UROVANT SCIENCES

Long-Term Safety and Efficacy in the Phase 3 EMPOWUR Extension Trial

GEMTESA® (vibegron) is a beta-3 adrenergic agonist indicated for the treatment of overactive bladder (OAB) with symptoms of urge urinary incontinence, urgency, and urinary frequency in adults. Please see accompanying full Prescribing Information.

Vibegron 75 mg once daily for 40 weeks and for 52 weeks demonstrated favorable long-term safety, tolerability, and efficacy in patients with OAB, consistent with results of the 12-week EMPOWUR trial. Nearly two-thirds of patients treated with vibegron experienced a ≥75% reduction in UUI episodes, and more than 40% became dry. Patients treated with vibegron had significantly greater reductions in UUI episodes and total incontinence episodes compared with tolterodine (active control).

No clinically meaningful differences between the vibegron and tolterodine (active control) groups were observed in overall incidence or severity of AEs or incidence of SAEs or AEs leading to treatment discontinuation. The incidence of AEs of hypertension was similar in both groups. Dry mouth occurred more frequently with tolterodine (active control) than with vibegron.

Phase 3 EMPOWUR Extension Trial

Following the 12-week EMPOWUR trial,[1] a 40-week extension trial was conducted with EMPOWUR completers.[2] Subjects previously randomized to receive vibegron 75 mg or tolterodine ER 4 mg (active control) continued their same once daily blinded treatment for an additional 40 weeks (52 total weeks of treatment). Subjects previously randomized to receive placebo were randomized 1:1 to receive blinded vibegron 75 mg or tolterodine ER 4 mg (active control) once daily for 40 weeks. Following enrollment in the extension study, subjects were evaluated at Weeks 16, 24, 36, 44 and 52 relative to Day 1 of 12-week EMPOWUR trial.

The primary outcome was safety and tolerability of vibegron including treatment-emergent adverse events (AEs), extent of exposure and treatment compliance, clinical laboratory evaluations, vital signs, physical examinations, electrocardiograms and post-void residual (PVR) urine volume measured via ultrasound.

Efficacy at Week 52 was a secondary endpoint and included the change from baseline (CFB) in average daily number of micturitions in all subjects, urge urinary incontinence (UUI) episodes in OAB wet patients, urgency episodes (need to urinate immediately) in all patients, and total urinary incontinence episodes in OAB wet patients.

Among 506 randomized subjects, 505 received ≥1 dose of double-blind study drug (vibegron, n=273; tolterodine (active control), n=232) with a high completion rate (85.0% overall) and similar completion rates across treatment groups. Discontinuations due to AEs occurred in 12 (2.4%) subjects, with a slightly lower proportion of subjects in the vibegron group discontinuing due to an AE compared with the tolterodine (active control) group (vibegron, n = 4 [1.5%]; tolterodine (active control), n = 8 [3.4%]).

Most subjects were female (78.2%) and most (78.2%) had wet OAB. The mean age of the study population was 61.1 years with 46.5% ≥65 years old. There were no notable differences between the two treatment groups in baseline or demographic factors.

In the efficacy endpoint analyses, once daily vibegron 75 mg for a total of 52 weeks demonstrated numerically greater decreases in CFB for average daily number of micturitions (Figure 1), UUI episodes (Figure 2), urgency episodes (Figure 3), and total urinary incontinence

episodes (Figure 4) compared to tolterodine (active control). Greater improvements in efficacy endpoints among vibegron-treated subject were observed at 2 weeks and was maintained throughout the total of 52-week study. Once daily vibegron 75 mg resulted in a numerically greater proportion of subjects with a ≥75% reduction from baseline in UUI episodes, with a 100% reduction from baseline in UUI episodes, and ≥50% reduction in total incontinence compared with the tolterodine (active control) treatment (Table 1)

Table 1. Urge Urinary Incontinence and Total Incontinence Responder Analyses (OAB Wet Subjects)

	52-weeks Vibegron 75mg n=143	**52-weeks Tolterodine ER 4mg (active control) n=106**
Subjects with at 75% Reduction in UUI from Baseline at 52 weeks		
Proportion (95% CI)	61.0 (52.6 – 69.4)	54.4 (44.5 – 54.3)
Subjects with at 100% Reduction in UUI from Baseline at 52 weeks		
Proportion (95% CI)	40.8 (32.4 – 49.2)	34.2 (24.7 – 43.8)
Subjects with at 50% Reduction in Total Incontinence from Baseline at 52 weeks		
Proportion (95% CI)	71.1 (63.3 – 78.9)	61.9 (52.3 – 71.6)

Figure 1. Change in Mean Daily Micturitions

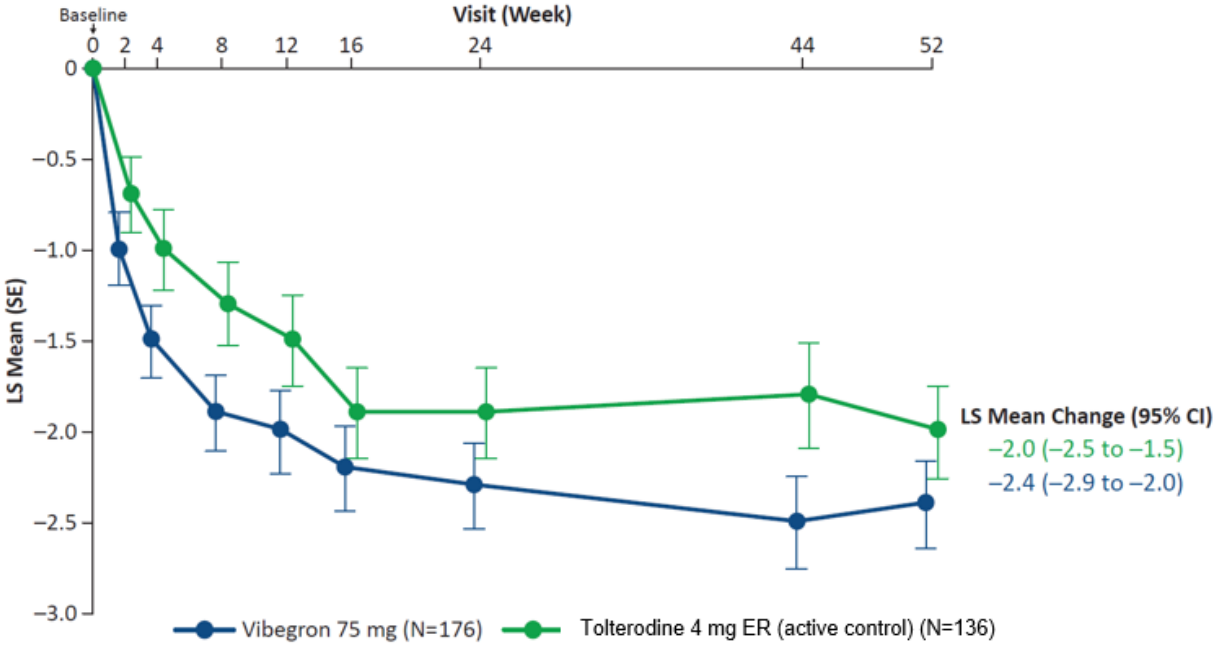
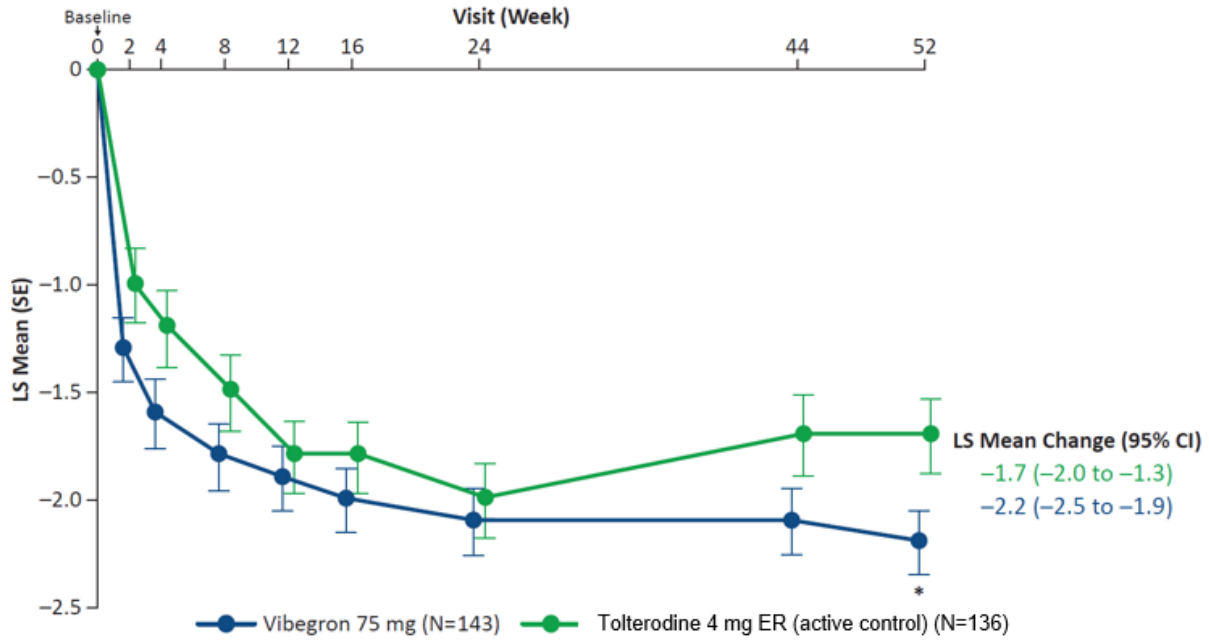
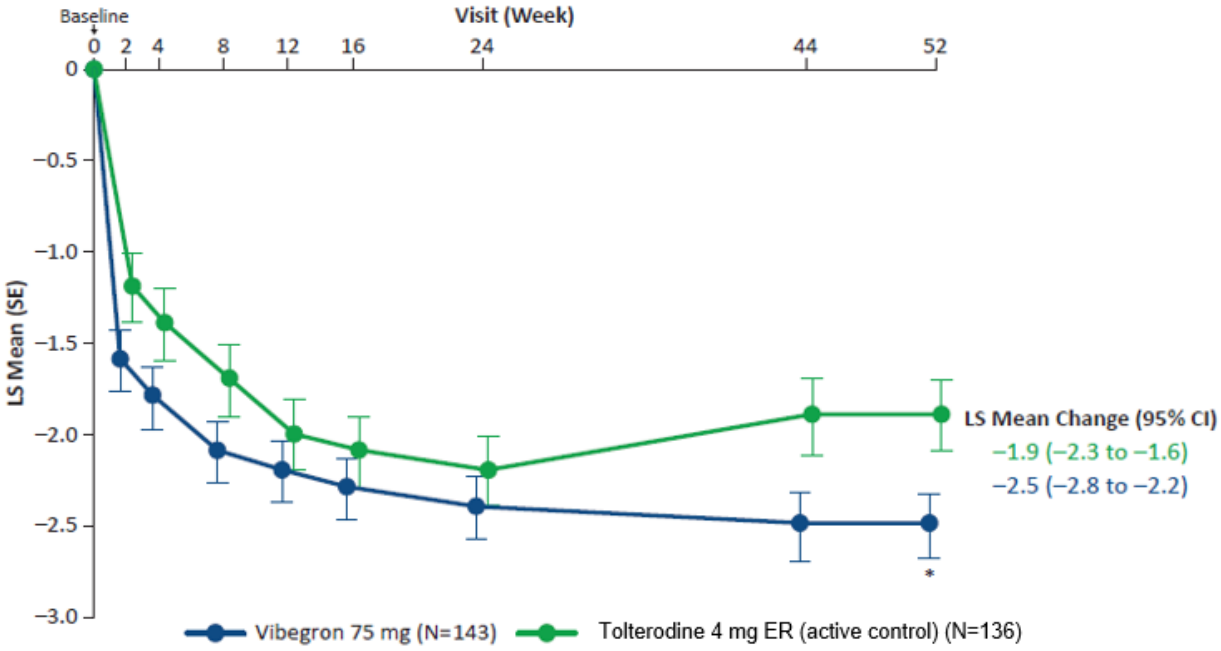


Figure 2. Change in Mean Daily UUI Episodes



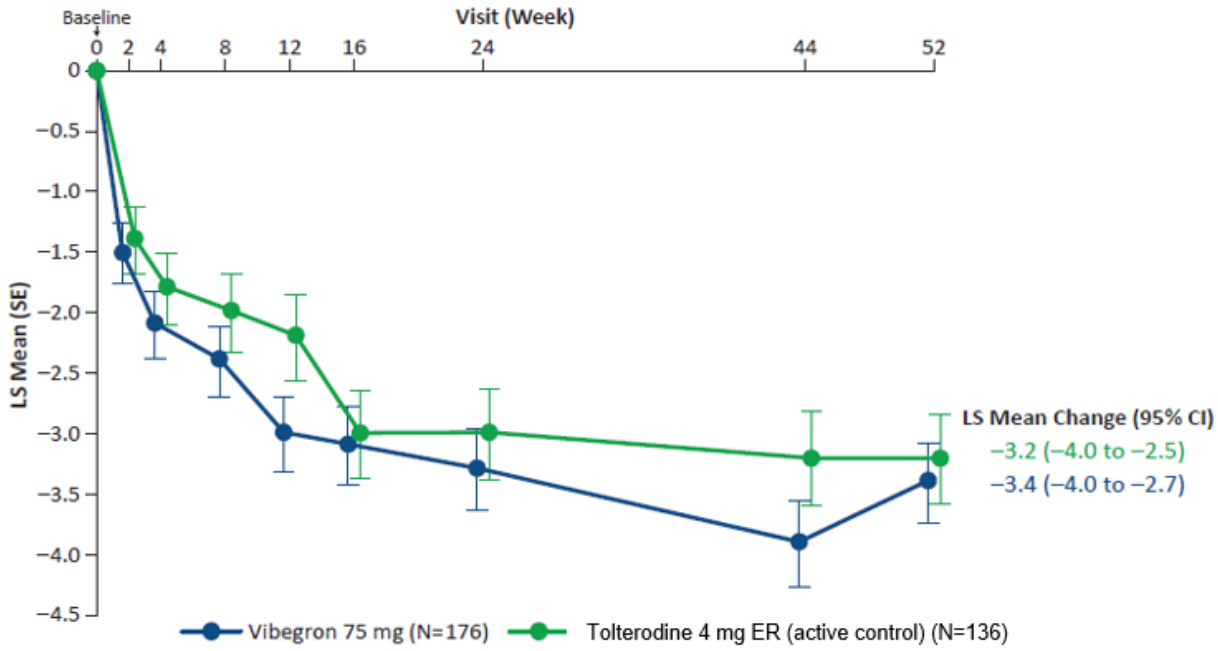
**P*<0.05

Figure 3. Change in Mean Daily Urgency Episodes



**P*<0.05

Figure 4. Change in Mean Daily Incontinence Episodes



Among subjects treated with vibegron (n=273), 171 subjects (62.6%) reported at least one AE and four subjects (1.5%) discontinued due to an AE. Among tolterodine-treated (active control) subjects (n=232), 126 subjects (54.3%) reported at least one AE and eight (3.4%) discontinued due to an AE. AEs reported with an incidence >5% among subjects receiving vibegron were hypertension (n=24, 8.8%), urinary tract infection (n=18, 6.6%), and headache (n=15, 5.5%). These AEs were reported by 20 (8.6%), 17 (n=7.3) and 9 (3.9%), respectively, by subjects in the tolterodine group (active control).

At Week 52, there was no clinically relevant change from baseline in mean PVR urine volume for subjects treated with vibegron or with tolterodine (active control). Consistent with the PVR data, few subjects reported an AE of “residual urine volume increased” for vibegron subjects (n=7; 2.6%) reported eight events and tolterodine (active control) subjects (n=3; 1.3%) reported three events. Long-term treatment with vibegron did not result in increased urinary retention in subjects.

References

1. Staskin D, Frankel J, Varano S, et al. International phase III, randomized, double-blind, placebo and active controlled study to evaluate the safety and efficacy of vibegron in patients with symptoms of overactive bladder: EMPOWUR. J Urol. 2020;204:316-324. https://www.auajournals.org/doi/10.1097/JU.0000000000001574

2. Staskin D, Frankel J, Varano S, et al. Once-daily vibegron 75 mg for overactive bladder: long-term safety and efficacy from a double-blind extension study of the international phase 3 trial (EMPOWUR), The Journal of Urology® 2020, doi:10.1097/JU.0000000000001574.