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AN OPEN-LABEL, PROSPECTIVE INTERVENTIONAL STUDY OF THE TOLERABILITY AND EFFICACY OF ORAL HARNALIDGE® OCAS® (TAMSULOSIN) 0.4 MG IN PATIENTS WHO ARE UNSATISFIED WITH THE TREATMENT OF TAMSULOSIN 0.2 MG

Hypothesis / aims of study
Tamsulosin is an α1a -selective alpha blocker proven to be effective in treating benign prostatic hyperplasia (BPH). Doses of 0.2 mg and 0.4 mg are available yet the tolerability and efficacy of Oral Controlled Absorption System (OCAS) formulation remain to be studied in Asian men. This is the first data in the real world setting about the tolerability and efficacy of dose increase to Harnalidge® OCAS® 0.4 mg in Taiwanese males who are unsatisfied with tamsulosin 0.2 mg for the treatment of lower urinary tract symptoms (LUTS) associated with BPH.

Study design, materials and methods
This is a phase IV, prospective, open-label, single-arm study. After obtaining Institute Review Board approval and patient informed consents, subjects who met the inclusion criteria and not violating the exclusion criteria were enrolled to receive three-month treatment with Harnalidge® OCAS® 0.4 mg.
Subjects were eligible if they were diagnosed as LUTS associated BPH and had been taking oral Tamsulosin 0.2 mg for at least 4 weeks but still not satisfied with the treatment. Those who underwent prostatectomy; with neurogenic bladder dysfunction; bladder neck sclerosis; urethral stricture; prostatic cancer; cystolithiasis; severe vesical diverticulum; urinary tract infection or any other complication which may cause voiding dysfunction were excluded. Patients who had severe medical conditions, such as hepatic, renal, cardiovascular, orthostatic hypotension and senile dementia were not included.
The primary efficacy measures were changes from baseline in total scores of International Prostate Symptom Score (IPSS) at week 4, 8 & 12. The secondary efficacy measures were respective changes from baseline in IPSS subscores; Quality of life (QOL) index (IPSS-QOL); Uroflowmetry parameters (Qmax, Qave & post void residual volume.) and treatment satisfaction Visual Analogue Scale (VAS) at week 4, 8 & 12. Safety was assessed by physical examination, vital signs and adverse event reporting.

Results
A total of 100 patients were enrolled and 81(81%) patients completed the study. The mean age of study subjects was 64.8. After 12-week treatment with 0.4 mg Harnalidge OCAS® 0.4 mg, significant change in the total IPSS (15.2 to 7.8, $p<0.001$) from moderate to mild was observed. All the IPSS subscores of storage, voiding & nocturia improved significantly (-2.0; -5.1 &-0.5 respectively, all $P<0.001$). The impact of disease on the quality of life was alleviated (-1.9 in IPSS-QoL score). Patient reported treatment satisfaction VAS also increased from 40.2 to 73.2 ($p<0.001$).
There were 15 adverse events reported during the entire study period, three out of the fifteen recorded adverse events were rated as serious adverse events (including leukemia, recurrent HCC and epigastric hernia) which resulted in discontinuation of the study medication, however, none of them was considered related to the study medication. About 6-7% developed orthostatic hypotension in the current study as compared to 16% of patients in the US studies who received 0.4 mg tamsulosin, according to the package insert of Tamsulosin.

Interpretation of results
The overall efficacy of Harnalidge OCAS (tamsulosin 0.4 mg) is encouraging for subjects who were unsatisfied with previous 0.2mg tamsulosin treatment. The IPSS score including storage, voiding and nocturia subscores demonstrated significant improvement in both the “Full Analysis Set” (all participants who received any amount of study drug) and the “Per Protocol Set” (only those who completed the treatment originally assigned) population. Safety profile was in favour of 0.4mg and adverse events were mild to moderate in severity. Gradual titration by switching from 0.2 mg to 0.4 mg dose in this study may help reducing the incidence of orthostatic hypotension. Therefore, 0.4mg OCAS formulation may be recommended before switch the patients to another drug.

Concluding message
Harnalidge OCAS (tamsulosin 0.4 mg) demonstrates a good safety profile for the management of LUTS secondary to BPH in Taiwanese males who do not respond satisfactorily to 0.2 mg treatment. Increase the dose of tamsulosin results in further improvement in symptom scores and QoL without impacting the safety of the patients.

Disclosures
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