Efficacy of elinzanetant for the treatment of vasomotor symptoms associated with menopause: pooled data from two Phase 3 studies

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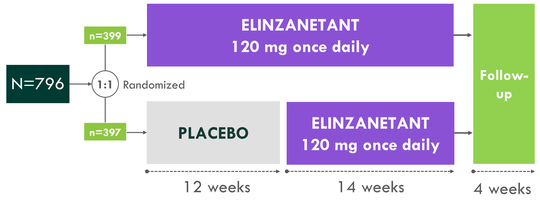
INTRODUCTION

Elinzanetant (EZN) is a non-hormonal compound in development for the treatment of vasomotor symptom (VMS; also known as hot flashes) associated with menopause that specifically targets both neurokinin-1 and -3 receptors. In both the OASIS-1 and OASIS-2 pivotal randomized Phase 3 trials, EZN significantly reduced menopausal VMS frequency and severity compared with placebo (PBO), improved sleep disturbances and menopause-related quality of life, and had a favorable safety profile.[1] This exploratory pooled analysis provides combined data from both OASIS-1 and OASIS-2 studies.

METHODS

Participants and interventions

Naturally/surgically postmenopausal women aged 40–65 years with ≥50 moderate-to-severe VMS episodes per week were randomized 1:1 to receive EZN 120 mg for 26 weeks or PBO for 12 weeks followed by EZN for 14 weeks.



Endpoints summary

- Mean change in **frequency** of moderate-to-severe VMS from baseline to **weeks 1, 4, and 12**
- Mean change in **severity** of moderate-to-severe VMS from baseline to **weeks 4 and 12**
- Mean change in **Patient-Reported Outcomes Measurement Information System Sleep Disturbance Short Form 8b (PROMIS SD SF 8b) total T-score** from baseline to **week 12 (sleep disturbance)**
- Mean change in **Menopause-Specific Quality of Life (MENQOL) questionnaire total score** from baseline to **week 12 (menopause-related quality of life)**

Data were pooled from OASIS 1 and 2 trials. Endpoints were analyzed by a mixed model with repeated measures; p values were indicative, not confirmatory.

ACKNOWLEDGEMENTS

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REFERENCES

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

DISCLOSURES

JoAnn V. Pinkerton was principal investigator on the OASIS 2 clinical trial, fees to the University of Virginia, and has been a consultant with Bayer HealthCare Pharmaceuticals and Pfizer. James A. Simon was principal investigator on the OASIS 1 trial; has grant/research support from AbbVie, Inc., Bayer Healthcare LLC., Daré Bioscience, Ipsen, Mylan/Viatris Inc., Myovant Sciences, ObsEva SA, Sebela Pharmaceuticals Inc., Viveve Medical; has been a consultant/advisory boards of Bayer HealthCare Pharmaceuticals Inc., Besins Healthcare, California Institute of Integral Studies (CIIS), Camargo Pharmaceutical Services, LLC, Covance Inc., Daré Bioscience, DEKA M.E.L.A. S.r.l., Femasys Inc., KaNDy/NeRRe Therapeutics Ltd., Khyria, Madorra Pty Ltd., Mitsubishi Tanabe Pharma Development America, Inc., QUE Oncology Pty, Limited, Scynexis Inc., Sebela Pharmaceuticals, Inc., Sprout Pharmaceuticals, Inc., Vella Bioscience Inc.; has served on the Speaker's bureaus of Mayne Pharma, Inc., Myovant Sciences, Inc., Pfizer Inc., Pharmavite LLC., Scynexis Inc., TherapeuticsMD; and is a stockholder (direct purchase) in Sermonix Pharmaceuticals. Hadine Joffe has received grants from NIH, Merck, Pfizer, and has performed consultancy work for Bayer, Merck, Hello Therapeutics. Pauline M. Maki has performed consultancy work for Abbott, Astellas, Bayer HealthCare AG, and Pfizer, and received speaking honorarium from Mithra, equity in Alloy, MidiHealth, and Estrigenix. Rossella E. Nappi had past financial relationships (lecturer, member of advisory boards and/or consultant) with Boehringer Ingelheim, Ely Lilly, Endoceutics, Palatin Technologies, Pfizer Inc., Procter & Gamble Co, TEVA Women's Health Inc., and Zambon SpA. At present, she has on-going relationship with Abbott, Astellas, Bayer HealthCare AG, Besins Healthcare, Exeltis, Fidia, Gedeon Richter, HRA Pharma, Merck & Co, Novo Nordisk, Organon & Co, Shionogi Limited, Theramex, Viatris, and Vichy Laboratories. Nick Panay has lectured and acted in an advisory capacity for Abbott, Astellas, Bayer, Besins, Gedeon Richter, Mithra, Novo Nordisk, SeCur, Theramex, and Viatris. Claudio N. Soares has received research grants from Ontario Brain Institute, Clairvoyant Therapeutics, and Eisai Inc., and performed consultancy work for Otsuka, Bayer, Eisai, and Diamond Therapeutics. Rebecca C. Thurston has acted in an advisory capacity for Bayer, Astellas, and Hello Therapeutics. Senka Djordjevic and Lineke Zuurman are employees of Bayer CC AG. Christiane Ahler and Claudia Haberland are employees of Bayer AG.

RESULTS

Table 1. Participant demographics

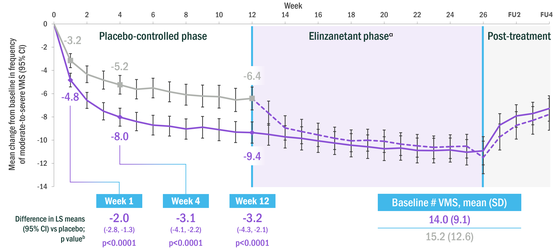
	EZN 120 mg (n=399)	PBO (n=397)
Age (years), mean (SD)	54.7 (4.9)	54.5 (4.7)
Race, n (%)		
White	314 (78.7%)	326 (82.1%)
Black or African American	73 (18.3%)	63 (15.9%)
Hispanic or Latino, n (%)	30 (7.5%)	38 (9.6%)
Weight (kg), mean (SD)	75.7 (14.2)	74.9 (13.5)
BMI (kg/m²), mean (SD)	27.8 (4.8)	27.8 (4.6)
Smoking history, n (%)		
Never	267 (66.9%)	250 (63.0%)
Former	67 (16.8%)	66 (16.6%)
Current	65 (16.3%)	81 (20.4%)
Hysterectomy, n (%)	153 (38.3%)	156 (39.3%)
Oophorectomy, n (%)	75 (18.8%)	89 (22.4%)
Duration of amenorrhea[a] (years), median (Q1, Q3)	3.9 (2.0, 7.0)[b]	3.0 (2.0, 6.0)[c]

[a]In participants without hysterectomy or oophorectomy; [b]n=241 (239 available for calculation); [c]n=230.
BMI, body mass index; EZN, elinzanetant; PBO, placebo; SD, standard deviation.

- Mean (SD) reductions from baseline to weeks 1, 4, and 12 in **daily frequency** (**Figure 1**) and weeks 4 and 12 in **severity** (**Figure 2**) of **moderate-to-severe VMS** were **nominally significantly greater with EZN** vs placebo
- Mean (SD) reductions from baseline to week 12 in **PROMIS SD SF 8b total T-score** (**Figure 3**) and week 12 in **MENQOL** (**Figure 4**) were **nominally significantly greater with EZN** vs placebo
- In those who switched from PBO to EZN after week 12, **further numerical improvements** were observed across **VMS, sleep disturbances, and quality of life** up to week 26 (**Figures 1–4**)

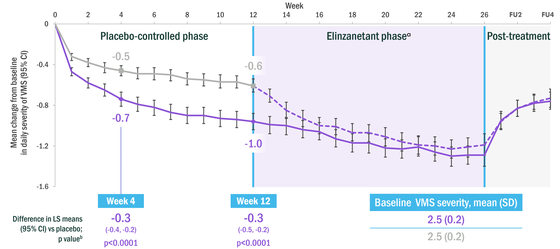
ELINZANETANT 120 MG — PLACEBO

Figure 1. Mean change from baseline in average daily frequency of moderate-to-severe VMS over time



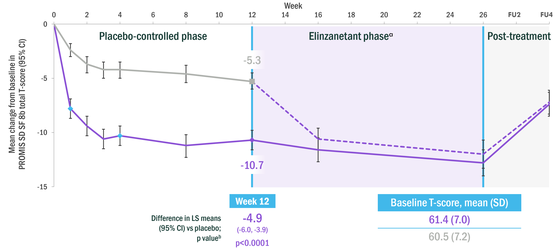
[a]Those who received placebo for the first 12 weeks switched to elinzanetant for the remainder of the trial; [b]nominal p value; one-sided.
CI, confidence interval; FU, follow-up; LS, least squares; SD, standard deviation; VMS, vasomotor symptoms.

Figure 2. Mean change from baseline in average daily severity of VMS over time



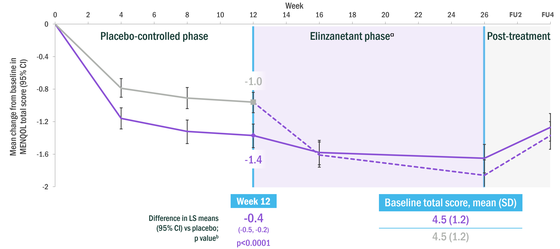
[a]Those who received placebo for the first 12 weeks switched to elinzanetant for the remainder of the trial; [b]nominal p value; one-sided.
CI, confidence interval; FU, follow-up; LS, least squares; SD, standard deviation; VMS, vasomotor symptoms.

Figure 3. Mean change from baseline in PROMIS SD SF 8b total T-score over time



[a]Those who received placebo for the first 12 weeks switched to elinzanetant for the remainder of the trial; [b]nominal p value; one-sided.
CI, confidence interval; FU, follow-up; LS, least squares; PROMIS SD SF 8b, Patient-Reported Outcomes Measurement Information System Sleep Disturbance Short Form 8b; SD, standard deviation.

Figure 4. Mean change from baseline in MENQOL total score over time



[a]Those who received placebo for the first 12 weeks switched to elinzanetant for the remainder of the trial; [b]nominal p value; one-sided.
CI, confidence interval; FU, follow-up; LS, least squares; MENQOL, Menopause-Specific Quality of Life questionnaire; SD, standard deviation.

CONCLUSIONS

Elinzanetant is an efficacious, novel non-hormonal treatment for postmenopausal women with moderate-to-severe VMS

Elinzanetant demonstrated reductions in VMS frequency as early as week 1, and reductions in VMS frequency and severity were maintained throughout treatment

Elinzanetant also improved sleep disturbances and menopause-related quality of life in postmenopausal women with moderate-to-severe VMS

The pooled safety analysis, which includes the recently completed OASIS 3 study, will be reported separately

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