POSTER 071

Effect of elinzanetant for the treatment of vasomotor symptoms associated with menopause across body mass index and smoking history subgroups: pooled data from two Phase 3 studies

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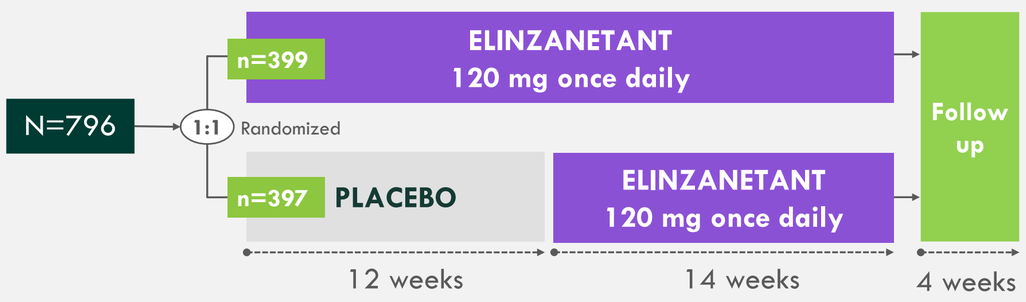
INTRODUCTION

In the pivotal randomized Phase 3 trials, OASIS 1 and 2, elinzanetant (EZN), a dual neurokinin-1 and -3 receptor antagonist, significantly reduced the frequency and severity of menopausal vasomotor symptoms (VMS; also known as hot flashes) compared with placebo (PBO).[1] It is important to understand the efficacy of EZN across body mass index (BMI) and smoking history subgroups as they are important aspects that could influence treatment choice. Therefore, this analysis aimed to evaluate the efficacy of EZN in pre-specified BMI and smoking history subgroups using pooled data from the OASIS 1 and 2 trials.

METHODS

Participants and interventions

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



Main outcome measures

Participants were evaluated by:

BMI (kg/m²):
- <18.5
- 18.5 to <25
- 25 to <30
- ≥30

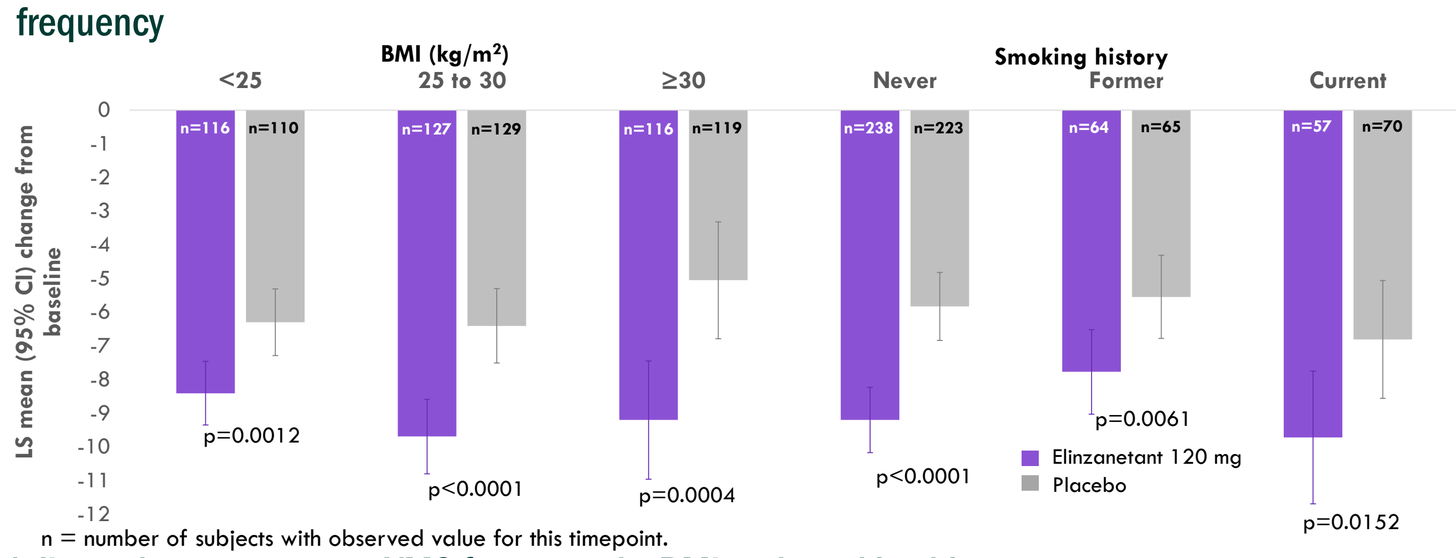
Smoking history:
- Never
- Former
- Current

Data were pooled from OASIS 1 and 2 trials. The <18.5 and 18–25 BMI subgroups were grouped for statistical analysis due to small sample size. Mean changes in daily moderate-to-severe VMS frequency from baseline to week 12 as well as the interaction between subgroup and treatment were analyzed by a mixed model with repeated measures. All p-values were nominal and one-sided (α level of 0.025).

RESULTS

- At **baseline,** daily moderate-to-severe VMS frequency was **similar** across BMI subgroups of <25 kg/m², 25 to <30 kg/m², and ≥30 kg/m², as well as never smokers, former smokers, and current smokers (**Table 2**).
- Mean (SD) reductions from baseline to week 12 in daily moderate-to-severe VMS frequency were nominally **significantly greater with EZN** than with PBO across **all BMI subgroups** of <25 kg/m², 25 to <30 kg/m², and ≥30 kg/m². The same was observed in subgroups of **never smokers, former smokers, and current smokers** (**Figure 1**).
- The differences in least square (LS) means between EZN and PBO were not nominally significantly different across BMI subgroups or smoking history subgroups.

Figure 1. LS mean change from baseline to week 12 in average daily moderate-to-severe VMS frequency



n = number of subjects with observed value for this timepoint.

Table 1. Participant BMI and smoking history

	EZN 120 mg (n=399)	PBO (n=397)
BMI (kg/m²), n (%)		
<25	129 (32.3%)	120 (30.2%)
25 to <30	142 (35.6%)	143 (36.0%)
≥30	128 (32.1%)	134 (33.8%)
Smoking history, n (%)		
Never	267 (66.9%)	250 (63.0%)
Former	67 (16.8%)	66 (16.6%)
Current	65 (16.3%)	81 (20.4%)

Table 2. Average daily moderate-to-severe VMS frequency by BMI and smoking history

	BMI (kg/m²)						Smoking history					
	<25		25 to <30		≥30		Never		Former		Current	
	EZN 120 mg (n=129)	PBO (n=120)	EZN 120 mg (n=142)	PBO (n=143)	EZN 120 mg (n=128)	PBO (n=134)	EZN 120 mg (n=267)	PBO (n=250)	EZN 120 mg (n=67)	PBO (n=66)	EZN 120 mg (n=65)	PBO (n=81)
Baseline, mean (SD)	13.5 (7.3)	13.8 (7.5)	13.5 (6.5)	15.8 (16.6)	15.1 (12.6)	15.9 (11.4)	14.0 (9.0)	15.8 (14.2)	13.2 (6.5)	13.0 (7.6)	14.9 (11.7)	15.3 (10.5)
LS mean change from baseline to week 12 (SE)	-8.4 (0.5)	-6.3 (0.5)	-9.7 (0.6)	-6.4 (0.6)	-9.2 (0.9)	-5.1 (0.9)	-9.2 (0.5)	-5.8 (0.5)	-7.8 (0.6)	-5.6 (0.6)	-9.7 (1.0)	-6.8 (0.9)
Difference in LS means (SE) [95% CI]	-2.1 (0.7) [-3.5, -0.8]		-3.3 (0.8) [-4.8, -1.7]		-4.2 (1.2) [-6.6, -1.7]		-3.4 (0.7) [-4.8, -2.0]		-2.2 (0.9) [-4.0, -0.5]		-2.9 (1.3) [-5.6, -0.3]	
p-value (one-sided)	p=0.0012		p<0.0001		p=0.0004		p<0.0001		p=0.0061		p=0.0152	

CONCLUSIONS

EZN was consistently efficacious in reducing moderate-to-severe VMS frequency in postmenopausal women across all BMI and smoking history subgroups

VMS can vary across BMI and smoking status; therefore, it is important to understand the efficacy of VMS treatments across these characteristics[2]

EZN demonstrated nominally significantly greater reductions than PBO in moderate-to-severe VMS frequency across all BMI and smoking history subgroups

These differences were consistent across individual BMI and smoking history subgroups

ACKNOWLEDGEMENTS

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REFERENCES

1. Pinkerton JV, et al. JAMA 2024. doi:10.1001/jama.2024.14618.
2. Anderson DJ, et al. Am J Obstet Gynecol 2020;222:478.e1–478.e17.

DISCLOSURES

JoAnn 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 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 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 Soares has received research grants from: Ontario Brain Institute, Clairvoyant Therapeutics, Eisai Inc. and performed consultancy work for: Otsuka, Bayer, Eisai, Diamond Therapeutics. Rebecca Thurston has acted in an advisory capacity for Bayer, Astellas, and Hello Therapeutics. Senka Djordjevic and Lineke Zuurman are employees of Bayer CC AG. Claudia Haberland is an employee of Bayer AG. Chenshuang Lu is an employee of Bayer U.S. LLC.