THE IMPACT OF ELINZANETANT TREATMENT ON BONE HEALTH AND BODY COMPOSITION IN POSTMENOPAUSAL WOMEN

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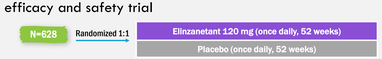
INTRODUCTION

- The neuropeptide substance-P and its receptor neurokinin-1 (SP-NK1R pathway) have been proposed to play a role in bone metabolism and remodeling.[1,2] However, the exact role of the pathway and the therapeutic potential of NK1R antagonists in diseases like osteoporosis remains unclear.[2]
- Preclinical evidence also points to a role of this pathway in energy homeostasis,[3-5] with NK1R antagonists suggested as potential therapies in obesity.[3]
- Elinzanetant is a dual NK1 and NK3 receptor antagonist in late-stage development for vasomotor symptoms (hot flashes) associated with menopause.[6]
- This post hoc analysis evaluates potential benefits of elinzanetant on the skeleton, body weight, and body composition in postmenopausal women.

METHODS

Data were gathered from exploratory endpoints of the 52-week, placebo-controlled OASIS-3 Phase III elinzanetant efficacy and safety trial



Bone measures

- Mean % change in bone mineral density: measured directly by dual-energy X-ray absorptiometry in femoral neck, total hip, and lumbar spine[a,b]
- Mean change in total bone mass (kg): measured indirectly by bioelectrical impedance analysis[c,d]
- Mean % change in bone turnover markers: OC and P1NP[c,e]

Body composition measures

- Mean change in body weight (kg)[c,d]
- Mean change in BMI (weight/height^2)[c,d]
- Mean change in waist circumference (cm)[c,d]
- Mean change in FMI (fat mass/height^2)[c,d]
- Mean change in LMI (lean mass/height^2)[c,d]
- Mean change in total body water[c,d]
- Subanalysis based on FMI at baseline (FMI ≤9 normal fat mass; >9 excess fat mass)[7,8]

Descriptive statistics were used to evaluate all parameters and trends

BMI, body mass index; DXA, dual-energy X-ray absorptiometry; FMI, fat mass index; HRT, hormone replacement therapy; LMI, lean mass index; OC, osteocalcin; P1NP, procollagen 1N-terminal propeptide.
[a]Mean change from baseline. Data collected at baseline and weeks 24 and 52. [b]BMD analysis set: all randomized participants in sites assigned to perform DXA, who have baseline and ≥1 post-baseline (week 24 and/or week 52) DXA scan available and have not used HRT or some other drugs affecting bone density (other than vitamin D and calcium) until that time point (n=173 elinzanetant; N=170 placebo). [c]Mean change from baseline. Data collected at baseline and weeks 4, 8, 12, 18, 24, 36, and 52. [d]Full analysis set: all randomized participants (n=313 elinzanetant; n=315 placebo). [e]Safety analysis set: all participants who receive ≥1 dose of study intervention (n=313 elinzanetant; n=314 placebo).

RESULTS

% CHANGE IN BMD WAS LOWER WITH ELINZANETANT VS PLACEBO

		Elinzanetant 120 mg (n=173)			Placebo (n=170)		
		n	Mean (SD)	Median	n	Mean (SD)	Median
Femoral neck	Baseline	172	0.82 (0.13)	0.80	165	0.83 (0.13)	0.82
	Week 52	143	0.83 (0.14)	0.81	147	0.82 (0.13)	0.80
	% change from BL (week 52)	142	0.00 (4.70)	-0.38	146	-1.22 (4.07)	-1.44
Total hip	Baseline	172	0.94 (0.13)	0.93	165	0.95 (0.12)	0.96
	Week 52	143	0.93 (0.14)	0.92	147	0.95 (0.12)	0.94
	% change from BL (week 52)	142	-0.70 (4.16)	-0.93	146	-1.37 (3.01)	-0.83
Lumbar spine	Baseline	168	1.07 (0.18)	1.06	168	1.07 (0.16)	1.07
	Week 52	140	1.07 (0.19)	1.06	150	1.06 (0.17)	1.07
	% change from BL (week 52)	139	-0.57 (3.33)	-0.62	149	-1.22 (3.08)	-1.18

Table 1. % change in BMD at week 52, mean (SD). BL, baseline; BMD, bone mineral density; SD, standard deviation.

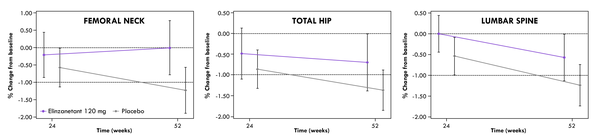


Figure 1. % change in BMD ± 95% CI are shown at weeks 24 and 52 in femoral neck (A), total hip (B), and lumbar spine (C), measured by DXA. BMD, bone mineral density; CI, confidence interval; DXA, dual-energy X-ray absorptiometry.

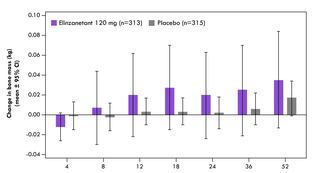


Figure 2. Mean change in bone mass (kg) from baseline up to 52 weeks of treatment, determined indirectly by bioelectrical impedance assessment. CI, confidence interval.

BONE TURNOVER MARKERS P1NP AND OSTEOCALCIN WERE LOWER WITH ELINZANTANT VS PLACEBO OVER 52 WEEKS OF TREATMENT

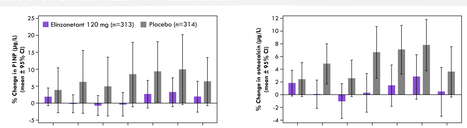


Figure 3. % change in bone turnover markers from baseline up to week 52: P1NP (µg/L) (A) and osteocalcin (µg/L) (B). CI, confidence interval; P1NP, procollagen 1N-terminal propeptide.

MILD REDUCTIONS IN WEIGHT, BMI, AND WAIST CIRCUMFERENCE WERE OBSERVED WITH ELINZANETANT VS PLACEBO OVER 52 WEEKS OF TREATMENT

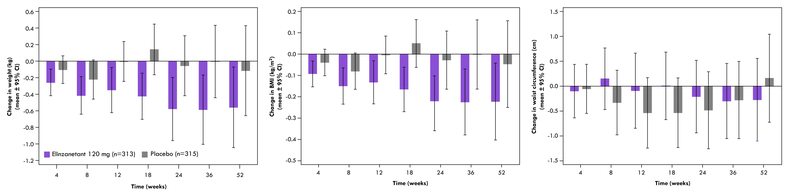


Figure 5. Mean change ± 95% CI in weight (kg), BMI (kg/m^2), and waist circumference (cm) from baseline up to week 52. BMI, body mass index; CI, confidence interval.

MILD REDUCTIONS IN FMI, AND MILD INCREASES IN LMI AND BODY WATER WERE OBSERVED WITH ELINZANETANT VS PLACEBO OVER 52 WEEKS OF TREATMENT

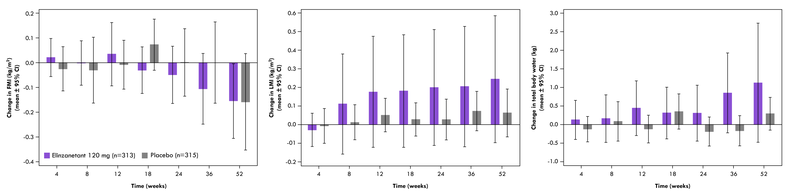
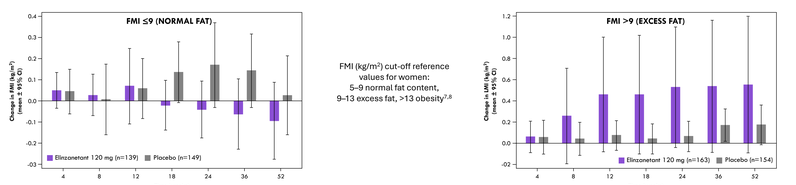


Figure 6. Mean change in FMI (kg/m^2) (A), LMI (kg/m^2) (B), and total body water (kg) (C) from baseline up to week 52. CI, confidence interval; FMI, fat mass index; LMI, lean mass index.

POSITIVE BODY RECOMPOSITION WAS OBSERVED IN PATIENTS TAKING ELINZANETANT VS PLACEBO OVER 52 WEEKS OF TREATMENT



FMI (kg/m^2) cut-off reference values for women: 5–9 normal fat content, 9–13 excess fat, >13 obesity[7,8]

Figure 7. Body recomposition is driven by lower FMI in patients with FMI ≤9 at baseline (A) or higher LMI in patients with FMI >9 at baseline (B). Plots show change in FMI and LMI (kg/m^2) over 52 weeks. CI, confidence interval; FMI, fat mass index; LMI, lean mass index.

CONCLUSIONS

Data from exploratory endpoints of the long-term safety Phase III OASIS-3 trial expand the safety profile of elinzanetant

This analysis provides preliminary but novel signals that a dual NK1R/NK3R antagonist may provide benefits in bone health and body composition of postmenopausal women

Further research is warranted to provide conclusive evidence of the benefits of elinzanetant, specifically in postmenopausal women with obesity/overweight status or osteoporosis

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DISCLOSURES

E. Michael Lewiecki: consultant and/or speaker for Amgen, Angitia, Ascendis, Kyowa Kirin, Radius, and Ultragenyx. Ekta Kapoor: consultant for Astellas, Estetra SRL, and Wellfound Inc, and participated in advisory boards for Exeltis, Novo Nordisk, Fresenius Kabi USA, and Kabi USA. Sandra Hurtado: Principal Investigator for the OASIS-2 and -3 studies. Victor M. Navarro: consultant/speaker for Bayer AG. Maria Jose Torres, Jeremy Beau: employees of Bayer U.S., LLC. Ioanna Gkioni: employee of Syneos Health LLC (providing service to Bayer). Kelly Genga: employee of Bayer SA, Sao Paulo, Brazil.

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