**Introduction**

Dyspareunia and vaginal dryness occur in postmenopausal women as a result of the decreased estradiol levels, thinning, drying, and loss of elasticity of the vaginal epithelium due to reduced estrogen levels, also known as vulvar and vaginal atrophy (VVA), a component of the genitourinary syndrome of menopause (GSM).

**TX-004HR** is a softgel vaginal insert of ultra-low-dose solubilized 17β-estradiol (E2), designed to be mucoadhesive and rapidly dissolving.

**Methods**

**Study Design**

- **REDOCE (NCT02255173)** was a 12-week, randomized, double-blind, placebo-controlled, multicenter trial that evaluated the E2 vaginal insert in postmenopausal women (≥67 years) with VVA and a most bothersome symptom of moderate to severe dyspareunia.

- Women were randomized to the E2 insert at 4 µg, 10 µg, or 25 µg or a matching placebo vaginal insert once a day for 2 weeks, and then twice weekly for 10 weeks.

- Co-primary efficacy endpoints analyzed for each dose were changes from baseline to week 12 compared with placebo for percentages of vaginal superficial and parabasal cells, vaginal pH, and dyspareunia severity.

- Women who received treatment had baseline values for all co-primary variables and at least one post-baseline value for the co-primary variable, completed the study at week 12, and were ≥80% overall study drug compliant; were included in the efficacy evaluable (EE) population.

**Responder Analyses**

- Responders were defined as responders who met all inclusion criteria and who had at least one post-baseline value for the co-primary variables, completed the study at week 12, and were ≥80% overall study drug compliant.

**Results**

When all women (independent of treatment) were analyzed in aggregate, a consistent effect of TX-004HR in menopausal women with moderate to severe dyspareunia was observed as early as 2 weeks of therapy as shown by the highest percentage of responders to TX-004HR at week 2 predicted a positive response at week 12.

- **Table 2** shows these data may inform clinicians counseling women with moderate to severe dyspareunia associated with menopause regarding the E2 vaginal insert (TX-004HR).

**Conclusions**

A consistent effect of TX-004HR in menopausal women with moderate to severe dyspareunia was observed as early as 2 weeks of therapy as shown by the highest percentage of responders.

**Acknowledgments**

Dr. Constantine consults for multiple pharmaceutical companies including but not limited to TherapeuticsMD and has stock options from TherapeuticsMD. Dr. Millheiser has served as consultant to or on the advisory boards of Allergan, Aytu Biologics, Duchesnay, Exploramed, Indevus Pharmaceuticals, Valeant, and Willow; is a stockholder in Aytu Biologics, Viveve, and Willow; is currently Chief Medical Officer of Sprout Pharmaceuticals. Dr. Kaunitz is serving as consultant to or on the advisory boards of AMAG Pharmaceuticals, Bayer Healthcare, Miltenyi, and Shionogi, and has received research support from the University of Florida College of Medicine-Jacksonville. Dr. Portman is a member of the TherapeuticsMD scientific advisory board. Dr. Graham, Bernick, and Mirkin are employees of TherapeuticsMD with stock options from TherapeuticsMD and has stock options from TherapeuticsMD.

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