Uterine Bleeding Rates with Hormone Therapies in Menopausal Women with Vasomotor Symptoms
James H Pickar, MD1; David F Archer, MD2; Steven R Goldstein, MD3; Risa Kagan, MD4; Brian Bernick, MD5; Sebastian Mirkin, MD5

1Columbia University Medical Center, New York, NY; 2Eastern Virginia Medical School, Norfolk, VA; 3New York University School of Medicine, New York, NY; 4University of California, San Francisco and Sutter East Bay Medical Foundation, Berkeley, CA; 5TherapeuticsMD, Boca Raton, FL

Introduction
• Women often discontinue the use of hormone therapy (HT) taken for vasomotor symptoms (VMS) because of bleeding and spotting1

The REPLENISH trial (NCT01942668) evaluated a single oral capsule combining bioidentical 17β-estradiol and progestogens (E2/PR, TherapeuticMD, Boca Raton, FL) in postmenopausal women with a uterus seeking relief of moderate to severe VMS2

• The 1 mg E2/100 mg P4 dose was FDA approved as Bijuva3

Objective
To report the incidence of amenorrhea over 1 year with this E2/P4 and other continuous-combined HT commercially available in the US for the treatment of menopausal women with a uterus

Methods
• A list of FDA-approved, continuous-combined HT products indicated for menopausal women with a uterus and vasomotor symptoms was compiled3

• PubMed was searched for English-language studies using the following keywords: menopause, bleeding and hormones found in the FDA-approved products

• Estrogens: conjugated estrogens (CE) or estradiol or ethinyl estradiol

• Progestogens: medroxyprogesterone acetate (MPA), norethindrone acetate or norethindrone acetate (NETA), drospirenone, levonorgestrel (LNG)

• Prescribing information (PI) for these FDA-approved HT products was also obtained

One-year bleeding data (12-13 cycles) from randomized, controlled trials and PI of the continuous-combined oral or transdermal HT with at least 25 women per treatment group were compared with those of E2/PR in REPLENISH

• Amenorrhea was defined as no bleeding or spotting

• Spotting was defined as not requiring sanitary protection, while bleeding was defined as requiring sanitary protection

Results

Cumulative Amenorrhea Rates with E2/P4
In the REPLENISH trial, rates of cumulative amenorrhea from cycles 1 to 13 increased over time with the E2/PR 1 mg/100 mg versus placebo (Figure 1)4

Other FDA-approved, Continuous-combined HT Products
Table 1 lists the prescription hormone preparations included in the review based on PI

Overall Results from Clinical Trials and PI Data
• Proportions of women with cumulative amenorrhea over one year, amenorrhea at cycle 12-13, and mean bleeding/spotting days based on data from the clinical trials and PI are shown in Table 2

Conclusions
• Compared with published bleeding data reported separately for other continuous-combined HT, E2/P4 appears to have a positive bleeding profile

• Note that comparisons were derived from separate studies with each product and not head-to-head trials

• The high rates of cumulative amenorrhea with Bijuva make it a therapeutic option for postmenopausal women seeking treatment for moderate to severe VMS who are concerned about bleeding

References

Appendix
Role of the funder(s): The sponsors had no role in the design, conduct, or reporting of this study.

Table 1. FDA-approved, continuous-combined HT formulations used to treat vasomotor symptoms, included in this comparison review

Table 2. Summary of amenorrhea rates and number of bleeding/spotting days with FDA-approved continuous HT

Figure 1. Cumulative amenorrhea rates over one year with E2/P4

Figure 2. Mean bleeding/spotting days with FDA-approved continuous HT

Figure 3. Mean bleeding/spotting days at cycle 12-13, ranked from least to most improved

Table 1. FDA-approved, continuous-combined HT formulations used to treat vasomotor symptoms, included in this comparison review

Table 2. Summary of amenorrhea rates and number of bleeding/spotting days with FDA-approved continuous HT