 (80.3)	295 (81.0)	1041 (80.9)
Dry	85 (18.5)	91 (19.7)	69 (19.0)	245 (19.1)
Mean (SD) micturitions per day§	11.7 (4.0)	11.3 (3.5)	11.4 (3.0)	11.5 (3.6)
Mean (SD) UUI episodes per day§	2.9 (3.0)	3.0 (3.2)	2.8 (2.6)	2.9 (3.0)
Mean (SD) urgency episodes per day§	8.0 (4.6)	8.1 (4.4)	7.8 (3.7)	8.0 (4.3)
Mean (SD) OAB-q score, n	443	447	351	1241
Total HRQL	63.2 (23.6)	62.6 (24.7)	64.4 (22.7)	63.3 (23.7)
Coping	57.8 (27.2)	57.1 (28.0)	59.6 (26.0)	58.0 (27.1)
Concern	62.9 (26.1)	61.6 (27.1)	63.2 (26.1)	62.5 (26.4)
Sleep	57.0 (26.7)	58.4 (27.9)	60.0 (25.1)	58.4 (26.7)
Social interaction‖	78.4 (25.3)	76.9 (25.8)	78.5 (24.5)	77.9 (25.2)
Symptom bother	50.8 (20.9)	50.2 (21.9)	48.7 (20.5)	50.0 (21.2)
Mean (SD) PGI score, n	444	448	352	1244
PGI-severity	3.0 (0.6)	3.0 (0.6)	3.0 (0.6)	3.0 (0.6)
PGI-control	3.2 (1.0)	3.3 (0.9)	3.2 (0.9)	3.2 (0.9)
PGI-frequency	3.8 (0.8)	3.8 (0.8)	3.6 (0.9)	3.7 (0.8)
PGI-leakage¶	3.4 (0.9)	3.4 (0.8)	3.3 (0.9)	3.4 (0.9)
PGI-change	3.6 (1.1)	3.6 (1.1)	3.5 (1.1)	3.5 (1.1)

*Analyzed in the safety set (all randomized women who took ≥1 dose of double-blind study treatment), except for OAB-q and PGI scores, which were analyzed in the FAS or FAS-I (all randomized women who took ≥1 dose of double-blind study treatment and had ≥1 evaluable change from baseline micturition or UUI measurement, respectively).

†Based on baseline vitals and prior medical history.

‡Based on randomization.

§Placebo, n = 457; vibegron, n = 462; tolterodine, n = 364; overall, n = 1283.

‖Placebo, n = 442; vibegron, n = 447; tolterodine, n = 352; overall, n = 1241.

¶Placebo, n = 364; vibegron, n = 360; tolterodine, n = 284; overall, n = 1008.

ER, extended release; FAS, full analysis set; FAS-I, FAS for incontinence; HRQL, health-related quality of life; HRT, hormone replacement therapy; OAB, overactive bladder; OAB-q, OAB questionnaire; PGI, patient global impression; UUI, urge urinary incontinence.

for 12 weeks resulted in statistically significant reductions from baseline compared with placebo in the average daily number of micturitions, UUI episodes, and urgency episodes. Women receiving vibegron demonstrated improvements in OAB symptoms as early as week 2, with statistically significant improvement

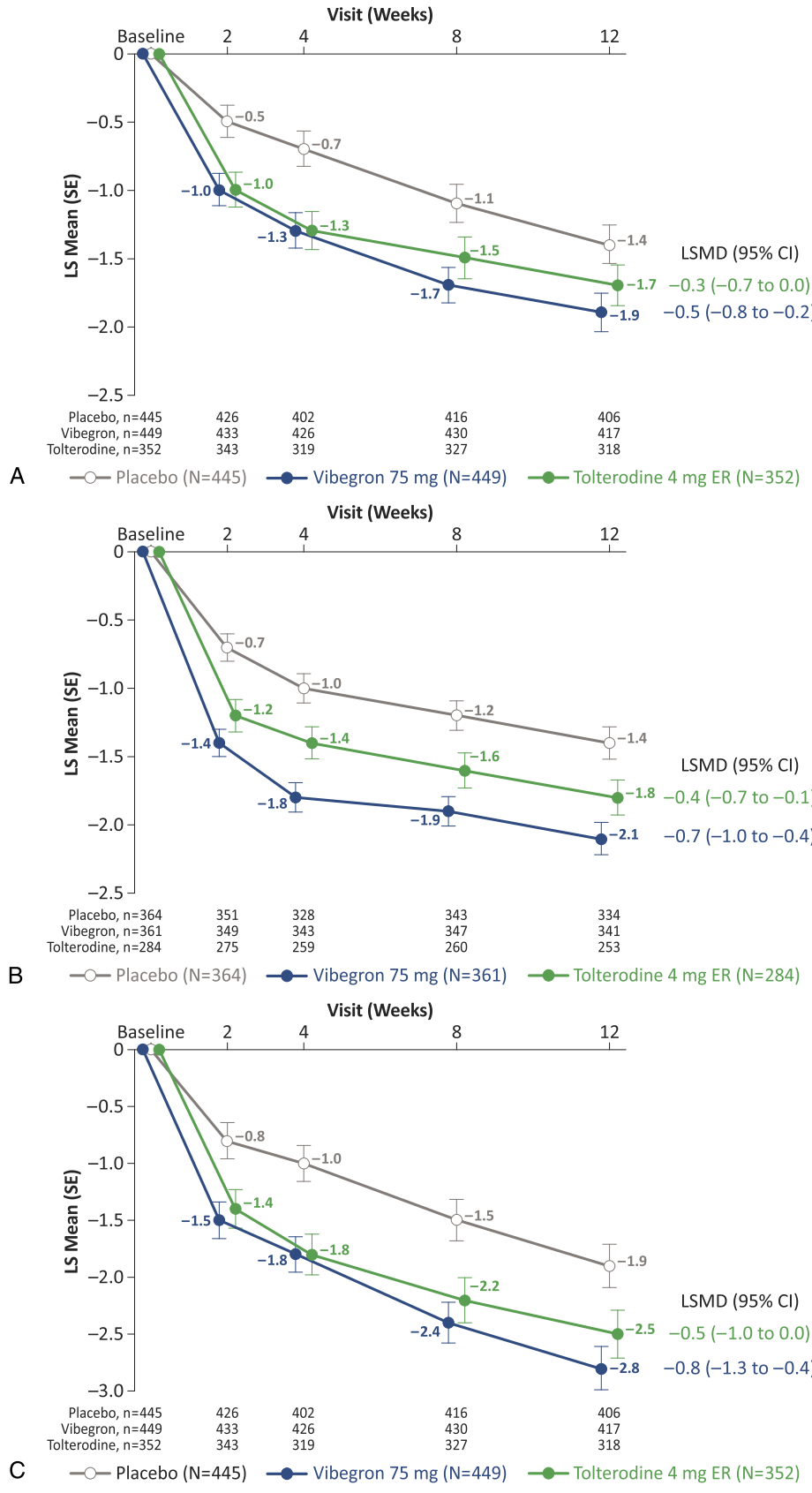
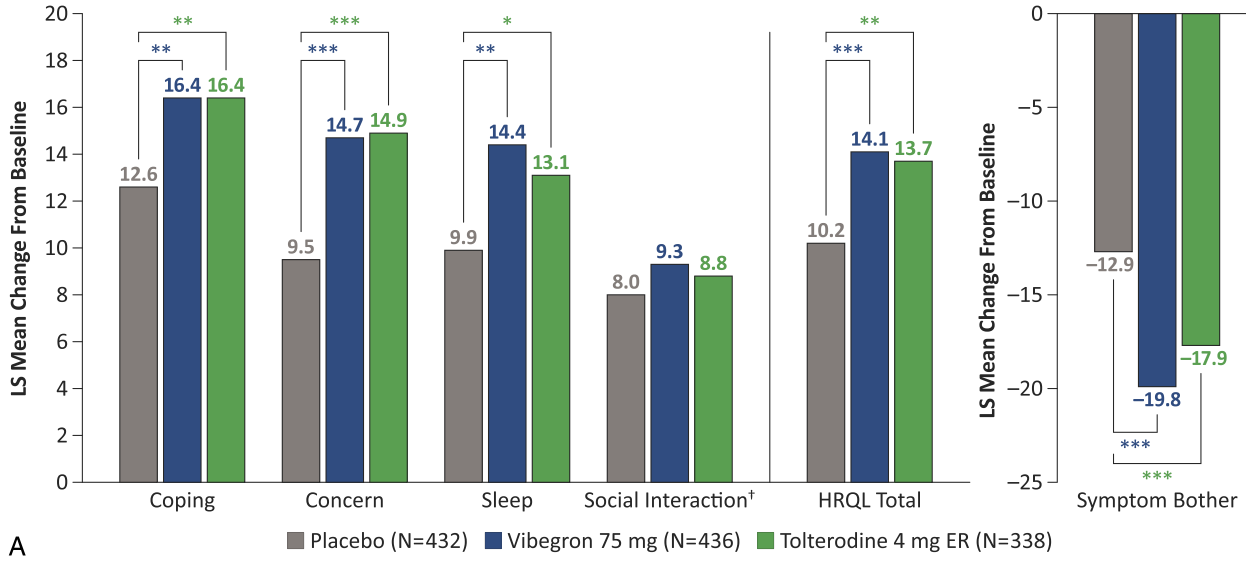


FIGURE 2. LS mean (SE) change from baseline in mean daily (A) micturitions, (B) UUI episodes, and (C) urgency episodes in women. CI, confidence interval; ER, extended release; LS, least squares; LSMD, LS mean difference; SE, standard error; UUI, urge urinary incontinence.



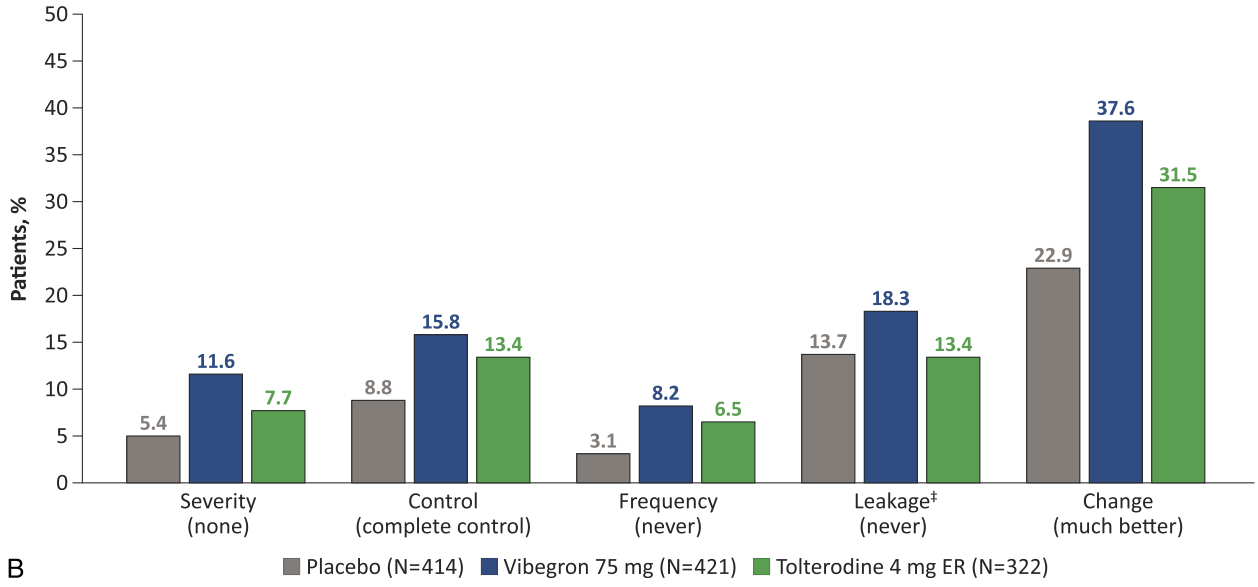


FIGURE 3. Quality of life outcomes in women. (A) LS mean change from baseline at week 12 in OAB-q scores. For coping, concern, sleep, social interaction, and HRQL total, increases indicate improvement; for symptom bother, decreases indicate improvement. (B) Percentage of women reporting the best response for each PGI measure at week 12. *$P<0.05$; **$P<0.01$; ***$P<0.001$. †Placebo, n = 431; vibegron, n = 436; tolterodine, n = 339. ‡Placebo, n = 340; vibegron, n = 341; tolterodine, n = 256. HRQL, health-related quality of life; LS, least squares; OAB-q, overactive bladder questionnaire; PGI, patient global impression.

versus placebo at week 12. Both vibegron and tolterodine showed improvement versus placebo in each outcome; however, the 95% CI of the LSMD for tolterodine versus placebo overlapped 0 (ie, was not statistically significant) for micturition and urgency episodes. Furthermore, the clinical meaningfulness of these improvements in OAB outcomes is supported by significant improvements in patient-reported outcomes related to OAB with vibegron versus placebo. Women receiving vibegron showed significantly greater improvements versus placebo at week 12 for OAB-q coping, concern, sleep, and symptom bother subscale scores and HRQL total score. Treatment with vibegron in women was also associated with greater improvement in PGI scores, with consistently higher percentages of women reporting the most favorable response in each PGI measures compared with placebo at week 12. Vibegron in women with OAB was generally safe and well tolerated, and no clinically meaningful differences were reported for vibegron versus placebo in the overall incidence of TEAEs.

The efficacy and safety results from this subgroup analysis of women with OAB were consistent with those observed in the overall study population of the

TABLE 2. Summary of Safety in Women (Safety Set*)

AE, n (%)	Placebo (n = 459)	Vibegron 75 mg (n = 463)	Tolterodine 4 mg ER (n = 364)
≥1 TEAE	160 (34.9)	182 (39.3)	144 (39.6)
≥1 treatment-related TEAE	51 (11.1)	62 (13.4)	57 (15.7)
≥1 TEAE leading to study drug discontinuation	5 (1.1)	7 (1.5)	14 (3.8)
≥1 serious TEAE	4 (0.9)	6 (1.3)	8 (2.2)
Resulting in death	0	0	1 (0.3)†
≥1 treatment-related serious TEAE	0	1 (0.2)‡	0
TEAEs occurring in ≥1% of women in the vibegron group and more than placebo			
Headache	12 (2.6)	20 (4.3)	10 (2.7)
Nasopharyngitis	9 (2.0)	15 (3.2)	9 (2.5)
Nausea	5 (1.1)	11 (2.4)	5 (1.4)
Diarrhea	6 (1.3)	9 (1.9)	9 (2.5)
Hypertension	8 (1.7)	9 (1.9)	10 (2.7)
Constipation	6 (1.3)	8 (1.7)	5 (1.4)
Dry mouth	4 (0.9)	8 (1.7)	24 (6.6)
Upper respiratory tract infection	4 (0.9)	8 (1.7)	2 (0.5)
Dizziness	4 (0.9)	5 (1.1)	3 (0.8)

*All randomized women who took ≥1 dose of double-blind study treatment.

†Patient reported AEs of urinary tract infection, sepsis, and cerebrovascular accident around the time of death; no AE was considered related to study treatment by the investigator.

‡Noncardiac chest pain, which resolved and was considered not related to study drug by the sponsor.

AE, adverse event; ER, extended release; TEAE, treatment-emergent AE.

EMPOWUR trial.[16] The LSMD for vibegron versus placebo was generally comparable in women and the overall population for micturitions (women, –0.5; overall, –0.5), UUI episodes (–0.7; –0.6), and urgency episodes (–0.8; –0.7). In an analysis of clinical meaningfulness of the EMPOWUR trial, significantly more patients receiving vibegron versus placebo achieved meaningful reductions in efficacy end points (ie, ≥15% reduction in micturitions, ≥50% reduction in urgency episodes, and ≥75% and 90% reduction in UUI episodes), which were associated with patient-perceived improvement.[18]

Although slightly higher rates of certain TEAEs, such as headache, occurred more frequently with vibegron than with placebo among women (4.3% vs 2.6%, respectively), the incidence of headache with vibegron versus placebo aligns with the overall safety results of the overall population from the EMPOWUR trial (4.0% vs 2.4%, respectively).[16] In addition, TEAEs of hypertension in women displayed similar rates for vibegron and placebo (1.9% and 1.7%, respectively).

Urinary incontinence (UI), and in particular UUI, is a common symptom of OAB that is highly prevalent in women. The use of anticholinergics to treat UI due to OAB is associated with adverse effects, particularly dry mouth,[19] limiting long-term treatment adherence and persistence.[8] Indeed, a systematic review of randomized controlled trials of anticholinergics for women with UI showed the incidence of dry mouth was 3 times more common with anticholinergics than placebo (relative risk, 3.00 [CI, 2.70–3.34]).[20] Similarly, this analysis showed that among women receiving tolterodine, the incidence of dry mouth was greater than with vibegron and placebo (6.6% vs 1.7% and 0.9%, respectively).

Although anticholinergics can be efficacious in treating symptoms of OAB, long-term anticholinergic use is being shown to be associated with an elevated risk of dementia[10] and falls or fractures.[21–23] This is especially concerning among older women as the prevalence of anticholinergic burden ≥3 is greater in women compared with men,[24] leading to recurrent falls in postmenopausal women.[22] Furthermore, a previous report showed falls to be more frequent in adults ≥65 years old (39.4%) with UUI compared with those without UUI.[25] Higher fall rates in this population may be partly due to a slower gait speed and increased variability in gait among older women (≥65 years) with severe UI experiencing urinary urgency.[26,27] As such, the significant improvements observed in this analysis with vibegron in both UUI episodes and urgency episodes suggest that vibegron may be a beneficial and safe treatment option among older women with OAB.

Simply Stated

Overactive bladder (OAB) is a condition that lowers quality of life. More women than men have OAB and related symptoms. Vibegron is in a newer class of drugs for treating OAB. Vibegron was approved after being tested in the EMPOWUR clinical trial. Here, we look at the effect of vibegron specifically on women from the EMPOWUR trial. Patients with OAB took either vibegron, placebo, or tolterodine once a day for 12 weeks. We looked at changes in the average daily number of urinations, the urgent need to urinate, and urgent need to urinate resulting in urine leakage. We also monitored patient safety throughout the trial. At the end of the study, women taking vibegron had 1.9 fewer urinations per day than at the start of the study. Women taking placebo had 1.4 fewer urinations. Leakages were down 2.1 episodes with vibegron, compared with down 1.4 episodes with placebo. Vibegron reduced urgency episodes by 2.8, compared with 1.9 with placebo. The percentage of women who had an adverse safety event was similar with vibegron (39%) and placebo (35%). These results in women were similar to the overall EMPOWUR results. Vibegron may be a safe and beneficial option for women with OAB.

Given the symptoms associated with OAB can be burdensome and significantly affect patient QoL, the International Continence Society recommends evaluating QoL measures in addition to symptom measures.[28] These subgroup analyses showed that women receiving vibegron experienced significant and clinically meaningful improvements versus placebo in patient-reported QoL measures, including the OAB-q and PGI. This is clinically important given that women with OAB show high rates of symptoms of depression, poor sleep quality, and relatively low QoL.[3] Notably, these results are consistent with previous analyses in patient-reported QoL measures in the overall population from the EMPOWUR trial.[17]

A limitation of the analysis was the relatively short study duration of 12 weeks. However, a 40-week double-blind extension of the EMPOWUR trial (52 total weeks of treatment)[29] demonstrated long-term efficacy and safety of vibegron. Sample size was calculated for the overall population, and therefore, power was reduced to identify differences between groups in this subgroup analysis. Consistent with the placebo-controlled trials of OAB and previously observed in other similar analyses,[30] a relatively high placebo response rate was observed. However, vibegron was associated with statistically significant improvements versus placebo in OAB symptoms in women despite the high placebo response.

CONCLUSIONS

The results of this subgroup analysis of women with OAB are consistent with results from the 12-week EMPOWUR trial, demonstrating that once-daily vibegron 75 mg was associated with statistically significant reductions versus placebo in efficacy end points, including UUI and urgency, with a favorable safety and tolerability profile. Furthermore, treatment with vibegron among women with OAB significantly improved QoL measures compared with placebo. These results suggest that vibegron is efficacious and safe for the treatment of women with OAB.

ARTICLE INFORMATION

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Portions of these data have been previously presented at the 2021 Pelvic Floor Disorders Week of the American Urogynecologic Society, Phoenix, AZ, October 12–15, 2021, and at the 2021 International Urogynecological Association 46th Annual Meeting, virtual, December 9–12, 2021.

Request for data from Urovant Sciences (e-mail: medinfo@urovant.com) will be considered from qualified researchers on a case-by-case basis.

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's website (www.urogynecologyjournal.org).

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