SKYLIGHT 4: Phase 3 Long-Term Safety Study of Fezolinetant for Vasomotor Symptoms Associated With Menopause

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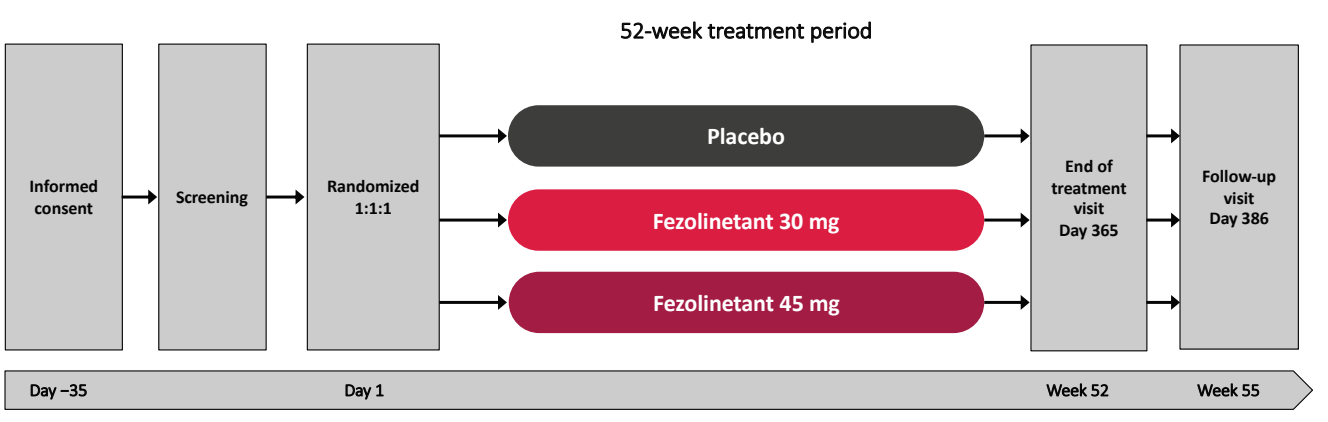
- Vasomotor symptoms (VMS, eg, hot flashes, night sweats) are experienced by most women during the menopausal transition and can have a substantial impact on quality of life

1. Why was this study done?

- Fezolinetant is a nonhormonal, selective neurokinin 3 receptor antagonist in development for treatment of moderate-to-severe VMS associated with menopause
- Results from the Phase 3 SKYLIGHT 1 (NCT04003155) and SKYLIGHT 2 (NCT04003142) studies showed that fezolinetant 30 mg and 45 mg met statistical significance in reducing VMS frequency and severity at weeks 4 and 12 vs placebo
  - Over the 12-week double-blind period, there was a low incidence of individual treatment-emergent adverse events (TEAEs) and few serious TEAEs with fezolinetant treatment
- SKYLIGHT 4 (NCT04003389) was conducted to provide 52-week, placebo-controlled safety data in a large cohort, with a focus on endometrial safety

2. What was the study design?



3. What was the study population?

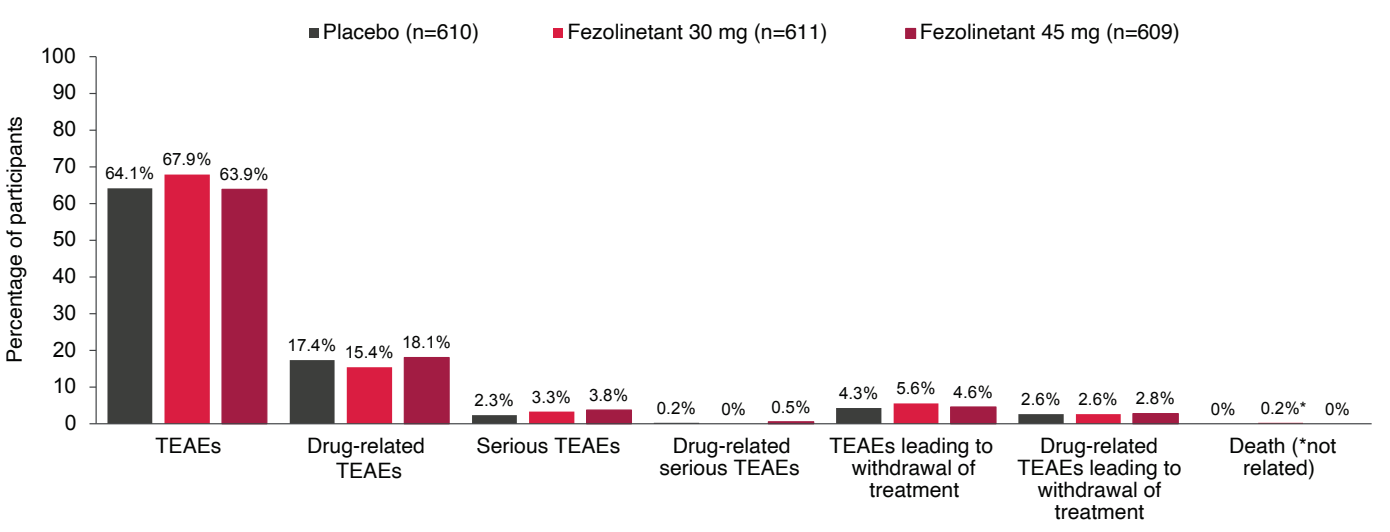
- Age ≥40 to ≤65 years
- Postmenopausal
- Seeking treatment for VMS associated with menopause
- Body mass index ≥18 kg/m² and ≤38 kg/m²
- Not had a hysterectomy (following protocol amendment)

4. What were the primary study endpoints?

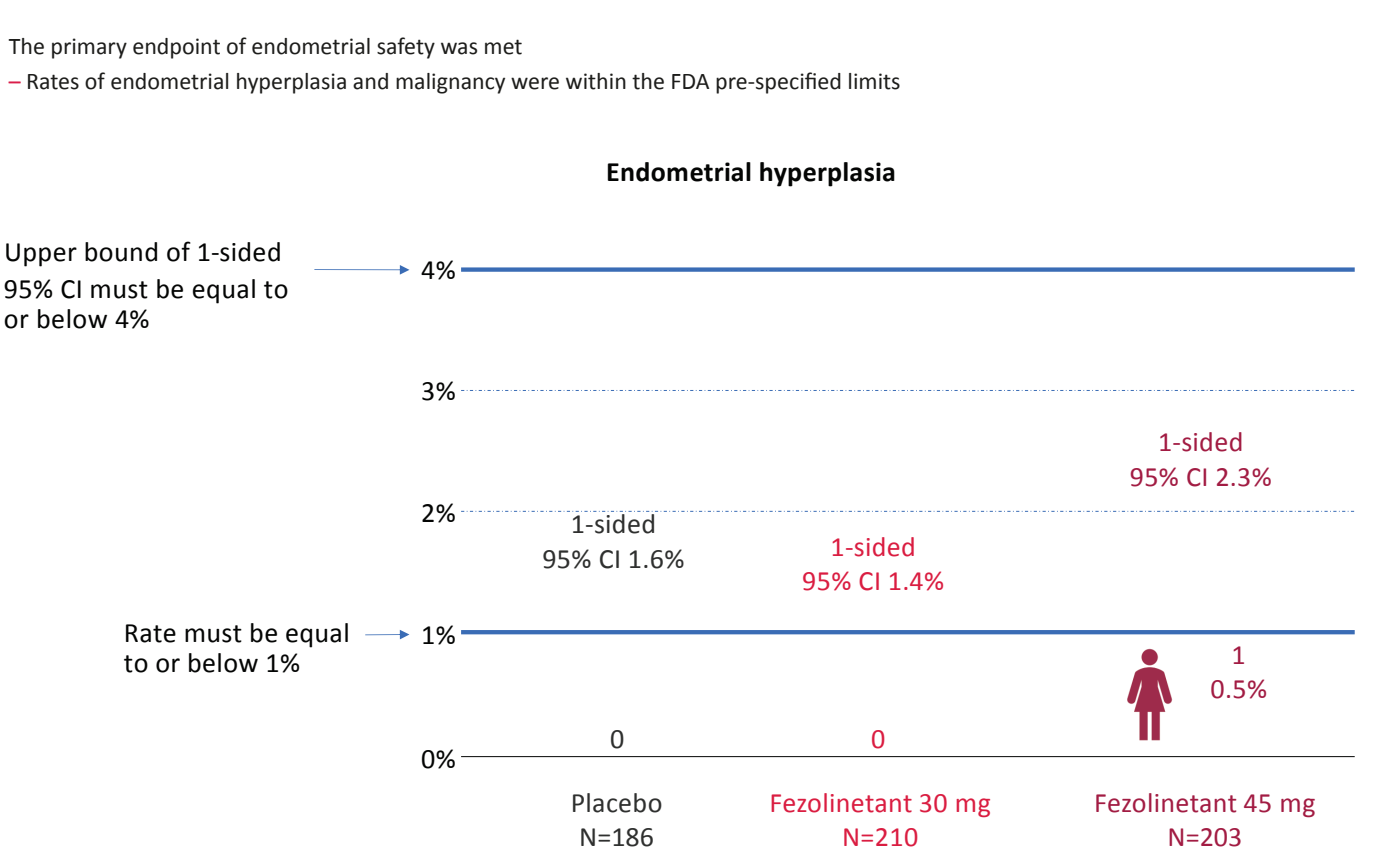
- Frequency and severity of TEAEs
- Percentages of participants with endometrial hyperplasia
- Percentages of participants with endometrial malignancy

5. What were the main results?

- TEAEs were similar across treatment groups



- The primary endpoint of endometrial safety was met
  - Rates of endometrial hyperplasia and malignancy were within the FDA pre-specified limits



6. What were the other key results?

The most common TEAEs were headache and COVID-19, with a similar incidence across treatment groups

There was no significant difference in endometrial thickness between fezolinetant- and placebo-treated participants

Overall, elevations in liver enzymes were low across treatment groups, asymptomatic, resolved on treatment or after treatment discontinuation, and no cases of Hy's Law were reported

A potential Hy's Law case is defined as: (alanine aminotransferase or aspartate aminotransferase >3 x upper limit of normal) and total bilirubin >2 x upper limit of normal, with no elevation of alkaline phosphatase and no other reason to explain the combination

7. What were the study conclusions?

- Safety data over 52 weeks of study support the use of fezolinetant for VMS associated with menopause
- Primary endpoints of endometrial hyperplasia or malignancy were each within the FDA pre-specified limits
- No significant difference in endometrial thickness between fezolinetant- and placebo-treated participants
- The safety data generated from 1830 participants in this study demonstrate the long-term safety and tolerability of fezolinetant 30 mg and 45 mg and support its long-term use

8. Further information

- The full article is called "Safety of Fezolinetant for Vasomotor Symptoms Associated With Menopause: A Randomized Controlled Trial"
- Fezolinetant is not currently approved for the treatment of vasomotor symptoms associated with menopause
- This summary reports the results of one study and may differ from the results of other studies
- This summary is not a substitute for medical advice. Always contact your healthcare provider if you have any health problems
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The original authors of the full article were involved in preparing this summary.
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Neal-Perry G, Cano A, Lederman S, Nappi RE, Santoro N, Wolfman W, et al. Safety of fezolinetant for vasomotor symptoms associated with menopause: a randomized controlled trial. Obstet Gynecol 2023;141.
The authors provided this information as a supplement to their article.