Deutsche Menopause Gesellschaft e.V.

FIRST TO KNOW

ON THE HORIZONT: SELECTIVE NEUROKININ-1,3-RECEPTOR-ANTAGONIST ELINZANETANT

Schweizerische Gesellschaft für Gynäkologische Endokrinologie, Kontrazeption und Menopause

NEWSLETTER OCTOBER 2024

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.

Elinzanetant for the Treatment of Vasomotor Symptoms Associated With Menopause: OASIS 1 and 2 Randomized Clinical Trials.

JAMA. 2024 Aug 22:e2414618. doi: 10.1001/jama.2024.14618.

BACKGROUND

The non-hormonal neurokinin-3 receptor antagonist fezolinetant (45 mg/day) was approved by the EMA in December 2023 for the treatment of vasomotor symptoms (VMS) associated with menopause. Results from the pivotal OASIS 1+2 studies for elinzanetant were published in August. Elinzanetant is a selective neurokinin 1,3 receptor antagonist being investigated for the treatment of menopausal VMS. The drug has already been submitted to the FDA for approval.

SUMMARY

OASIS 1+2 are two phase 3, randomised, double-blind, placebo-controlled trials (RCTs) involving 400 postmenopausal women aged 40-65 years with moderate to severe VMS. Women in the active treatment arm received oral elinzanetant at a dose of 120 mg/day for 26 weeks. Women in the placebo arm received placebo for 12 weeks, followed by 14 weeks of oral elinzanetant at 120 mg/day.

The primary outcome was the mean change from baseline in the frequency and severity of moderate-to-severe VMS at weeks 4 and 12, and the secondary outcomes were sleep quality (PROMIS SD SF 8b questionnaire) and menopause-related quality of life (MENQOL questionnaire). At baseline, participants in the elinzanetant and placebo groups had an average of 13-16 VMS per day. After 4 weeks, the number of VMS was significantly reduced by 55.9% (OASIS 1) to 57.9% (OASIS 2) with elinzanetant and by 65.2% (OASIS 1) to 67.0% (OASIS 2) after 12 weeks. In the placebo group, the number of VMS decreased by 31.4% / 35.7% (week 4; OASIS 1+2) and 42.2% / 45.9% (week 12; OASIS 1+2). Elinzanetant also improved VMS severity, sleep disturbance and menopause-related quality of life. Headache (7-9%) and fatigue (5.5-7%) were more common in the active treatment group than in the placebo group (2.6% and 1.5%, respectively). Details of liver function tests are not reported, only that there was no evidence of hepatic toxicity.

COMMENTARY

Elinzanetant could be another non-hormonal treatment option for menopausal VMS from 2025/2026. At first glance, fezolinetant and elinzanetant appear to reduce the incidence of VMS equally well, but a head-to-head RCT would be needed to make a definitive comparison. It is hoped that additional blockade of the NK1 receptor will further improve sleep. This would also require another RCT in women with menopausal sleep disorders, as OASIS 1+2 primarily

included women with menopausal hot flushes. The efficacy trials of elinzanetant were shorter (26 weeks) than those of fezolinetant (52 weeks) (1,2). Therefore, the results of the OASIS 3 safety study need to be awaited for more detailed information, such as liver function tests.

REFERENCES

(1) Santoro N, Nappi RE, Neal-Perry G, English M, King DD, Yamaguchi Y, Ottery FD. Fezolinetant treatment of moderate-to-severe vasomotor symptoms due to menopause: effect of intrinsic and extrinsic factors in two phase 3 studies (SKYLIGHT 1 and 2). *Menopause. 2024 Apr 1;31(4):247-257. doi: 10.1097/GME.0000000000002340. PMID: 38517210.*

(2) Johnson KA, Martin N, Nappi RE, Neal-Perry G, Shapiro M, Stute P, Thurston RC, Wolfman W, English M, Franklin C, Lee M, Santoro N. Efficacy and Safety of Fezolinetant in Moderate to Severe Vasomotor Symptoms Associated With Menopause: A Phase 3 RCT. *J Clin Endocrinol Metab. 2023 Jul 14;108(8):1981-1997. doi: 10.1210/clinem/dgad058. PMID: 36734148; PMCID: PMC10348473.*

HERAUSGEBER
Deutsche Menopause Gesellschaft e.V.
Präsidentin: Dr. Katrin Schaudig

REDAKTION
Prof. Dr. Petra Stute
Leitende Ärztin Gyn. Endokrionologie und Reproduktionsmedizin, Inselspital Bern

GESCHÄFTSSTELLE
Anne Becker, 35041 Marburg
E-mail: Info-DMG@email.de
www.menopause-gesellschaft.de