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van Kerrebroeck P[1], Sokol R[2], Traudtner K[3], Bongaerts D[3], van Charldorp K[3], Drake M[4]

1. *Maastricht University Medical Center, Maastricht, The Netherlands,* ***2.*** *Private Urological Care Center, Piaristicka, Trencin, Slovakia,* ***3.*** *Astellas Pharma Global Development Europe, Leiderdorp, The Netherlands,* ***4.*** *Bristol Urological Institute, Bristol, UK*

SAFETY OF A COMBINATION TABLET WITH SOLIFENACIN AND TAMSULOSIN OCAS™ IN MEN WITH LUTS ASSOCIATED WITH BPH IN THE NEPTUNE TRIAL

Hypothesis / aims of study

As part of the NEPTUNE trial, the safety and tolerability of a once-daily fixed-dose combination (FDC) tablet containing solifenacin (soli) and the oral controlled absorption system (OCAS™) formulation of tamsulosin were evaluated, in comparison with tamsulosin OCAS™ (TOCAS) monotherapy, in men with lower urinary tract symptoms (LUTS) associated with benign prostatic hyperplasia (BPH) who had both storage and voiding symptoms.

Study design, materials and methods

NEPTUNE was a randomised, double-blind, placebo-controlled, multicentre, 12-week, phase 3 trial (2-week placebo run-in). Men aged ≥45 years, diagnosed with LUTS (voiding and storage symptoms: total IPSS ≥13 and Q_{max} 4.0–12.0 mL/s, ≥8 micturitions/24 h and ≥2 grade 3 or 4 PPIUS urgency episodes/24 h) associated with BPH for ≥3 months were randomised to receive either TOCAS 0.4 mg (n=326), TOCAS 0.4 mg + soli 6 mg (n=337) or 9 mg (n=324), or placebo (n=341 [number of patients included in the safety population]).

Results

Treatment-emergent adverse events (TEAEs) were reported by 87 patients (25.5%) in the placebo group, 74 (22.7%) in the TOCAS 0.4 mg group, 99 (29.4%) in the TOCAS 0.4 mg + soli 6 mg group and 100 (30.9%) in the TOCAS 0.4 mg + soli 9 mg group. Treatment-related AEs (TRAEs) occurred in 30 patients (8.8%) in the placebo group, 27 (8.3%) in the TOCAS 0.4 mg group, 57 (16.9%) in the TOCAS 0.4 mg + soli 6 mg group and 65 (20.1%) in the TOCAS 0.4 mg + soli 9 mg group. Dry mouth and constipation were the most common TRAEs (Table). A total of 42 serious adverse events (SAEs) were reported in 27 patients. The incidence of treatment-related SAEs was 0.3% in the placebo group, 1.2% in the TOCAS 0.4 mg group, 0% in the TOCAS 0.4 mg + soli 6 mg group and 1.5% in the TOCAS 0.4 mg + soli 9 mg group. The FDCs were generally well tolerated, with the majority of AEs described as mild to moderate and consistent with the safety profiles of each monotherapy. Two patients died during the study, but the causes of death were not considered to be related to study medication. Discontinuation rates owing to TEAEs were 3.9% (6 mg) and 3.1% (9 mg) for the FDC groups. Five patients experienced acute urinary retention (AUR) that required catheterisation, including 1 (0.3%) in the TOCAS 0.4 mg group, 1 (0.3%) in the TOCAS 0.4 mg + soli 6 mg group and 3 (0.9%) in the TOCAS 0.4 mg + soli 9 mg group. Two of the patients receiving TOCAS 0.4 mg + soli 9 mg discontinued the study due to AUR. There was a small increase in mean post-void residual (PVR) volume for patients receiving TOCAS 0.4 mg + soli 6 mg (mean change from baseline 3.8 mL) and TOCAS 0.4 mg + soli 9 mg (mean change from baseline 12.3 mL). These increases were not considered clinically significant and were not associated with AUR.

Interpretation of results

Combination therapy with TOCAS 0.4 mg + soli 6 mg or 9 mg was well tolerated in men with LUTS/BPH. The most common TEAEs were dry mouth and constipation, which is consistent with the safety profiles of both monotherapies. Reported AUR rates were low, as expected in a population of patients with LUTS/BPH.

Concluding message

Treatment with the FDC tablets containing TOCAS + soli 6 mg or 9 mg was well tolerated in men with LUTS/BPH with a substantial storage component.

Summary of patients with adverse events

	Placebo (n=341)	TOCAS 0.4 mg (n=326)	TOCAS + 6 mg soli (n=337)	TOCAS + 9 mg soli (n=324)
Any TRAE	30 (8.8%)	27 (8.3%)	57 (16.9%)	65 (20.1%)
Dry mouth	4 (1.2%)	1 (0.3%)	27 (8.0%)	34 (10.5%)
Constipation	1 (0.3%)	1 (0.3%)	9 (2.7%)	16 (4.9%)
Dyspepsia	1 (0.3%)	1 (0.3%)	6 (1.8%)	4 (1.2%)
Nausea	1 (0.3%)	4 (1.2%)	1 (0.3%)	0
Headache	2 (0.6%)	2 (0.6%)	4 (1.2%)	0
Urinary retention	0	1 (0.3%)	2 (0.6%)	4 (1.2%)
Fatigue	2 (0.6%)	2 (0.6%)	4 (1.2%)	1 (0.3%)
Retrograde ejaculation	0	0	1 (0.3%)	4 (1.2%)
SAEs	3 (0.9%)	10 (3.1%)	5 (1.5%)	9 (2.8%)
Treatment-related SAEs	1 (0.3%)	4 (1.2%)	0	5 (1.5%)
Deaths	0	1 (0.3%)	1 (0.3%)	0

Discontinuations				
Due to AEs	5 (1.5%)	9 (2.8%)	13 (3.9%)	10 (3.1%)
Due to TRAEs	3 (0.9%)	5 (1.5%)	9 (2.7%)	8 (2.5%)

Disclosures
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