EFFICACY OF ELINZANETANT ON VASOMOTOR SYMPTOMS AND SLEEP DISTURBANCE

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BACKGROUND AND OBJECTIVES

OASIS-1 AND -2

- Elinzanetant, a dual neurokinin (NK)-targeted therapy (NK1 and NK3 receptor antagonist), significantly reduced moderate-to-severe vasomotor symptom (M/S VMS) frequency and severity, improved sleep disturbance and menopause-related quality of life compared with placebo, and had a favorable safety profile in women with M/S VMS in 2 global Phase III trials (OASIS-1 and OASIS-2)[1]

Post hoc analyses

VMS BY TIME OF DAY

Characterize the effect of elinzanetant on VMS frequency at different times of day (daytime and nighttime) over 12 weeks

SLEEP BY BASELINE VMS

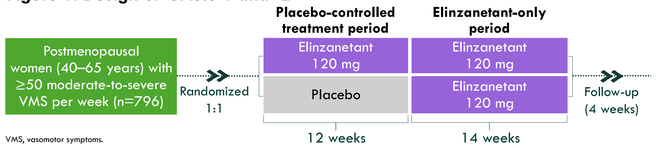
Assess the effect of elinzanetant on sleep disturbance across subgroups defined by baseline VMS frequency

METHODS

Study design and participants

- OASIS-1 (NCT05042362) and OASIS-2 (NCT05099159) were Phase III, randomized, placebo-controlled, multicenter, multicountry, double-blind trials with similar designs
- The trials enrolled naturally or surgically (bilateral oophorectomy with or without hysterectomy) postmenopausal women aged 40–65 years and experiencing ≥50 M/S VMS over 7 days during screening
- Participants were randomly assigned in a 1:1 ratio to receive either elinzanetant 120 mg for 26 weeks or placebo for 12 weeks followed by elinzanetant for 14 weeks; presented here are results for a post hoc pooled exploratory analysis from the US population (**Figure 1**)

Figure 1. Design of OASIS-1 and -2



VMS, vasomotor symptoms.

Table 2. Post hoc analyses from the OASIS-1 and -2 trials

Moderate-to-severe VMS assessed by time of day	
Subgroups	Daytime VMS vs nighttime VMS
Assessment	VMS frequency recorded via the hot flash daily diary completed morning and evening: • Daytime VMS: from evening entries • Nighttime VMS: from morning entries
Analysis	• Mean frequency of daytime and nighttime VMS for each week on treatment was calculated using available data for that week and averaged to a mean daily frequency per period • Baseline values were calculated using diary entries from the 14 days prior to treatment start • This analysis included only moderate-to-severe VMS
Statistical method	MMRM to analyze differences in LS mean change from baseline between elinzanetant and placebo; 1-sided p values are indicative, not confirmatory
Time points	Baseline; weeks 1, 4, and 12
PROMIS SD SF 8b by moderate-to-severe VMS frequency	
Subgroups	Stratified by baseline mean daily VMS frequency: • ≥12/day (higher VMS group) • <12/day (lower VMS group)
Assessment	Sleep disturbance measured using the PROMIS SD SF 8b (higher score = worse sleep disturbance)
Analysis	Mean change from baseline in total T-scores compared between treatment arms within each VMS burden subgroup
Statistical method	MMRM to analyze differences in LS mean change from baseline between elinzanetant and placebo; p values are indicative, not confirmatory
Time points	Baseline; weeks 1, 4, and 12

LS, least squares; MMRM, mixed model for repeated measures; PROMIS SD SF 8b, Patient-Reported Outcomes Measurement Information System Sleep Disturbance Short Form 8b; VMS, vasomotor symptoms.

RESULTS

- Baseline characteristics were generally balanced between the elinzanetant and placebo groups (**Table 1**)

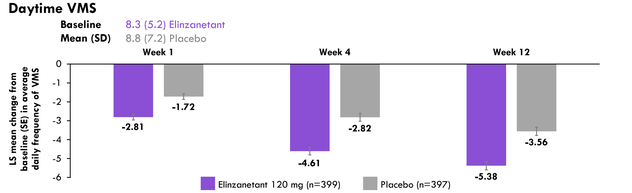
Table 1. Baseline demographics and characteristics

Characteristic	Elinzanetant 120 mg (n=399)	Placebo → Elinzanetant 120 mg (n=397)	Total (N=796)
Age, y, mean (SD)	54.7 (4.9)	54.5 (4.7)	54.6 (4.8)
Race, n (%)			
American Indian or Alaska Native	2 (0.5)	2 (0.5)	4 (0.5)
Asian	2 (0.5)	2 (0.5)	4 (0.5)
Black or African American	73 (18.3)	63 (15.9)	136 (17.1)
White	314 (78.7)	326 (82.1)	640 (80.4)
Multiple	3 (0.8)	1 (0.3)	4 (0.5)
Not reported	5 (1.3)	3 (0.8)	8 (1.0)
Hispanic or Latino, n (%)	30 (7.5)	38 (9.6)	68 (8.5)
BMI, kg/m^2, mean (SD)	27.78 (4.82)	27.80 (4.63)	27.79 (4.72)
Smoking status, n (%)			
Never	267 (66.9)	250 (63.0)	517 (64.9)
Former	67 (16.8)	66 (16.6)	133 (16.7)
Current	65 (16.3)	81 (20.4)	146 (18.3)

BMI, body mass index; SD, standard deviation.

Figure 2. Mean moderate-to-severe VMS frequency at week 12

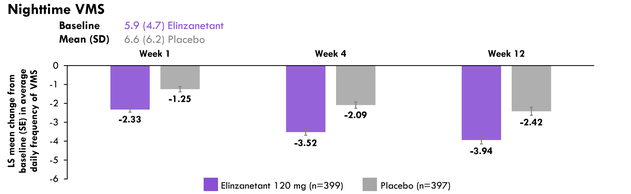
Daytime VMS



In the MMRM analysis, reductions from baseline in M/S VMS daily frequency by daytime VMS (LS mean change [95% CI]) were greater with elinzanetant vs placebo at week 1 (-1.1 [-1.5, -0.7]), week 4 (-1.8 [-2.3, -1.2]), and week 12 (-1.8 [-2.4, -1.2]) (all p<0.0001)

p values are indicative, not confirmatory. CI, confidence interval; LS, least squares; MMRM, mixed model for repeated measures; M/S, moderate-to-severe; SD, standard deviation; SE, standard error; VMS, vasomotor symptoms.

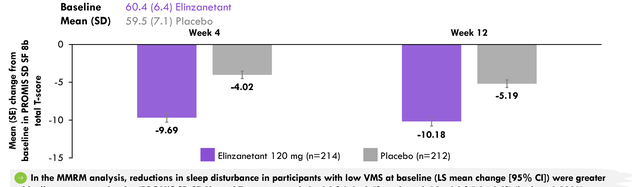
Nighttime VMS



In the MMRM analysis, reductions from baseline in M/S VMS daily frequency by nighttime VMS (LS mean change [95% CI]) were greater with elinzanetant vs placebo at week 1 (-1.1 [-1.5, -0.7]), week 4 (-1.4 [-1.9, -1.0]), and week 12 (-1.5 [-2.1, -0.9]) (all p<0.0001)

p values are indicative, not confirmatory. CI, confidence interval; LS, least squares; MMRM, mixed model for repeated measures; SD, standard deviation; SE, standard error; VMS, vasomotor symptoms.

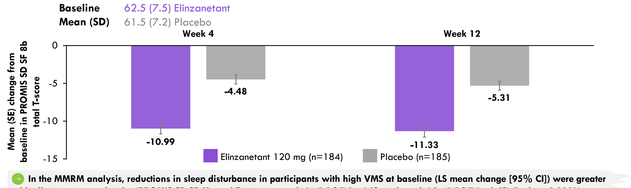
Lower VMS group (<12/day; n=426)



In the MMRM analysis, reductions in sleep disturbance in participants with low VMS at baseline (LS mean change [95% CI]) were greater with elinzanetant vs placebo (PROMIS SD SF 8b total T-score at week 4: -4.9 [-6.4, -3.5]; and week 12: -4.3 [-5.8, -2.9]) (both p<0.0001)

p values are indicative, not confirmatory. CI, confidence interval; LS, least squares; MMRM, mixed model for repeated measures; PROMIS SD SF 8b, Patient-Reported Outcomes Measurement Information System Sleep Disturbance Short Form 8b; SD, standard deviation; SE, standard error; VMS, vasomotor symptoms.

Higher VMS group (≥12/day; n=369)



In the MMRM analysis, reductions in sleep disturbance in participants with high VMS at baseline (LS mean change [95% CI]) were greater with elinzanetant vs placebo (PROMIS SD SF 8b total T-score at week 4: -5.8 [-7.3, -4.3]; and week 12: -5.5 [-7.1, -3.9]) (both p<0.0001)

p values are indicative, not confirmatory. CI, confidence interval; LS, least squares; MMRM, mixed model for repeated measures; PROMIS SD SF 8b, Patient-Reported Outcomes Measurement Information System Sleep Disturbance Short Form 8b; SD, standard deviation; SE, standard error; VMS, vasomotor symptoms.

CONCLUSIONS

Consistent reductions of M/S VMS frequency during the day and the night

Elinzanetant demonstrated greater reductions than placebo in M/S VMS during both daytime and nighttime, with improvements seen as early as week 1 and sustained through week 12

Sleep improvement possibly independent of VMS burden

Greater reductions in sleep disturbance were observed with elinzanetant vs placebo, regardless of baseline VMS frequency (≥12/day or <12/day)

These results underscore the potential of elinzanetant to improve VMS and sleep disturbance, 2 of the most frequent and disruptive menopausal symptoms

REFERENCES

1. Pinkerton JV, et al. JAMA. 2024;332(16):1343–1354.

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