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A DOUBLE-BLIND, PLACEBO-CONTROLLED CLINICAL PHARMACOLOGICAL STUDY OF TAS-303 IN FEMALE PATIENTS WITH STRESS URINARY INCONTINENCE

Hypothesis / aims of study

TAS-303, a selective noradrenaline reuptake inhibitor, is currently at the stage of Phase II development for stress urinary incontinence (SUI) in Japan. In animal studies, TAS-303 has been shown to increase the noradrenaline-induced contraction in urethral preparations. The aim of this study was to evaluate pharmacological effect, safety and pharmacokinetics of TAS-303 in female patients with SUI.

Study design, materials and methods

A double-blind, single-dose, placebo-controlled crossover study of 18 mg TAS-303 was conducted in 16 female patients with SUI. Patients had to have the predominant symptom of SUI with ≥ 2 incontinent episodes per week and with moderate to severe leakage on 1-hour pad test. The urethral pressure profiles at rest were measured before and 6 hours after administration of TAS-303 or placebo. This study was approved by the institutional review board at Hakata Clinic in Fukuoka, Japan and registered at ClinicalTrials.gov as NCT02562807.

Results

The female patients had a mean age of 48.9 years and a mean body mass index of 21.9 kg/m². Ten of the 16 patients had SUI and the other 6 had mixed urinary incontinence. There was no statistically significant difference in the change in maximal urethral closure pressure (MUCP) from baseline to 6 hours between TAS-303 and placebo administration. In 2 of the patients, however, the MUCP increased by more than 10 cmH₂O after administration of TAS-303. Furthermore, one of these 2 patients had particularly high MUCP of more than 100 cmH₂O with TAS-303. After single oral administration of 18 mg TAS-303, there appeared to be no clinically significant difference in pharmacokinetic parameters between female SUI patients and healthy adult male subjects. There were no reports of serious adverse events, significant changes in blood pressure, or abnormal results on urinalysis.

Interpretation of results

The MUCP in 2 of 16 patients increased by more than 10 cmH₂O after single administration of TAS-303.

Concluding message

Considering the limitation of a single-dose study, the efficacy of TAS-303 should not be conclusively determined only by the results of this study. Instead, the efficacy of this drug should be evaluated more accurately in a Phase II study in which the primary endpoint is improvement of SUI symptoms.

Disclosures

Funding: Funding: Taiho Pharmaceutical Co., Ltd., Tokyo, Japan **Clinical Trial:** Yes **Registration Number:** This study was registered at ClinicalTrials.gov as NCT02562807. **RCT:** Yes **Subjects:** HUMAN **Ethics Committee:** This study was approved by the institutional review board at Hakata Clinic in Fukuoka, Japan. **Helsinki:** Yes **Informed Consent:** Yes