PRESS RELEASE

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Late-stage study finds menopause drug fezolinetant safely reduces hot flushes for almost 6 months

Fezolinetant reduces the frequency and severity of hot flushes during menopause for 24 weeks, without serious side effects, according to research presented at the 26th European Congress of Endocrinology in Stockholm. These findings provide further evidence of the benefits of using this non-hormonal preventative drug in women experiencing hot flushes during menopause.

Hot flushes and night sweats, also known as vasomotor symptoms (VMS), affect up to 80% of women going through menopause and can severely impact daily life, exercise and sleep. Hormone replacement therapy (HRT) is the most effective treatment, but these drugs are not suitable for some women, such as survivors of endocrine cancer or those who have untreated high blood pressure; and others choose not to take them mainly due to the potential side effects.

The new type of non-hormonal drug, fezolinetant – approved by the US Food and Drug Administration (FDA) and the European Medicines Agency (EMA) last year – acts directly on the temperature-control pathway and alleviates these symptoms. Specifically, it works by blocking a brain protein called neurokinin-3 (NK-3), involved in regulating body temperature. But unlike hormone therapy which replaces estrogen, fezolinetant will not alleviate other menopausal symptoms such as mood changes or vaginal dryness.

Previous late-stage clinical trials (SKYLIGHT 1 and SKYLIGHT 2) have shown that fezolinetant reduces both the frequency and severity of hot flushes in women with moderate or severe symptoms compared to placebo over 12 weeks. This phase 3b study, known as DAYLIGHT and supported by Astellas Pharma, investigated the effect of fezolinetant use over 24 weeks.

Researchers examined 453 menopausal women aged 40–65 with moderate or severe hot flushes who were unsuitable for hormone replacement therapy, after giving them 45mg of fezolinetant or placebo, and found that women who took fezolinetant had less frequent and severe hot flushes throughout the 24 weeks. Women taking fezolinetant had consistently fewer hot flushes in the first week, with the strongest decrease during the first 3 days. The severity of their hot flushes was also reduced dramatically by the drug in the first week from the second day. No safety issues were found for the 45mg fezolinetant dose over the 24 weeks.

“DAYLIGHT is the first study of fezolinetant to investigate placebo-controlled efficacy over 24 weeks”, said Professor Antonio Cano from the INCLIVA Research Institute in Valencia, Spain, who was involved in the study.

“Fezolinetant was effective and well tolerated for 24 weeks and the effect was observed as early as day 1 of treatment. While there are other NK antagonists, none have shown a similar concurrence of efficacy and safety in clinical studies with a sufficiently high number of participants.”

“A safe and effective non-hormonal molecule may be available for the very high number of menopausal women who suffer from vasomotor symptoms and improve their overall health, quality of life and work performance. However, these symptoms vary in prevalence or intensity depending on ethnicity – for example, VMS are more frequent and severe in black women – so more clinical data are needed in different populations or geographical areas in the world.”

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Abstract
P352

Early Response with Fezolinetant Treatment of Moderate-to-Severe Vasomotor Symptoms Associated with Menopause in Women Considered Unsuitable for Hormone Therapy: Phase 3b DAYLIGHT Study

Introduction
There is a need for well tolerated and effective nonhormonal therapies for vasomotor symptoms (VMS) associated with menopause. Fezolinetant is a nonhormonal, selective neurokinin 3 receptor antagonist that is approved for the treatment of moderate-to-severe VMS associated with menopause.

Objective
To assess how early a response to fezolinetant in frequency and severity of moderate-to-severe VMS was observed in the 24-week placebo-controlled DAYLIGHT study.

Methods
DAYLIGHT (NCT05033886) was a phase 3b, randomised, double-blind, 24-week placebo-controlled study. Participants were women aged ≥40 to ≤65 years with moderate-to-severe VMS who were unsuitable for hormone therapy (HT) based on four categories - contraindications, caution (prior medical history), stoppers (lack of efficacy, side effects, or medical advice), or averse (made informed choice not to take HT after discussion with clinician) - and randomised 1:1 to placebo or fezolinetant 45 mg once daily. The primary endpoint was mean change in daily VMS frequency of moderate-to-severe episodes from baseline to week 24. Mean change in VMS severity (key secondary endpoint) and safety were also assessed.

Results
Overall, 453 women were enrolled (placebo n=226; fezolinetant n=227), including HT contraindicated (51, 11%), caution (165, 36%), stoppers (69, 15%), and averse (168, 37%).
Participants treated with fezolinetant 45 mg had a greater reduction from baseline in the daily mean change in frequency of moderate-to-severe VMS compared with placebo during the first week of treatment (day 7 least squares [LS] mean difference: –2.20; 95% CI: –2.78, –1.61; p<0.001). VMS frequency consistently decreased from days 1 to 6, with the strongest decrease during the first 3 days. Participants treated with fezolinetant 45 mg had a greater reduction from baseline in the daily mean change in VMS severity compared with placebo from days 2 to 7 (day 7 LS mean difference: –0.17; 95% CI: –0.23, –0.10; p<0.001). Improvements in VMS frequency and severity were sustained through week 24. No safety signals of concern were apparent for the 45 mg fezolinetant dose through week 24.

Conclusions
DAYLIGHT is the first study of fezolinetant to investigate efficacy versus placebo over 24 weeks. Fezolinetant 45 mg was efficacious and well tolerated for moderate-to-severe VMS in women considered unsuitable for HT. An effect on VMS frequency was seen as early as day 1 and maintained through the 24-week placebo-controlled period, demonstrating a rapid onset of action and sustained efficacy with fezolinetant treatment.

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Notes for Editors

1. For further information about the study, and to arrange an interview with the authors, please contact the ECE 2024 press office:

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2. The study **"Early Response with Fezolinetant Treatment of Moderate-to-Severe Vasomotor Symptoms Associated with Menopause in Women Considered Unsuitable for Hormone Therapy: Phase 3b DAYLIGHT Study"** is a poster presentation that will take place on Saturday 11 May 2024 at the European Congress of Endocrinology at the Stockholm International Fairs (Stockholmsmässan) in Stockholm, Sweden.

3. The 26th European Congress of Endocrinology (ECE) is held at the Stockholm International Fairs (Stockholmsmässan) in Stockholm, Sweden, on 11-14 May 2024. See the full scientific programme here: https://ese-hormonesapps.m-anage.com/ece2024/en-GB/pag

4. The European Society of Endocrinology (ESE) is at the centre of Europe's endocrine community. Its vision is to shape the future of endocrinology to improve science, knowledge and health. Through its events, publications, grants and advocacy work, ESE shares the best knowledge in endocrine science and medicine across Europe and beyond. ESE and its partner societies jointly represent a community of over 20,000 endocrinologists. ESE informs policymakers on health decisions at the highest level through advocacy efforts across Europe