Systematic Review

Fezolinetant and Elinzanetant Therapy for Menopausal Women Experiencing Vasomotor Symptoms

A Systematic Review and Meta-analysis

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OBJECTIVE: To assess the efficacy and safety of fezolinetant and elinzanetant for vasomotor symptoms in menopausal women.

DATA SOURCES: MEDLINE, EMBASE, and Cochrane databases were systematically searched until August 22, 2024. Because the Cochrane Library included all the identified randomized controlled trials (RCTs), it was unnecessary to search ClinicalTrials.gov. The following words made up the search strategy, which was applied to the three databases: fezolinetant, elinzanetant, vasomotor symptoms, and menopause.

METHODS OF STUDY SELECTION: Only RCTs comparing fezolinetant and elinzanetant with placebo for vasomotor symptoms in menopausal women were included.

TABULATION, INTEGRATION, AND RESULTS: We extracted the number of patients, mean age, body mass index (BMI), and number of patients who underwent oophorectomy. Data were examined with the Mantel–Haenszel method and 95% CIs. Heterogeneity was assessed with I^2 statistics. R 4.3.2 was used for statistical analysis. Seven RCTs with 4,087 patients were included in the analysis. Fezolinetant and elinzanetant were associated with diminished vasomotor symptom frequency: fezolinetant 30 mg (mean difference 2.16, 95% CI, 1.54–2.79, I^2=0%), fezolinetant 45 mg (mean difference 2.54, 95% CI, 1.86–3.21, I^2=0%), and elinzanetant 120 mg (mean difference 2.99, 95% CI, 1.74–4.23, I^2=0%). Both drugs also showed a decrease in vasomotor symptom severity: fezolinetant 30 mg (mean difference 0.20, 95% CI, 0.09–0.33, I^2=0%), fezolinetant 45 mg (mean difference 0.24, 95% CI, 0.13–0.34, I^2=0%), and elinzanetant 120 mg (mean difference 0.36, 95% CI, 0.26–0.46, I^2=0%). Elinzanetant 120 mg showed a significant improvement in sleep quality (mean difference 4.65, 95% CI, 3.73–5.56, I^2=0%). Elinzanetant 120 mg was associated with the occurrence of drug-related adverse events (11.70% vs 20.75%, risk ratio [RR] 0.57, 95% CI, 0.39–0.82, I^2=19%) and headache (2.54% vs 8.0%, RR 0.32, 95% CI, 0.16–0.64, I^2=0%).

CONCLUSION: In this meta-analysis, consistent results suggest that fezolinetant and elinzanetant are associated with beneficial outcomes in menopausal women with vasomotor symptoms. Elinzanetant provided a larger effect size in vasomotor symptom frequency and severity reduction and greatly improved sleep quality compared with fezolinetant.

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See related editorial on page 245.

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Menopause is a physiologic event that represents a milestone in a woman's reproductive life. Women approaching or undergoing menopause are

susceptible to experiencing the climacteric syndrome. Menopause commonly leads to bothersome vasomotor symptoms, which include hot flushes and night sweats and afflict up to 70% of women.[1,2] Mittelman-Smith et al[3] demonstrated the role of the thermoregulatory center in the hypothalamus in causing such symptoms. This area of the brain is innervated by kisspeptin–neurokinin B–dynorphin neurons, which are modulated by estrogen. Estrogen withdrawal during the menopausal transition disrupts this cascade, resulting in kisspeptin–neurokinin B–dynorphin neuron hypertrophy and hyperactivation. Consequently, the thermoregulatory center gets disrupted, leading to heat dissipation through hot flushes.[4]

Hormone therapy is the most effective treatment for climacteric syndrome symptoms. Although the safety of hormonal therapy has been questioned, long-term analyses from the Women's Health Initiative (WHI) trials have demonstrated that hormone therapy is appropriate for treating vasomotor symptoms in women in early menopause without contraindications.[5–7] However, nonhormonal therapies have gained attention in recent years.[1,8,9] Until 2023, low-dose paroxetine salt was the only U.S. Food and Drug Administration–approved treatment option for vasomotor symptoms.[2,10]

Fezolinetant is an oral nonhormone NK3 antagonist approved by the U.S. Food and Drug Administration for treating moderate and severe vasomotor symptoms related to menopause.[11] Elinzanetant, a dual NK1 and NK3 inhibitor, has also been assessed for the same purpose in the OASIS (A Study to Learn More About How Well Elinzanetant Works and How Safe it is for the Treatment of Vasomotor Symptoms [Hot Flashes] That Are Caused by Hormonal Changes Over 26 Weeks in Women Who Have Been Through the Menopause) 1 and 2 phase III randomized controlled trial (RCTs), showing promising effects.[12] Although some meta-analyses examined fezolinetant in menopausal women, no pooled analysis has directly compared both fezolinetant and elinzanetant with placebo. The objective of this study was to perform a systematic review and meta-analysis of RCTs comparing fezolinetant and elinzanetant with placebo in menopausal women experiencing vasomotor symptoms.

SOURCES

Eligibility criteria were: 1) randomized controlled trial, 2) studies examining fezolinetant or elinzanetant with placebo, 3) inclusion of menopausal women, and 4) reporting at least one relevant outcome. No restrictions were imposed regarding publication date. Exclusion criteria were: 1) any other neurokinin 1 and 3 receptor antagonist other than fezolinetant, 2) women receiving other treatments that might have interfered with the results, and 3) conference abstracts.

MEDLINE, EMBASE, and Cochrane Central Register of Controlled Trials were chosen as the sources of information for this meta-analysis and were systematically searched from inception to August 22, 2024. Since the Cochrane Library included all the identified RCTs, it was unnecessary to search ClinicalTrials.gov.

The present systematic review and meta-analysis was conducted according to Cochrane Collaboration and PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. MEDLINE, EMBASE, and Cochrane Central Register of Controlled Trials were searched with the following search strategy: (fezolinetant OR elinzanetant) AND "vasomotor symptoms" AND menopause.

STUDY SELECTION

Two authors (A.M.d.A. and P.O.) independently screened titles and abstracts and evaluated the studies in full for eligibility. We also reviewed the references of selected articles to identify any relevant additional publications. Two authors (A.M.d.A. and P.O.) independently conducted data extraction, collecting the following information from each study: study population, number of patients, age in years, race, body mass index (BMI, calculated as weight in kilograms divided by height in meters squared), and concentration of intervention. The primary outcomes measuring efficacy were vasomotor symptom frequency and severity. Secondary outcomes included the PROMIS-SD-SF (Patient-Reported Outcomes Measurement Information System Sleep Disturbance Short Form) 8b total T score and the MENQOL (Menopause-Specific Quality of Life) questionnaire total score. The safety analysis included the occurrence of drug-related adverse events, headache, adverse events leading to discontinuation, serious adverse events, and treatment-emergent adverse events.

Assessment of risk of bias in individual studies was conducted with the Cochrane Risk of Bias tool for randomized trials. Two independent authors evaluated the bias risk of each study and documented their observations. Disagreements were resolved through discussion and consensus.

We used R 4.3.2 and the extension package meta for all statistical analyses. Binary outcomes were analyzed with odds ratios; continuous outcomes were assessed through mean difference, both with 95% CIs.

Statistical significance was set as $P<.05$. Heterogeneity was examined with I^2 statistics, and significance was attributed to cases with $I^2>25\%$. For all outcomes, the Mantel–Haenszel random-effects model was applied. Studies were eligible for synthesis if all necessary data were available, including the number of events, mean number of events for each group, or SDs.

RESULTS

In total, 138 studies were identified from the initial search. After duplicates were removed, the titles and abstracts of 44 articles were screened, and 15 potential articles underwent full-text review. Of these, 7 RCTs[12–17] and 4,087 patients met the inclusion criteria and were included in the study, as described in the flow diagram (Fig. 1).

Tables 1 and 2 outline the main characteristics of the included studies assessing fezolinetant and elinzanetant, respectively. The minimum and maximum sample sizes were 87 and 1,830, respectively. All included patients presented with vasomotor symptoms associated with a diagnosis of menopause. Of the 4,087 included patients, 2,252 (55.10%) received fezolinetant, 399 (9.72%) received elinzanetant, and 1,436 (35.13%) received a placebo (Table 3).

In the pooled analysis of data from 1,979 menopausal women, both fezolinetant and elinzanetant were associated with a decrease in the frequency of vasomotor symptom events: fezolinetant 30 mg (mean difference 2.16, 95% CI, 1.54–2.79, $I^2=0\%$, Fig. 2A), fezolinetant 45 mg (mean difference 2.54, 95% CI, 1.86–3.21, Fig. 2A), and elinzanetant 120 mg (mean difference 2.99, 95% CI, 1.74–4.23, Fig. 2A) (total vasomotor symptom frequency reduction with NK-inhibitor administration: mean difference 2.41, 95% CI, 1.98–2.84, $I^2=0\%$, Fig. 2A).

Fezolinetant and elinzanetant significantly attenuated the vasomotor symptom severity in the 12-week period: fezolinetant 30 mg (mean difference 0.20, 95% CI, 0.09–0.33, $I^2=0\%$, Fig. 2B), fezolinetant 45 mg (mean difference 0.24, 95% CI, 0.13–0.34, Fig. 2B), and elinzanetant 120 mg (mean difference 0.36, 95% CI, 0.26–0.46, Fig. 2B) (total vasomotor symptom severity reduction with NK-inhibitor administration: mean difference 0.27, 95% CI, 0.20–0.33, $I^2=21\%$, Fig. 2B).

Only fezolinetant 45 mg promoted a statistically significant change in the sleep quality of menopausal women experiencing vasomotor symptoms: fezolinetant 30 mg (mean difference 0.24, 95% CI, −0.03 to 0.51, Fig. 3A), fezolinetant 45 mg (mean difference 0.50, 95% CI, 0.23–0.77, Fig. 3A), and elinzanetant 120 mg (mean difference 4.65, 95% CI, 3.73–5.56, Fig. 3A) (total sleep quality improvement with NK-inhibitor administration: mean difference 1.79, 95% CI, 0.79–2.78, $I^2=94\%$, Fig. 3A).

Fezolinetant and elinzanetant significantly improved the quality of life in menopausal women experiencing vasomotor symptoms, which was measured through the MENQOL questionnaire score: fezolinetant 30 mg (mean difference 0.32, 95% CI,

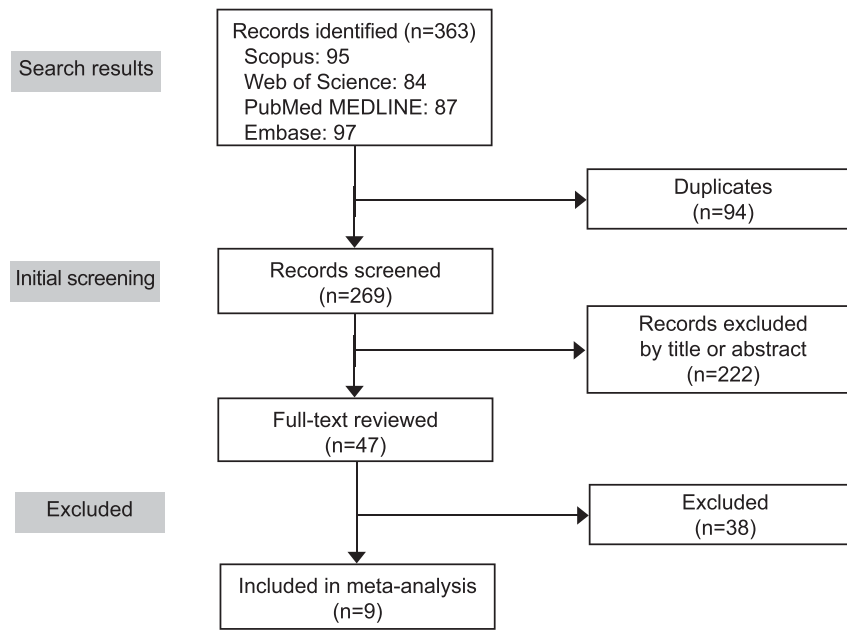


Fig. 1. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram with systematic review of detailed searches.

Menegaz de Almeida. Fezolinetant and Elinzanetant for Vasomotor Symptoms. Obstet Gynecol 2025.

Table 1. Baseline Characteristics of Included Studies Assessing Fezolinetant

	No. of Patients				Mean Age (y)				BMI (kg/m²)				Oophorectomy			
		Fezolinetant				Fezolinetant				Fezolinetant				Fezolinetant		
Study	Placebo	30 mg	45 mg	90 mg	Placebo	30 mg	45 mg	90 mg	Placebo	30 mg	45 mg	90 mg	Placebo	30 mg	45 mg	90 mg
Depypere et al, 2019	44	NA	NA	43	53.7	NA	NA	53.3	26.5	NA	NA	25.1	NA	NA	NA	NA
Fraser et al, 2020	43	43	NA	NA	54.8	53.9	NA	NA	27.3	28.3	NA	NA	NA	NA	NA	NA
SKYLIGHT 1, 2023	175	174	173	NA	54.7	54.2	54.2	NA	28.1	28.1	28.2	NA	38	37	37	NA
SKYLIGHT 2, 2023	167	166	167	NA	54.7	53.9	54.3	NA	28.1	27.9	27.9	NA	37	34	28	NA
SKYLIGHT 4, 2023	610	611	609	NA	54.9	54.7	54.7	NA	28.2	28.4	28.4	NA	86	75	86	NA

BMI, body mass index; NA, not applicable; SKYLIGHT, A Study to Find Out if Fezolinetant Helps Reduce Moderate to Severe Hot Flashes in Women Going Through Menopause.

0.13–0.52, Fig. 3B), fezolinetant 45 mg (mean difference 0.49, 95% CI, 0.30–0.67, Fig. 3B), elinzanetant 120 mg (mean difference 0.41, 95% CI, 0.24–0.58, Fig. 3B) (total quality of life improved with NK-inhibitor administration: mean difference 0.41, 95% CI, 0.30–0.51, I^2=0%, Fig. 3B).

Only elinzanetant 120 mg was associated with the occurrence of drug-related adverse events (see Appendix 1, available online at http://links.lww.com/AOG/D951): fezolinetant 30 mg (14.27% vs 13.68%; risk ratio [RR] 0.97, 95% CI, 0.57–1.67, I^2=59%), fezolinetant 45 mg (15.02% vs 25.50%, RR 0.72, 95% CI, 0.33–1.56, I^2=82%), fezolinetant 180 mg (16.09% vs 25.28%, RR 0.62, 95% CI, 0.28–1.40), and elinzanetant 120 mg (11.70% vs 20.75%, RR 0.57, 95% CI, 0.39–0.82) (total occurrence of drug-related adverse events: 14.21% vs 19.87%, RR 0.73, 95% CI, 0.54–0.99, I^2=75%).

Only elinzanetant 120 mg was associated with the occurrence of headache (see Appendix 2, available online at http://links.lww.com/AOG/D951): fezolinetant 30 mg (7.5% vs 6.9%, RR 1.09, 95% CI, 0.79–1.49, I^2=0%), fezolinetant 45 mg (7.66% vs 7.58%, RR 1.01, 95% CI, 0.74–1.38, I^2=0%), fezolinetant 180 mg (9.19% vs 9.30%, RR 0.96, 95% CI, 0.38–2.42), and elinzanetant 120 mg (2.54% vs 8.0%, RR 0.32, 95% CI, 0.16–0.64) (total occurrence of headache: 6.83% vs 7.45%, RR 0.94, 95% CI, 0.77–1.16, I^2=19%).

The occurrence of serious adverse events was statistically significantly different only in the pooled analysis of all fezolinetant doses and elinzanetant 120 mg (see Appendix 3, available online at http://links.lww.com/AOG/D951): fezolinetant 30 mg (1.50% vs 2.51%, RR 0.64, 95% CI, 0.34–1.20, I^2=0%), fezolinetant 45 mg (1.57% vs 2.84%, RR 0.57, 95% CI, 0.31–1.06, I^2=0%), and elinzanetant 120 mg (0.76% vs 1.25%, RR 0.62, 95% CI, 0.15–2.60) (total occurrence of serious adverse events 1.40% vs 2.34%, RR 0.62, 95% CI, 0.41–0.94, I^2=0%).

No other analyzed adverse event showed a statistically significant difference tending for NK-inhibitor administration: adverse events leading to discontinuation (total occurrence: 4.32% vs 4.85%, RR 0.79, 95% CI, 0.60–1.04, I^2=1%, Appendix 4, available online at http://links.lww.com/AOG/D951) and treatment-emergent adverse events (total occurrence:

Table 2. Baseline Characteristics of Included Studies Assessing Elinzanetant

	No. of Patients		Mean Age (y)		BMI		Oophorectomy	
Study	Placebo	Elinzanetant	Placebo	Elinzanetant	Placebo	Elinzanetant	Placebo	Elinzanetant
OASIS 1, 2024	197	199	54.5±4.9	54.6±4.9	27.7±4.5	27.8±4.8	49	51
OASIS 2, 2024	200	200	54.4±4.5	54.8±5.0	28.0±4.7	27.8±4.8	40	24

BMI, body mass index; OASIS, A Study to Learn More About How Well Elinzanetant Works and How Safe it is for the Treatment of Vasomotor Symptoms (Hot Flashes) That Are Caused by Hormonal Changes Over 26 Weeks in Women Who Have Been Through the Menopause.

Data are mean±SD unless otherwise specified.

Table 3. Outcomes Measurements

Outcome	Drug	Effect Size	Measure of Association	95% CI	I^2 Statistics (%)
Vasomotor symptoms frequency	Fezolinetant 30 mg	2.16	MD	1.54–2.79	0
	Fezolinetant 45 mg	2.54	MD	1.86–3.21	NA
	Elinzanetant 120 mg	2.99	MD	1.74–4.23	NA
	NK inhibitor (general)	2.41	MD	1.98–2.84	0
Vasomotor symptoms severity	Fezolinetant 30 mg	0.20	MD	0.09–0.33	0
	Fezolinetant 45 mg	0.24	MD	0.13–0.34	NA
	Elinzanetant 120 mg	0.36	MD	0.26–0.46	NA
	NK inhibitor (general)	0.27	MD	0.20–0.33	21
PROMIS SD SF	Fezolinetant 30 mg	0.24	MD	0.03–0.51	NA
	Fezolinetant 45 mg	0.50	MD	0.23–0.77	NA
	Elinzanetant 120 mg	4.65	MD	3.73–5.56	NA
	NK inhibitor (general)	1.79	MD	0.79–2.78	94
MENQOL	Fezolinetant 30 mg	0.32	MD	0.13–0.52	NA
	Fezolinetant 45 mg	0.49	MD	0.30–0.67	NA
	Elinzanetant 120 mg	0.41	MD	0.24–0.58	NA
	NK inhibitor (general)	0.41	MD	0.30–0.51	0
Drug-related AEs	Fezolinetant 30 mg	0.97	RR	0.57–1.67	59
	Fezolinetant 45 mg	0.72	RR	0.33–1.56	82
	Fezolinetant 180 mg	0.62	RR	0.28–1.40	NA
	Elinzanetant 120 mg	0.57	RR	0.39–0.82	NA
	NK inhibitor (general)	0.73	RR	0.54–0.99	75
Headache	Fezolinetant 30 mg	1.09	RR	0.79–1.49	0
	Fezolinetant 45 mg	1.01	RR	0.74–1.38	0
	Fezolinetant 180 mg	0.96	RR	0.38–2.42	NA
	Elinzanetant 120 mg	0.32	RR	0.16–0.64	NA
	NK inhibitor (general)	0.94	RR	0.77–1.16	19
Serious AEs	Fezolinetant 30 mg	0.64	RR	0.34–1.20	0
	Fezolinetant 45 mg	0.57	RR	0.31–1.06	0
	Elinzanetant 120 mg	0.62	RR	0.15–2.60	NA
	NK inhibitor (general)	0.62	RR	0.41–0.94	0
AEs leading to discontinuation	NK inhibitor (general)	0.79	RR	0.60–1.04	1
Treatment-emergent AEs	NK inhibitor (general)	0.98	RR	0.93–1.03	0

MD, mean difference; NA, not applicable; NK, neurokinin; PROMIS SD SF, Patient-Reported Outcomes Measurement Information System Sleep Disturbance Short Form; MENQOL, Menopause-Specific Quality of Life; RR, risk ratio; AE, adverse event.

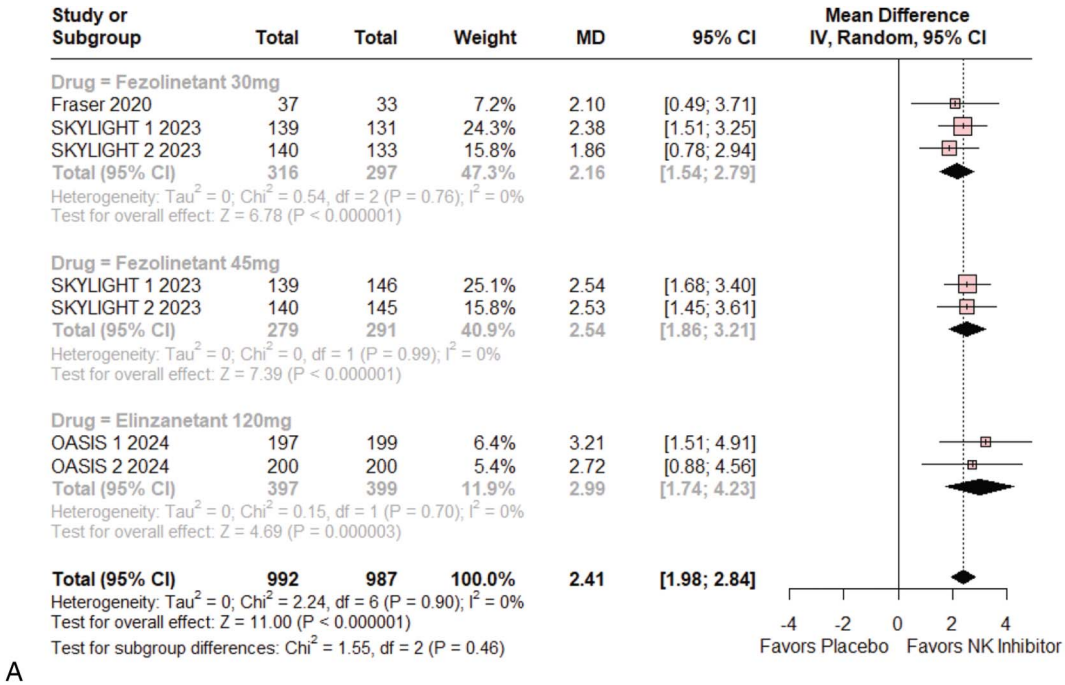
53.27% vs 54.73%, RR 0.98, 95% CI, 0.93–1.03, I^2=0%, Appendix 5, available online at http://links.lww.com/AOG/D951). The risk of Bias 2 tool was used for quality assessment. Individual RCT appraisal is reported in Figure 4. Because no biases were identified, all studies were considered to be at low risk of bias.

DISCUSSION

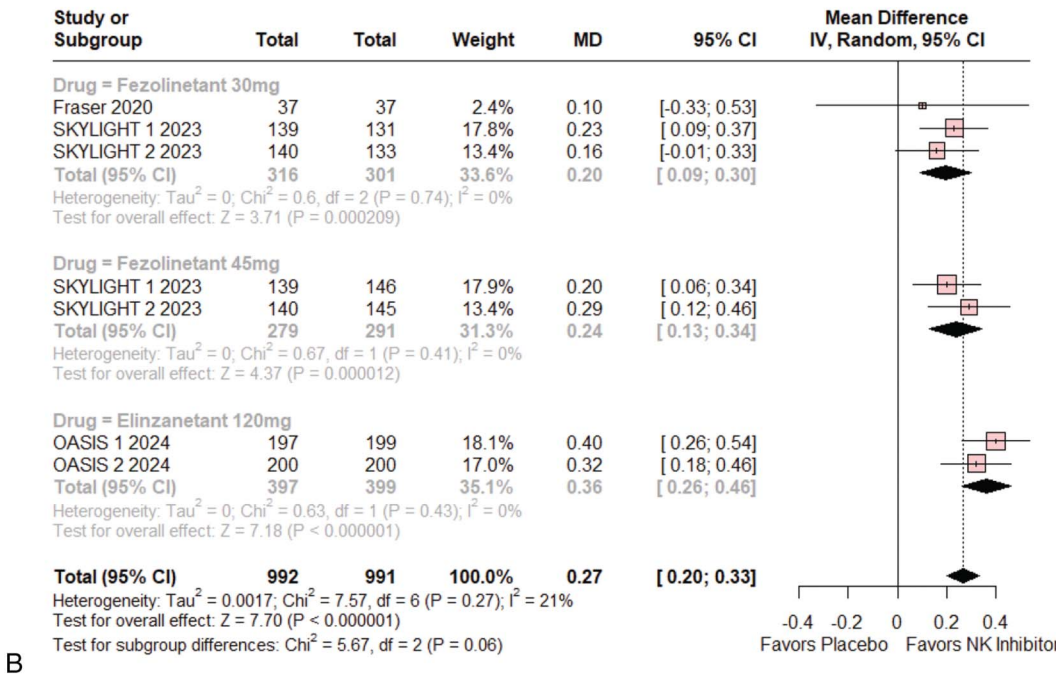
In this meta-analysis involving 4,087 patients from seven RCTs, all doses of fezolinetant and elinzanetant significantly lowered vasomotor symptom frequency and severity, with elinzanetant showing a greater size effect. Although fezolinetant was not associated with an increased risk of adverse events, elinzanetant showed an increased occurrence of drug-related adverse events and headache. Both fezolinetant and elinzanetant improved quality of life, and elinzanetant was associated with a stronger effect on sleep quality.

The effects that vasomotor symptoms can have on a woman's life are often undervalued. Given the prevalence of vasomotor symptoms among women transitioning into menopause, the frequency and severity of symptoms significantly decrease quality of life, leading to sleep disturbances and reduced productivity.[18] Reducing vasomotor symptom frequency and severity should be the primary objective of any investigational drug targeting such patients. In our study, both fezolinetant and elinzanetant effectively achieved this goal and further contributed to a global improvement in various factors affecting patients' quality of life. All of our efficacy outcomes strongly support the use of neurokinin inhibitors for menopausal women requiring treatment for vasomotor symptoms.

Because the phase 2b dose range–finding study of elinzanetant demonstrated a significant improvement in sleep quality for such patients, this agent has been suggested to potentially improve insomnia related to



A



B

Fig. 2. A. Vasomotor symptoms frequency change from baseline. **B.** Vasomotor symptoms severity change from baseline. MD, mean difference; IV, inverse variance; SKYLIGHT, A Study to Find Out if Fezolinetant Helps Reduce Moderate to Severe Hot Flashes in Women Going Through Menopause; OASIS, A Study to Learn More About How Well Elinzanetant Works and How Safe it is for the Treatment of Vasomotor Symptoms (Hot Flashes) That Are Caused by Hormonal Changes Over 26 Weeks in Women Who Have Been Through the Menopause; df, degrees of freedom; NK, neurokinin.

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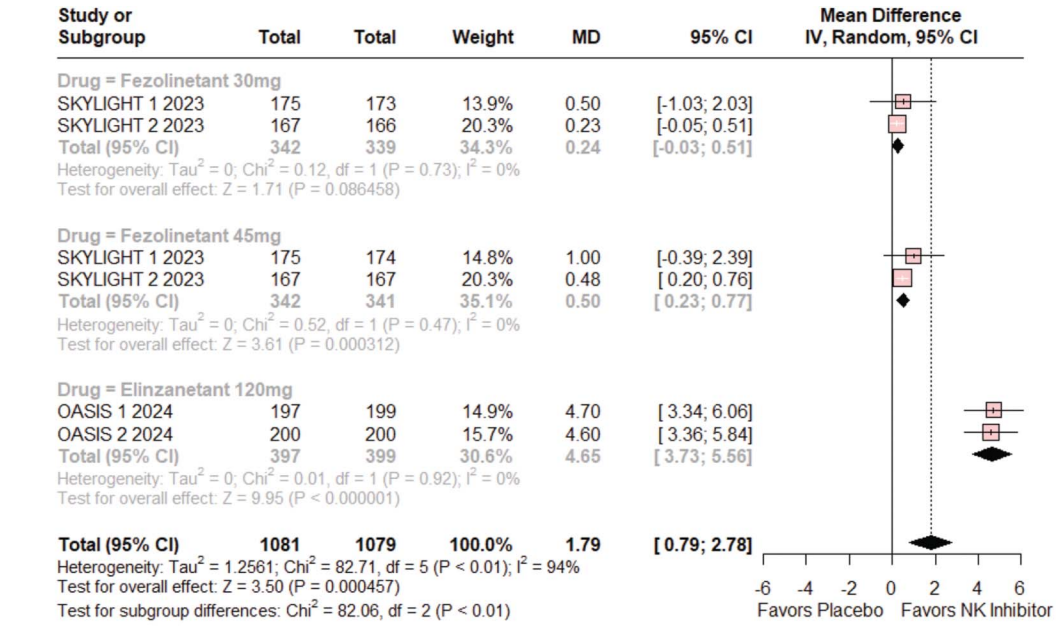
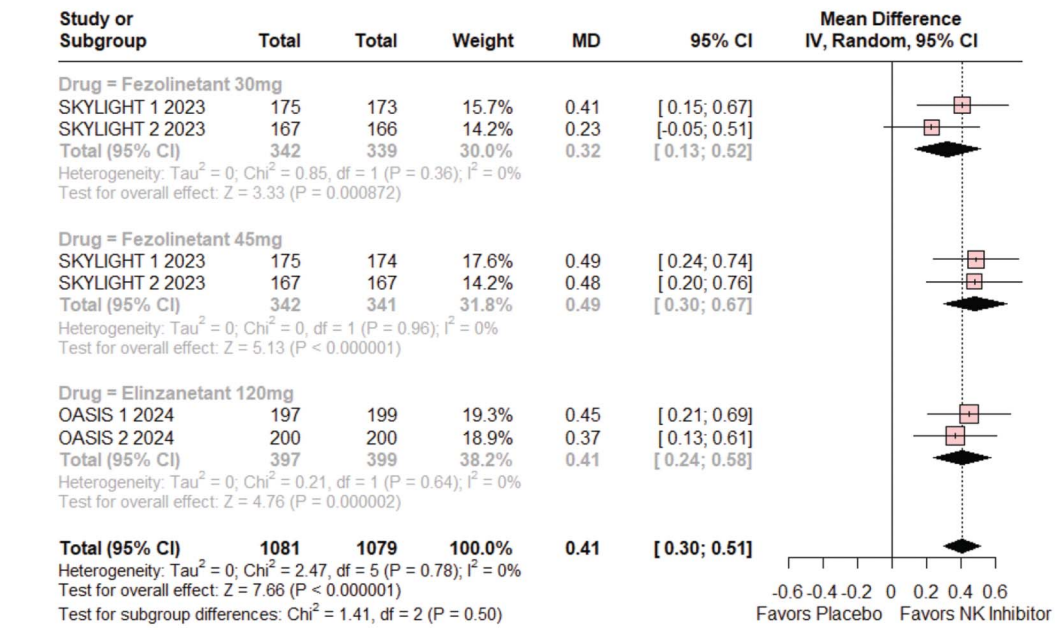


A



B

Fig. 3. A. PROMIS-SD-SF (Patient-Reported Outcomes Measurement Information System Sleep Disturbance Short Form) score change from baseline. **B.** MENQOL (Menopause-Specific Quality of Life) score change from baseline. MD, mean difference; IV, inverse variance; SKYLIGHT, A Study to Find Out if Fezolinetant Helps Reduce Moderate to Severe Hot Flashes in Women Going Through Menopause; OASIS, A Study to Learn More About How Well Elinzanetant Works and How Safe it is for the Treatment of Vasomotor Symptoms (Hot Flashes) That Are Caused by Hormonal Changes Over 26 Weeks in Women Who Have Been Through the Menopause; df, degrees of freedom; NK, neurokinin.

Menegaz de Almeida. Fezolinetant and Elinzanetant for Vasomotor Symptoms. Obstet Gynecol 2025.

menopause.[19] Although the mechanism of action still needs to be elucidated, it may be directly linked to the reduction in nighttime vasomotor symptoms, which probably disrupts the circadian rhythm, thus causing continued insomnia. An intriguing finding was that, although only fezolinetant 45 mg showed a statistically

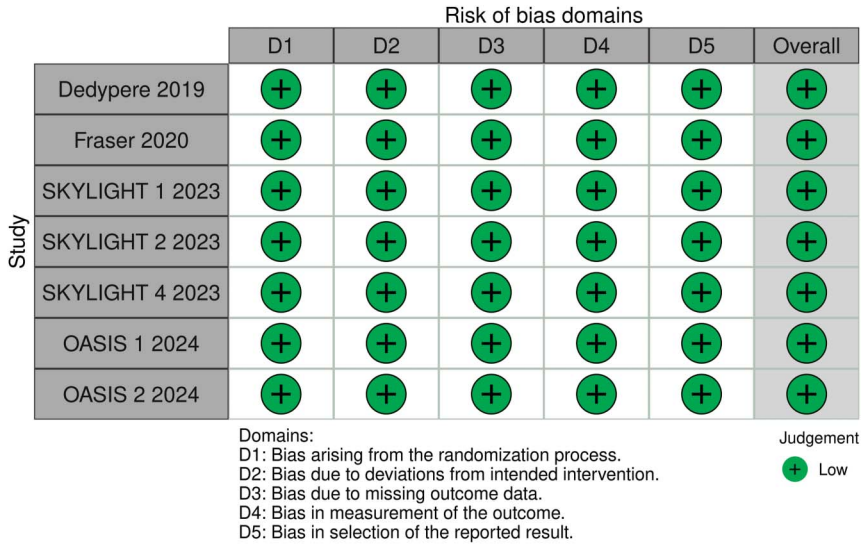


Fig. 4. Risk of bias individual assessment. SKYLIGHT, A Study to Find Out if Fezolinetant Helps Reduce Moderate to Severe Hot Flashes in Women Going Through Menopause; OASIS, A Study to Learn More About How Well Elinzanetant Works and How Safe it is for the Treatment of Vasomotor Symptoms (Hot Flashes) That Are Caused by Hormonal Changes Over 26 Weeks in Women Who Have Been Through the Menopause.

Menegaz de Almeida. Fezolinetant and Elinzanetant for Vasomotor Symptoms. Obstet Gynecol 2025.

significant very small improvement in sleep quality, elinzanetant had a nine times larger effect size in promoting this benefit when indirectly compared with fezolinetant. This characteristic may be linked to the inhibitory pattern of elinzanetant in blocking NK1 and NK3, whereas fezolinetant blocks only NK3.

Bias associated with hormone therapy is one of the factors driving the search for new interventions capable of reducing vasomotor symptoms as effectively as hormone replacement therapy. Ensuring that a new drug carries no risk of breast cancer or cardiovascular disease will likely improve treatment adherence. Although both fezolinetant and elinzanetant appear to lack mechanisms that induce cancer or acute myocardial infarction, adverse events were still significantly observed in patients treated with elinzanetant. Although studies of fezolinetant report the possibility of drug-related adverse events, our analysis found no significant difference between the groups for this drug, whereas a significant association was observed with elinzanetant. In addition, headaches were reported with elinzanetant but not with fezolinetant. Thus, given the efficacy differences identified through indirect comparisons between fezolinetant and elinzanetant, the decision to prescribe an NK inhibitor for women experiencing vasomotor symptoms should be individualized, taking into account patient-specific factors such as the severity of vasomotor symptoms and the presence of insomnia because climacteric syndrome presents heterogeneously. Furthermore, it is important to note that nonhormonal interventions do not address other menopausal symptoms such as genital symptoms, which should also be considered when deciding whether to prescribe these drugs.

Because of the greater effect size in reducing vasomotor symptom frequency and severity observed with elinzanetant, along with the occurrence of more adverse events, it is possible that low-dose fezolinetant may emerge as a first option for women with mild to moderate vasomotor symptoms in future guidelines. In addition, patients experiencing any grade of insomnia may benefit more from elinzanetant administration. The underlying mechanism of this benefit requires further investigation to clarify the correlation between NK1 inhibition and improved sleep quality, especially because fezolinetant, which primarily blocks NK3, demonstrated only a small effect on sleep. Further direct comparisons of NK inhibitors and other nonhormonal interventions, specifically paroxetine, are necessary to better elucidate safety and efficacy differences; previous meta-analyses have also demonstrated the efficacy of paroxetine in reducing vasomotor symptoms.[20,21]

Our study has several limitations. First, there were slight differences between the included RCTs in terms of administered dose, which made it difficult to assess a varied arrange of doses. However, all assessed groups demonstrated very significant *P* values mainly along with no heterogeneity. Second, our findings may not apply to all women with vasomotor symptoms. In general, most of the participants were White patients. Third, despite a low number of studies screened in the initial search, the included RCTs showed a consistent and satisfactory assessment of risks of bias through multivariate analysis.

Fezolinetant and elinzanetant are both effective in reducing the frequency and severity of vasomotor symptoms in menopausal women. In addition, fezolinetant was not associated with any adverse events and showed a very slight improvement in sleep quality, whereas elinzanetant had an increased occurrence of drug-related adverse events and headaches, along with a strong effect on sleep quality. Our findings suggest that further studies are needed to better analyze dose-escalation differences and the individual effects of NK1 receptor blockade on insomnia.

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