

17 β -Estradiol/Progesterone in a Single Oral Softgel Capsule (TX-001HR) Significantly Reduced Moderate-to-Severe Vasomotor Symptoms without Endometrial Hyperplasia

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[CHARACTER LIMIT: 2000 including spaces; currently 1989]

Objective

To evaluate the efficacy, endometrial safety, and overall safety of TX-001HR in women with moderate-to-severe (mod-sev) menopausal vasomotor symptoms (VMS) and an intact uterus. TX-001HR is an investigational combination of 17 β -estradiol and progesterone (E2/P4) in a single, oral, softgel capsule.

Methods

The REPLENISH trial was a phase 3, 12-month, double-blind, multicenter trial. Women with mod-sev hot flashes (≥ 7 /day or ≥ 50 /week) were randomized (1:1:1:1:1) to E2/P4 (mg/mg) 1/100, 0.5/100, 0.5/50, 0.25/50, or placebo (VMS substudy); other women were randomized (1:1:1:1) to E2/P4 doses only; the endometrial and general safety analyses included all. In the VMS substudy, mod-sev VMS frequency and severity were tested from baseline to wks 4 and 12 vs placebo (4 co-primary endpoints). Incidence of endometrial hyperplasia and overall safety were also assessed.

Results

Participants had a mean age of 55 years, a mean BMI of 27 kg/m²; 65% were white and 32% were African American. E2/P4 1/100 or 0.5/100 vs placebo significantly improved ($P < .05$) the VMS frequency and severity at wks 4 and 12 from baseline. E2/P4 0.5/50 significantly improved ($P < .05$) frequency and severity at wk 12 from baseline, while E2/P4 0.25/50 significantly improved ($P < .05$) frequency, but not severity, at wks 4 and 12. Significantly more women were 50% responders (73–81% with E2/P4 vs 58% with placebo) and 75% responders (50–68% vs 32%). The mean daily number of mod-sev VMS decreased from 10–11 at baseline to 2–4 with TX-001HR (5 for placebo) at wk 12. No cases of endometrial hyperplasia or cancer were noted up to 12 mos. Changes in lipid and coagulation parameters were minimal. Treatment-emergent adverse events were of low incidence.

Conclusion

TX-001HR combinations of E2/P4 1/100 and 0.5/100 improved mod-sev VMS (all co-primary endpoints) with no unexpected safety signals. If approved, TX-001HR may provide a new option for treating mod-sev VMS in menopausal women with an intact uterus.