Introduction

The incidence of endometrial cancer differed between medroxyprogesterone acetate (MPA) and conjugated equine estrogens (CEE) in the PEPI and SAT-278 trials. In the PEPI trial, the combination of CEE and MPA effectively prevented endometrial hyperplasia. The SAT-278 trial showed that MPA prevented endometrial hyperplasia with various CEE doses.

Study Design

Women's HOPE Study

- 12-month randomized, double-blind, placebo-controlled, multicenter trial in menopausal women
- Evaluated the endometrial safety and uterine bleeding of doses of continuous combined CEE and MPA or CEE alone in cycles 1–13

Table 1. Endometrial Hyperplasia Incidence in the REPLENISH Trial

<table>
<thead>
<tr>
<th>Treatment (mg)</th>
<th>Endometrial safety and uterine bleeding incidence (%)</th>
</tr>
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<tr>
<td>CEE 0.625/MPA 2.5</td>
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Conclusions

- TX-001HR (E2/P4) provided endometrial protection in the 1-year REPLENISH trial.
- Incidence rates of endometrial hyperplasia at year 1 with all P4 doses combined were lower than with placebo.
- Cumulative safety Incidence rates increased over time. At 12 months, bleeding rates were 61–72%, with 68–85% with placebo.
- If approved, TX-001HR may be an appropriate alternative combination hormone therapy for treating menopausal women with uterine hyperplasia, while protecting the endometrium.

Disclosures

Presented at the 2018 ENDO Meeting, March 17-20, 2018 in Chicago, IL.

References


Figure 4. Cumulative Amenorrhea from Cycle 1 to 13 in the Women's HOPE Study and the REPLENISH Trial

Figure 5. REPLENISH Trial Disposition

Endometrial Hyperplasia Assessment

- Endometrial biopsies were performed and evaluated similarly in both studies.
- Incidence of endometrial hyperplasia at 1 year was a primary endpoint of both trials.
- CEE 0.625/2.5 mg with placebo in the PEPI trial
- Endometrial biopsies were performed at baseline and Month 12 and treatment (as cycles 1 and 6 in the Women's HOPE study).
- Biopsy specimens were processed by a central laboratory.
- Biopsy slides were reviewed by 2–3 pathologists.
- A pretest of the 17\β-estradiol was required to diagnose endometrial hyperplasia.
- No hyperplasia on biopsy at baseline for study eligibility.
- Patients who developed endometrial hyperplasia was withdrawn from the study and given the appropriate treatment.

Bleeding and Spotting Assessment

- A complete daily vaginal bleeding and spotting profile was assessed between treatment groups over thirteen 28-day cycles.
- Bleeding profiles, including cumulative amenorrhea (no bleeding or spotting) were assessed.

- Endometrial safety and uterine bleeding incidence were 0% after 1 year (Table 1).

Table 2. Endometrial Hyperplasia Incidence in the REPLENISH Trial

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- Endometrial hyperplasia incidence was 0% after 1 year (Table 2).
- No endometrial malignancies detected with any TX-001HR dose or placebo.

Figure 6. Women's HOPE Study

- The Women's Health, Osteoporosis, Progestin, Estrogen (Women's HOPE) study also showed that MPA prevented endometrial hyperplasia with various CEE doses.

Figure 2. Disposition and Demographics

- Women had a mean age of 53 years, and mean BMI of 24 kg/m².
- 19% of women discontinued the study.

Majority was white (88%), followed by African American (6%) or Hispanic (4%).

- Women in both studies completed diaries of daily vaginal bleeding and spotting up to month 12.

Results

- Evaluating endometrial safety and uterine bleeding of continuous combined doses of TX-001HR vs placebo on the endometrium.

Figure 3. Endometrial Safety

- TX-001HR is an investigational combination of solubilized E2 and micronized and suspended estradiol and natural progesterone (P4) when used with estrogens for endometrial protection.

TX-001HR (TherapeuticsMD, Boca Raton, FL) is an investigational vaginal E2 drug not yet approved by the U.S. FDA.