

TX-001HR Improved the Medical Outcomes Study-Sleep (MOS-Sleep) questionnaire in Menopausal Women with Vasomotor Symptoms

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Menopausal VMS Treatment

- Vasomotor symptoms (VMS) in menopausal women can
 - Be bothersome¹⁻³
 - Negatively impact quality of life,^{1,4} sleep,^{1,5} and work productivity^{4,6}
- **REPLENISH trial**
 - TX-001HR (TherapeuticsMD, Boca Raton, FL) is an investigational combination of 17 β -estradiol and progesterone in a single oral softgel capsule
 - One secondary objective was to evaluate the effects of four TX-001HR (E2/P4) doses versus placebo on sleep parameters when used for the treatment of moderate-to-severe VMS

E2: estradiol; P4: progesterone.

Study Design: Randomization

VMS substudy (12 wks)

- ≥ 7 /day or ≥ 50 /week moderate-to-severe hot flushes
- Randomized 1:1:1:1:1

Treatment Groups

- 1.0 mg E2/100 mg P4
- 0.5 mg E2/100 mg P4
- 0.5 mg E2/50 mg P4
- 0.25 mg E2/50 mg P4
- Placebo

General study (12 mos)

- Did not qualify for VMS substudy
- Randomized 1:1:1:1

- Both populations were assessed for sleep parameters using the Medical Outcomes Study (MOS)-Sleep Questionnaire

Medical Outcomes Study (MOS)-Sleep Questionnaire

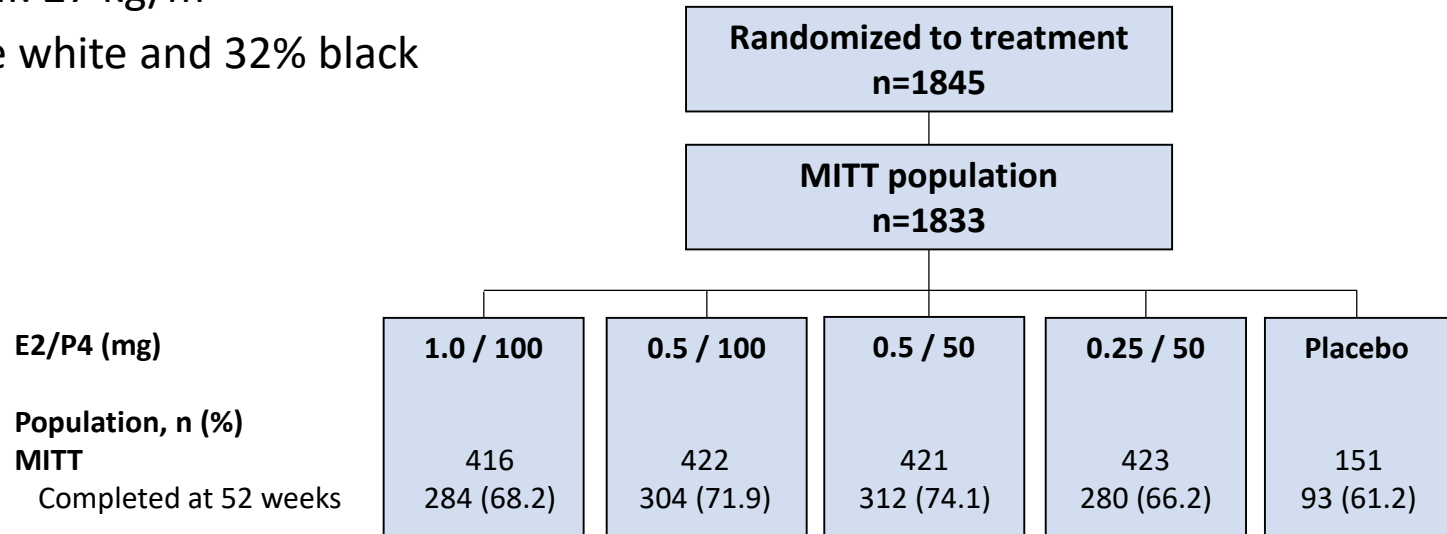
- MOS-Sleep is a 12-item questionnaire measuring 6 sleep dimensions over the past 4 weeks
 - The last 4 items* were scored using a 6-item Likert scale ranging from “All of the time” to “None of the time”

Sleep Dimensions	Subscales (derived from sleep dimensions)
<ul style="list-style-type: none">• Initiation (time to fall asleep)• Quantity (hours of sleep each night)• Maintenance*• Respiratory problems*• Perceived adequacy*• Somnolence*	<ul style="list-style-type: none">• Sleep Problems Index I (short form)• Sleep Problems Index II (long form)• Sleep disturbance• Sleep somnolence• Snoring• Sleep shortness of breath or headache

- MOS-Sleep questionnaire was administered at baseline, week 12 and months 6 and 12
- Change from baseline in total and subscale scores were analyzed for each treatment versus placebo at each time point in the MITT population

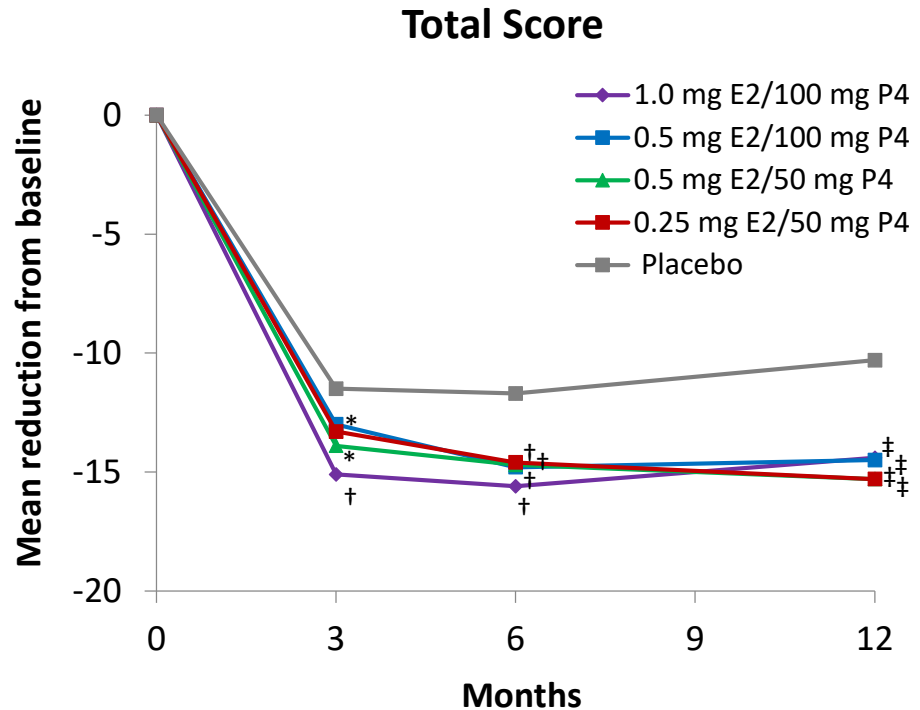
Disposition and Demographics

- 69% of women completed at 52 weeks
- Mean age: 55 years (40–66)
- Mean BMI: 27 kg/m²
- 65% were white and 32% black



Improvements in MOS-Sleep Total Score

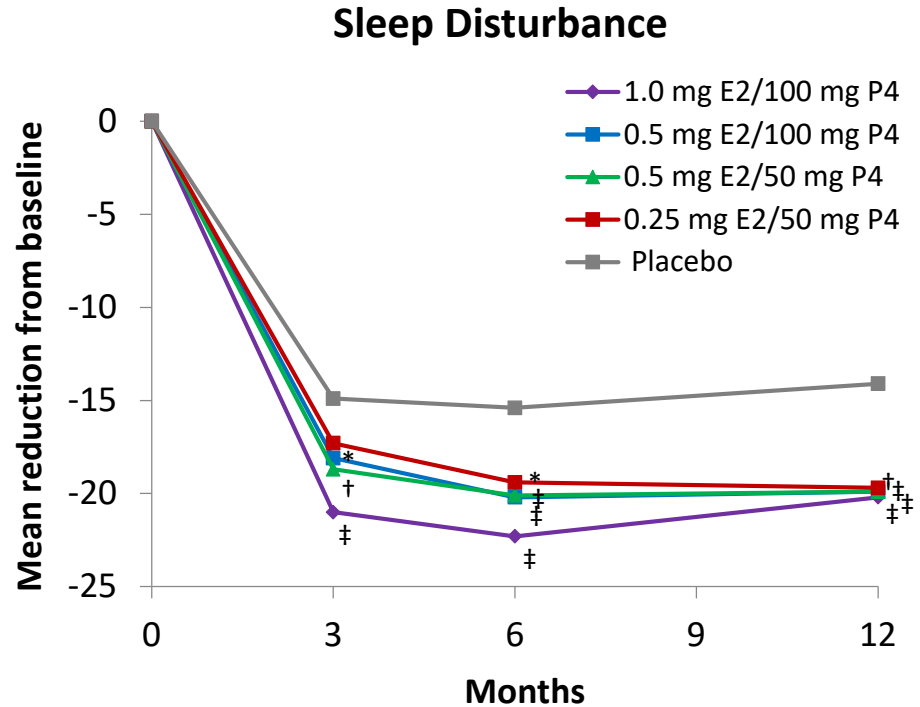
- All doses of TX-001HR significantly improved the MOS-Sleep total score versus placebo at week 12 and months 6 and 12
 - Except for those treated with the lowest dose at week 12
- Total scores ranged from 43.2–48.1 at baseline and were 27.5–29.4 with TX-001HR and 37.4 with placebo at month 12



* $P < 0.05$; † $P < 0.01$; ‡ $P < 0.001$ vs placebo.

Improvements in Sleep Disturbance Subscale

- Sleep disturbance subscale significantly decreased from baseline with TX-001HR versus placebo at all timepoints
 - Except for the lowest TX-001HR dose at week 12



* $P < 0.05$; † $P < 0.01$; ‡ $P < 0.001$ vs placebo.

Improvements in Sleep Problems Index I Subscale

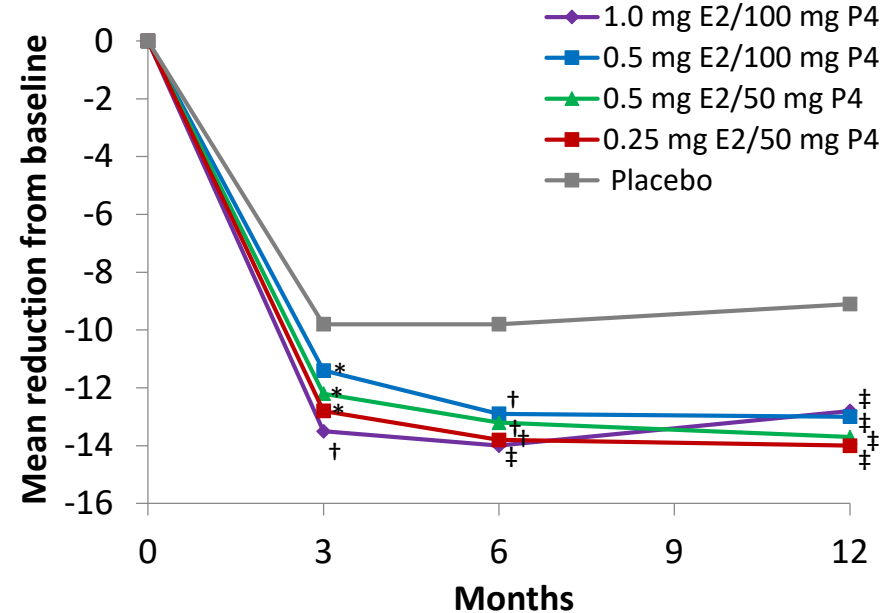
- All doses of TX-001HR significantly improved the Sleep Problems Index I subscale from baseline versus placebo to all timepoints

Sleep problems index I based on

How often during the past 4 weeks did you...

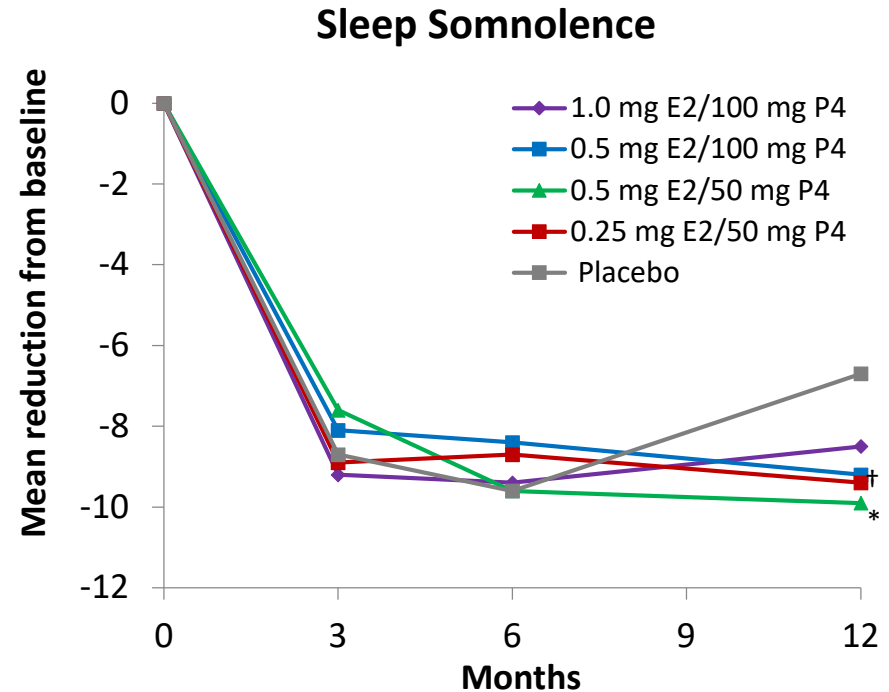
- Get enough sleep to feel rested upon waking?
- Awaken short of breath or with a headache?
- Have trouble falling asleep?
- Awaken and have trouble falling asleep again
- Have trouble staying awake during the day?
- Get the amount of sleep you needed?

Sleep Problems Index I



Improvements in Sleep Somnolence Subscale

- Sleep somnolence subscale significantly improved from baseline with TX-001HR doses 0.5 mg E2/100 mg P4 and 0.5 mg E2/50 mg P4 compared with placebo at month 12
 - TEAE incidence of somnolence was low (0.2% to 1.2%) with TX-001HR
- TX-001HR had no effects on the snoring subscale, or the sleep shortness of breath or headache subscale



* $P < 0.05$; † $P < 0.01$ vs placebo.

Conclusions

- All doses of TX-001HR significantly improved sleep parameters typically associated with menopause from baseline up to 12 months compared with placebo
 - Some improvements with the lowest dose was not significant at 12 weeks
 - The reported incidence of somnolence was also very low
- If approved, TX-001HR may provide the first oral combination of E2/P4 for treating moderate-to-severe VMS and could represent a new treatment option for menopausal women currently using unapproved and unregulated compounded bioidentical HT