Introduction

Vaginal bleeding associated with hormone therapy (HT) is one of the most common reasons for treatment discontinuation. Cumulative amenorrhea rates (no bleeding or spotting for 13 cycles) range from 5% to 70% with current HT options. In October 2018, the US Food and Drug Administration (FDA) approved the first bioidentical HT containing 17β-estradiol and progesterone (E2/P4; 1 mg/100 mg) as BiEstra® (TherapeuticsMD, Boca Raton, FL), in a softgel capsule for the treatment of menopausal vasomotor symptoms (VMS) in women with a uterus.

The efficacy and safety of four E2/P4 doses were evaluated in the REPLENISH trial (NCT01942668) and results have been published.

- Proportions of women with amenorrhea (36%-73%) and no bleeding (74%-90%) were high with up to 1 year of treatment and both were ≥90% by cycle 13.
- Similar predictors were noted for bleeding at cycle 3, except for baseline VMS severity, which was not a significant predictor.

Methods

Study Design

REPLENISH (NCT01942668) was a phase 3, randomized, double-blind, placebo-controlled, multicenter trial that evaluated four E2/P4 doses in postmenopausal women with a uterus. Women with moderate to severe vasomotor symptoms (VMS) in women with a uterus were randomized 1:1:1:1 to dosages of 0.25 mg E2/P4 (reduction in risk of bleeding/spotting ≥4 days/week vs <4 days/week with respect to serum E2 and estrone (E1) concentrations; E2: 0.45 mg, E1: 0.53 mg, E2: 0.97 mg, E1: 0.52 mg) or placebo (4-13 cycles). Study treatments were taken orally at bedtime with food. Women were allowed to use any VMS treatment (non-HRT, oral HRT, or vaginal cream/patch) other than the study regimens. Concomitant use of non-contraceptive estrogen therapy was allowed.

The number of days with bleeding and spotting was summarized by cycle and treatment.

Conclusions

- Even though the rate/amount of bleeding was relatively low overall, these data may help clinicians inform women who may be more likely to experience vaginal bleeding while being combined, bioidentical E2/P4 for menopausal symptoms.

References