SAFETY OF ORAL OSPEMIFENE IN PHASE 2/3 PLACEBO-CONTROLLED CLINICAL TRIALS
S. Goldstein, D. Archer, S. Graham

Objective: To report the overall safety from the clinical development program of ospemifene, a tissue selective estrogen agonist/antagonist approved by the Food and Drug Administration (FDA) for the treatment of dyspareunia in postmenopausal women.

Design: Seven Phase 2/3 double-blind, placebo-controlled trials, ranging in duration from 6 to 52 weeks, assessed the safety of ospemifene in subjects receiving at least 1 dose of study drug ranging from <=15 to 90 mg/day, compared to placebo. Subjects were postmenopausal with a mean age of 59 years. Most subjects had an intact uterus. Endometrial biopsies were performed at Baseline, 12 weeks and 12 months for incidence of endometrial hyperplasia and carcinoma.

Results: No endometrial hyperplasia or carcinoma was reported in the ospemifene or placebo groups at 12 months. The safety population included 1696 women in the ospemifene group and 958 in placebo, and treatment emergent adverse events (TEAEs) were reported in 1118 (65.9%) vs 518 (54.1%) subjects, respectively. The majority of TEAEs were classified as mild or moderate in severity. No clear dose-related increase in adverse events (AEs) was seen with ospemifene. For ospemifene, the most commonly reported TEAE was hot flush (8.5% vs 3.3% for placebo) and incidence of venous thrombotic events was low (0.1%). Discontinuation due to TEAEs was <=7% in both groups. Overall discontinuation due to hot flush was 0.9% for ospemifene vs 0.3% for placebo. Serious adverse events (SAEs) were experienced by 2.3% ospemifene vs 1.8% placebo subjects. No deaths were reported in any of the trials.

Conclusion: Ospemifene was well tolerated in 7 double-blind, Phase 2/3, placebo-controlled trials that evaluated safety up to 52 weeks in postmenopausal women with VVA. These results support the use of ospemifene as the first oral alternative to estrogen prescription therapies for the treatment of dyspareunia in postmenopausal women.