Effects of Vibegron on Ambulatory Blood Pressure in Patients With Overactive Bladder: Results From a Double-Blind, Placebo-Controlled Trial

Supplementary Information

Supplementary Table 1. Change From Baseline to Day 28 in Maximum* Ambulatory Systolic BP, Diastolic BP, and Heart Rate From 0.5 to 6.5 Hours

Ambulatory BP Parameter	Placebo (N=101)	Vibegron (N=96)
Systolic BP, mmHg		
Mean (SD) baseline	136.1 (12.7)	135.0 (13.9)
LS mean change at day 28 (90% CI)†	0.3 (–1.8 to 2.3)	2.0 (–0.1 to 4.0)
LS mean difference vs placebo (90% CI)	1.7 (–0.8 to 4.2)	
Diastolic BP, mmHg		
Mean (SD) baseline	84.2 (9.5)	83.1 (9.2)
LS mean change at day 28 (90% CI)†	–0.5 (–1.8 to 0.8)	0.6 (–0.7 to 2.0)
LS mean difference vs placebo (90% CI)	1.2 (–0.4 to 2.8)	
Heart rate, bpm		
Mean (SD) baseline	85.3 (13.4)	86.2 (12.6)
LS mean change at day 28 (90% CI)†	0.3 (–1.8 to 2.4)	1.8 (–0.4 to 3.9)
LS mean difference vs placebo (90% CI)	1.5 (–1.1 to 4.0)	

BP, blood pressure; LS, least squares.

*Defined as the maximum of the hourly means between 0.5 and 6.5 hours post cuff fitting, corresponding to the time to maximum concentration of vibegron.

†Placebo, N=96; vibegron, N=92.

Supplementary Table 2. Change From Baseline to Day 28 in Ambulatory Systolic BP, Diastolic BP, and Heart Rate by Age Subgroup

Ambulatory BP Parameter, Mean (SD)	Age ≤75th Percentile*		Age >75th Percentile*	
	Placebo (N=75)	Vibegron (N=76)	Placebo (N=26)	Vibegron (N=20)
Daytime systolic BP, mmHg				
Baseline	125.4 (9.7)	125.3 (11.3)	130.0 (12.1)	127.9 (10.4)
Change from baseline at day 28	0.2 (6.6)	0.7 (7.9)	–1.6 (6.9)	0.6 (8.8)
Daytime diastolic BP, mmHg				
Baseline	76.4 (7.9)	77.1 (7.8)	73.7 (9.3)	71.5 (7.3)
Change from baseline at day 28	0.5 (4.5)	0.2 (5.5)	–0.4 (4.9)	–0.3 (4.7)
Daytime heart rate, bpm				
Baseline	77.2 (8.5)	77.6 (8.4)	73.6 (9.1)	74.2 (7.7)
Change from baseline at day 28	0.7 (4.8)	1.5 (5.0)	–0.7 (5.2)	0.3 (4.4)
24-h systolic BP, mmHg				
Baseline	121.5 (9.2)	121.5 (11.3)	127.3 (11.3)	124.3 (9.9)
Change from baseline at day 28	0.2 (5.8)	0.7 (7.3)	–1.3 (6.7)	0.0 (8.0)
24-h diastolic BP, mmHg				
Baseline	73.1 (7.6)	73.9 (7.6)	71.1 (8.7)	68.9 (6.6)
Change from baseline at day 28	0.6 (3.8)	0.4 (5.2)	0.2 (4.6)	–0.7 (4.3)
24-h heart rate, bpm				
Baseline	74.9 (8.0)	75.0 (7.7)	71.9 (8.8)	72.1 (7.2)
Change from baseline at day 28	0.4 (4.4)	1.3 (4.7)	–0.9 (5.2)	0.0 (3.3)

Ambulatory BP Parameter, Mean (SD)	Age ≤75th Percentile*		Age >75th Percentile*	
	Placebo (N=75)	Vibegron (N=76)	Placebo (N=26)	Vibegron (N=20)
Maximum (0.5–6.5 h) systolic BP, mmHg†				
Baseline	134.7 (11.9)	134.5 (14.6)	140.2 (14.2)	136.8 (10.8)
Change from baseline at day 28‡	–0.1 (9.5)	1.3 (11.4)	–1.0 (11.0)	3.1 (13.0)
Maximum (0.5–6.5 h) diastolic BP, mmHg†				
Baseline	84.7 (8.8)	84.3 (9.1)	82.9 (11.4)	78.6 (8.3)
Change from baseline at day 28‡	–0.9 (6.1)	0.4 (7.1)	–1.8 (8.8)	0.2 (7.7)
Maximum (0.5–6.5 h) heart rate, bpm†				
Baseline	86.7 (12.9)	86.9 (12.7)	81.1 (14.3)	83.3 (12.1)
Change from baseline at day 28‡	0.9 (10.1)	1.4 (11.5)	–1.2 (14.0)	1.1 (12.6)

BP, blood pressure.

*75th percentile, 66 years.

†Defined as the maximum of the hourly means between 0.5 and 6.5 hours post cuff fitting, corresponding to the time to maximum concentration of vibegron.

‡Age ≤75th percentile: placebo, N=70; vibegron, N=72.

Supplementary Table 3. Percentage of Patients Meeting Predefined Thresholds for Change From Baseline to Day 28 in Ambulatory Systolic BP, Diastolic BP, and Heart Rate by Age Subgroup

Ambulatory BP Parameter, n (%)	Age ≤75th Percentile*		Age >75th Percentile*	
	Placebo (N=75)	Vibegron (N=76)	Placebo (N=26)	Vibegron (N=20)
Systolic BP, ≥15 mmHg				
Mean daytime	2 (2.7)	2 (2.6)	0 (0)	0 (0)
Mean 24-h	0 (0)	2 (2.6)	0 (0)	0 (0)
Maximum (0.5–6.5 h)†‡	4 (5.7)	3 (4.2)	0 (0)	3 (15.0)
Diastolic BP, ≥10 mmHg				
Mean daytime	2 (2.7)	2 (2.6)	0 (0)	0 (0)
Mean 24-h	0 (0)	1 (1.3)	0 (0)	0 (0)
Maximum (0.5–6.5 h)†‡	2 (2.9)	7 (9.7)	3 (11.5)	2 (10.0)
Heart rate, ≥10 bpm				
Mean daytime	3 (4.0)	2 (2.6)	1 (3.8)	1 (5.0)
Mean 24-h	2 (2.7)	2 (2.6)	1 (3.8)	1 (5.0)
Maximum (0.5–6.5 h)†‡	14 (20)	16 (22.2)	3 (11.5)	4 (20.0)

BP, blood pressure.

*75th percentile, 66 years.

†Defined as maximum of the hourly means between 0.5 and 6.5 hours post cuff fitting, corresponding to the time to maximum concentration of vibegron.

‡Age ≤75th percentile: placebo, N=70; vibegron, N=72.

Supplementary Table 4. Percentage of Patients Meeting Predefined Thresholds for Change From Baseline to Day 28 in Ambulatory Systolic BP, Diastolic BP, and Heart Rate by Pre-existing Hypertension

	With Pre-existing Hypertension		Without Pre-existing Hypertension	
Ambulatory BP Parameter, n (%)	**Placebo (N=31)**	**Vibegron (N=38)**	**Placebo (N=70)**	**Vibegron (N=58)**
Systolic BP, ≥15 mmHg				
Mean daytime	1 (3.2)	1 (2.6)	1 (1.4)	1 (1.7)
Mean 24-h	0 (0)	1 (2.6)	0 (0)	1 (1.7)
Maximum (0.5–6.5 h)*†	1 (3.3)	3 (8.3)	3 (4.5)	3 (5.4)
Diastolic BP, ≥10 mmHg				
Mean daytime	1 (3.2)	1 (2.6)	1 (1.4)	1 (1.7)
Mean 24-h	0 (0)	1 (2.6)	0 (0)	0 (0)
Maximum (0.5–6.5 h)*†	2 (6.7)	6 (16.7)	3 (4.5)	3 (5.4)
Heart rate, ≥10 bpm				
Mean daytime	1 (3.2)	1 (2.6)	3 (4.3)	2 (3.4)
Mean 24-h	1 (3.2)	1 (2.6)	2 (2.9)	2 (3.4)
Maximum (0.5–6.5 h)*†	5 (16.7)	7 (19.4)	12 (18.2)	13 (23.2)

BP, blood pressure.

*With pre-existing hypertension: placebo, N=30; vibegron, N=36; without pre-existing hypertension: placebo, N=66; vibegron, N=56

†Defined as the maximum of the hourly means between 0.5 and 6.5 hours post cuff fitting, corresponding to the time to maximum concentration of vibegron.

Supplementary Table 5. Summary of Adverse Events

AE, n (%)	Placebo (N=108)	Vibegron (N=106)
≥1 TEAE	27 (25.0)	49 (46.2)
≥1 study treatment–related TEAE	10 (9.3)	20 (18.9)
≥1 serious TEAE	1 (0.9)	1 (0.9)
≥1 study treatment–related serious TEAE	0	0
Deaths	0	0
TEAEs occurring in ≥2% of patients in either group		
Hypertension*	4 (3.7)	5 (4.7)
Upper respiratory tract infection	1 (0.9)	5 (4.7)
Headache	2 (1.9)	4 (3.8)
Nasopharyngitis	3 (2.8)	3 (2.8)
Diarrhea	1 (0.9)	3 (2.8)
Dry mouth	1 (0.9)	3 (2.8)
Nausea	1 (0.9)	3 (2.8)
Urinary tract infection	1 (0.9)	3 (2.8)
Fatigue	0	3 (2.8)
Hematuria	0	3 (2.8)

AE, adverse event; BP, blood pressure; TEAE, treatment-emergent AE.

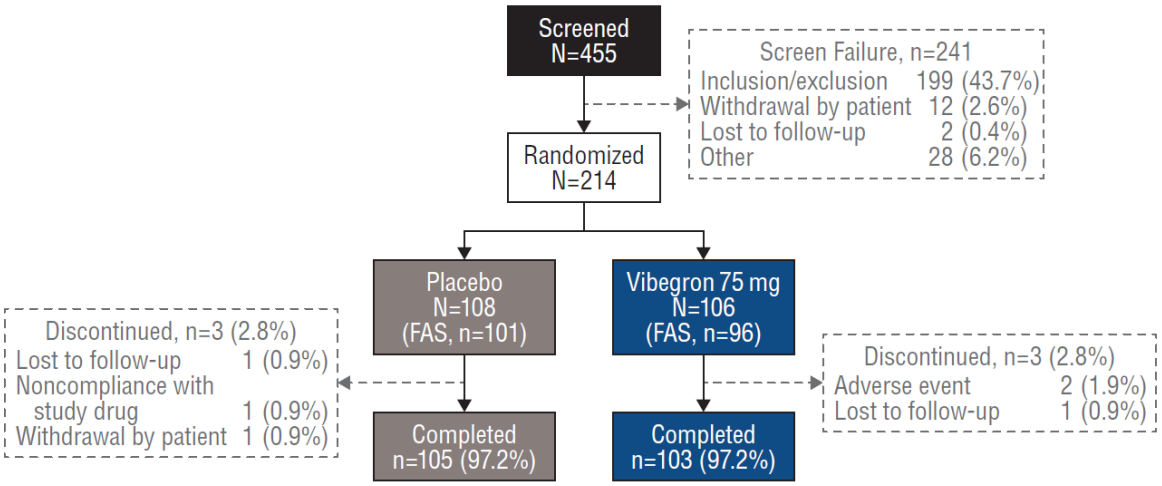
*Hypertension was recorded as an AE of clinical interest if the following criteria applied: for patients without hypertension at baseline, systolic BP ≥140 mmHg or diastolic BP ≥90 mmHg (at 2 consecutive visits for the average of 3 measurements); for patients with baseline hypertension, systolic BP increase of ≥20 mmHg or diastolic BP increase of ≥10 mmHg (at 2 consecutive visits for the average of 3 measurements); or the initiation of, or increase in dose of, medication for the treatment of hypertension.

Supplementary Table 6. Change From Baseline to Day 28 in In-Clinic Systolic BP, Diastolic BP, and Heart Rate (Safety Set)

Parameter, Mean (SD)	Placebo (N=108)	Vibegron (N=106)
Systolic BP, mmHg		
Baseline	122.3 (14.3)	119.6 (15.1)
Day 28	119.9 (12.7)	120.3 (15.2)
Change from baseline at day 28	–2.6 (13.5)	0.4 (10.9)
Diastolic BP, mmHg		
Baseline	76.5 (8.3)	75.2 (8.6)
Day 28	74.7 (8.5)	75.2 (7.9)
Change from baseline at day 28	–1.8 (8.1)	–0.2 (6.5)
Heart rate, bpm		
Baseline	70.4 (8.9)	71.9 (9.6)
Day 28	69.1 (10.1)	71.2 (9.4)
Change from baseline at day 28	–1.1 (7.4)	–0.8 (7.3)

BP, blood pressure.

Supplementary Figure 1. Patient disposition. FAS, full analysis set.



Supplementary Figure 2. Mean 24-hour ambulatory heart rate for placebo (left) and vibegron (right).