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Drake M[1], Sokol R[2], Klaver M[3], Traudtner K[3], Drogendijk T[3], van Kerrebroeck P[3]
1. *Bristol Urological Institute, Bristol, UK,* ***2.*** *Private Urological Care Center, Piaristicka, Trencin, Slovakia,* ***3.*** *Astellas Pharma Global Development Europe, Leiderdorp, The Netherlands*

EVALUATING THE LONG-TERM SAFETY AND EFFICACY OF FIXED DOSE COMBINATIONS OF SOLIFENACIN AND TAMSULOSIN OCAS™ IN MALE LUTS WITH STORAGE AND VOIDING SYMPTOMS: RESULTS FROM THE NEPTUNE II STUDY

Hypothesis / aims of study
The NEPTUNE II study was designed to investigate the long-term safety and efficacy of a fixed-dose combination (FDC) tablet containing solifenacin (soli) and the oral controlled absorption system (OCAS™) formulation of tamsulosin (TOCAS) in patients with lower urinary tract symptoms (LUTS) associated with benign prostatic hyperplasia (BPH) who had both storage and voiding symptoms.

Study design, materials and methods
The NEPTUNE II study was a long-term (40 weeks), open-label, flexible-dosing, phase 3 safety study enrolling patients who had completed 12 weeks of double-blind treatment within the NEPTUNE study (1,2). Main exclusion criteria were a post-void residual volume >150 mL or a symptomatic urinary tract infection. All patients started with TOCAS 0.4 mg + soli 6 mg. After 4 weeks, patients could request to increase the dose to soli 9 mg, during subsequent visits patients could request to increase or decrease the soli dose at 3-month intervals. Data on FDC treatment from the NEPTUNE and NEPTUNE II studies have been combined to cover a 52-week period. The efficacy endpoints included the changes in total IPSS (International Prostate Symptom Score) and TUS (total urgency score; sum of the patients perception of intensity of urgency scale [PPIUS] score averaged over 3 days) from baseline to end of treatment.

Results
Of 1067 patients enrolled in NEPTUNE II, 1066 received at least one dose of study medication (safety population), and 1009 had either IPSS or TUS scores both at baseline and at least one time point after first dose (full analysis set). After 4 weeks of treatment, adjusted mean (SE) changes from baseline in total IPSS and TUS were –6.8 (0.28) and –8.7 (0.42), respectively, indicating improvements in symptoms. Reductions were maintained until the end of the study (–8.4 and –10.1, respectively, after 52 weeks treatment). Overall, treatment-emergent adverse events (TEAEs) were reported in 499 patients (46.8%); the most common were dry mouth and constipation. Urinary retention was reported by 8 patients (0.8%); 6 of these cases required catheterization and were reported as a serious adverse event (SAE) and 5 were treatment related. Treatment-related AEs (TRAEs) were reported in 23.9% of patients and serious TRAEs in 1.1% of patients. Overall, 106 (9.9%) patients discontinued prematurely and few discontinuations were due to TRAEs (28 [2.6%]). There were 3 deaths, none of which were related to the study medication.

Interpretation of results
Treatment for up to 1 year with TOCAS + soli is well tolerated in men with both storage and voiding LUTS.

Concluding message
Long-term treatment with TOCAS + soli administered in a single tablet was efficacious and well tolerated in men with LUTS/BPH with storage and voiding symptoms.

Summary of patients with TEAEs during up to 52 weeks TOCAS + soli treatment

	Total (n=1066)
Any AE	499 (46.8%)
AEs of interest	
Dry mouth	132 (12.4%)
Constipation	55 (5.2%)
Urinary retention	8 (0.8%)
Blurred vision	6 (0.6%)
TRAEs	255 (23.9%)
SAEs	64 (6.0%)
Treatment-related SAEs	12 (1.1%)
Deaths	3 (0.3%)
Discontinuations	106 (9.9%)
Due to AEs	42 (3.9%)
Due to TRAEs	28 (2.6%)

References
1. Drake M et al. Evaluating the efficacy and safety of fixed dose combinations of tamsulosin OCAS and solifenacin in male LUTS with storage and voiding symptoms: An overview of the NEPTUNE trial. Urology 2011; 78(Suppl 3A): 858 (Abstract MP-05.01).
2. Drake M et al. Efficacy of combination therapy with tamsulosin OCASTM and solifenacin in NEPTUNE: Results from a randomised, phase 3 trial in men with LUTS. Poster presented at the 27th Annual EAU Congress, Paris, 2012 (Abstract: 746).

Disclosures
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EudraCT 2008-001212-20 **RCT:** Yes **Subjects:** HUMAN **Ethics Committee:** The study was started after written approval from the South West Research Ethics Committee, Bristol, UK, at the principal study site, and local Independent Ethics Committees at other study sites, and after obtaining Clinical Trial Authorization from the relevant Competent Authority. **Helsinki:** Yes **Informed Consent:** Yes