Elinzanetant for the treatment of vasomotor symptoms in menopause – results of the OASIS-3 study

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Elinzanetant for the Treatment of Vasomotor Symptoms Associated With Menopause: A Phase 3 Randomized Clinical Trial.

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BACKGROUND

Vasomotor symptoms (VMS) are among the most common complaints during perimenopause and postmenopause. Up to 80% of women are affected. In addition, sleep disturbances often occur in about 60% of those affected. Hormone replacement therapy (HRT) is effective, but not suitable for all women – either due to contraindications or personal preferences. Elinzanetant, an NK-1/3 receptor antagonist, is a non-hormonal treatment option for menopausal VMS, alongside the already approved NK-3 receptor antagonist fezolinetant. The efficacy studies on elinzanetant OASIS 1 and 2 over 26 weeks have already been published (1).

SUMMARY

The current randomised, double-blind, placebo-controlled phase 3 study OASIS-3 included 628 postmenopausal women aged between 40 and 65 with moderate to severe VMS. The subjects were randomised in a 1:1 ratio and received either elinzanetant 120 mg daily (n = 313) or placebo (n = 315) over 52 weeks. The primary endpoint was the change in the frequency of moderate to severe VMS between baseline and week 12. Secondary endpoints included the change in sleep disturbances (PROMIS SD-SF-8b) and menopause-specific quality of life (MENQOL).

At baseline, the women reported an average of 6.7 (SD 7.2) and 6.8 (SD 6.2) VMS episodes per day, respectively. After 12 weeks, the frequency decreased by −5.4 episodes (95% CI −6.3 to −4.5) in the elinzanetant group compared to −3.5 episodes (95% CI −4.1 to −2.9) in the placebo group. Relative to baseline, this corresponded to a reduction of 73.8% (95% CI −78.6% to −69.1%) in the verum group compared to 47.0% (95% CI −56.5% to −37.4%) under placebo. The severity of VMS also decreased more in week 12 with elinzanetant (−1.2 [95% CI −1.3 to −1.1]) than with placebo (−0.8 [95% CI −0.9 to −0.7]). Sleep disturbances improved by −9.4 points (95% CI −10.7 to −8.0) on the PROMIS scale by week 52, while the placebo group achieved an improvement of −5.7 points (95% CI −7.0 to −4.5). MENQOL total scores decreased by −1.3 points (95% CI −1.5 to −1.1) with elinzanetant compared with −1.1 points (95% CI −1.3 to −0.9) with placebo.

The overall safety profile was favourable. Adverse events occurred in 70.0% of women receiving elinzanetant and 61.1% receiving placebo. Treatment-related adverse events were observed in 30.4% of the verum group and 14.6% of the placebo group. The most common treatment-related adverse events were somnolence (4.8% vs. 1.0%), fatigue (4.2% vs. 1.6%) and headache (3.2% vs. 1.6%). Serious adverse events occurred in 4.2% vs. 1.9% ( ), but were not classified as therapy-related. Important safety endpoints showed no abnormalities: no cases of endometrial hyperplasia, no hepatotoxic effects, no clinically relevant changes in bone density.

COMMENT

In summary, OASIS-3 shows that elinzanetant causes a statistically significant and clinically relevant reduction in VMS over 52 weeks, with additional benefits for sleep and quality of life. The safety profile appears favourable. However, there are also limitations: the study was only statistically powered for the primary endpoint, so the results on sleep and quality of life should be interpreted with caution. The transferability is limited because certain patient groups were excluded (e.g. women with cancer) and ethnic diversity remained limited (over 75% white). In addition, mammograms were only performed in around 40% of cases at the end of the study.

REFERENCES

(1) Pinkerton JV, Simon JA, Joffe H, Maki PM, Nappi RE, Panay N, Soares CN, Thurston RC, Caetano C, Haberland C, Haseli Mashhadi N, Krahn U, Mellinger U, Parke S, Seitz C, Zuurman L.
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