THE IMPACT OF ELINZANETANT TREATMENT ON BONE HEALTH 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]
- Elinzanetant is a dual neurokinin (NK)-targeted therapy (NK1 and NK3 receptor antagonist) approved in the United States for the treatment of menopausal vasomotor symptoms (VMS); however, its effects on skeletal health in postmenopausal women have not been fully characterized[3,4]
- This post hoc analysis of exploratory endpoints from the 52-week Phase III OASIS-3 study evaluated the impact of elinzanetant vs placebo on bone health in postmenopausal women

METHODS

Study design and participants

- Data were obtained from exploratory endpoints of the 52-week placebo-controlled Phase III OASIS-3 study, which evaluated the efficacy and safety of elinzanetant
- OASIS-3 included postmenopausal women aged 40–65 years with moderate-to-severe VMS, with no requirement for a minimum number of VMS events

N=628 — Randomized 1:1 → Elinzanetant 120 mg (once daily, 52 weeks); Placebo (once daily, 52 weeks)

Endpoints

- Mean % change from baseline in BMD at the femoral neck, total hip, and lumbar spine, measured by DXA, with post hoc analysis by baseline T-score (≥ -1.0 [normal] vs < -1.0 [low bone mass])[a,b]
- Mean change from baseline in total bone mass (kg): measured indirectly by bioelectrical impedance analysis[c,d]
- Mean % change from baseline in bone turnover markers: OC and P1NP[c,e]
- Descriptive statistics were used for all analyses

BMD, bone mineral density; DXA, dual-energy X-ray absorptiometry; HRT, hormone replacement therapy; OC, osteocalcin; P1NP, procollagen 1N-terminal propeptide.
[a]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 postbaseline (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 (elinzanetant, n=174; placebo, n=169). [c]Data collected at baseline and weeks 4, 8, 12, 18, 24, 36, and 52. [d]Full analysis set: all randomized participants (elinzanetant, n=313; placebo, n=315). [e]Safety analysis set: all participants who receive ≥1 dose of study intervention (elinzanetant, n=313; placebo, n=314).

RESULTS

		Elinzanetant 120 mg (n=174)			Placebo (n=169)		
		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). % change from baseline in BMD was less with elinzanetant vs placebo. BL, baseline; BMD, bone mineral density; SD, standard deviation.

			Elinzanetant 120 mg (n=174)			Placebo (n=169)		
			n	Mean (SD)	95% CI	n	Mean (SD)	95% CI
FEMORAL NECK	T-score at baseline ≥ -1.0: Normal	Baseline	90	0.90 (0.12)	0.88, 0.93	99	0.90 (0.11)	0.88, 0.92
		Week 52	75	0.91 (0.13)	0.88, 0.94	91	0.88 (0.11)	0.86, 0.91
		% change from BL (week 52)	75	**-0.58** (3.54)	-1.40, 0.23	91	**-1.91** (3.98)	-2.74, -1.08
	T-score at baseline < -1.0: Low bone mass	Baseline	82	0.73 (0.07)	0.72, 0.75	66	0.72 (0.08)	0.70, 0.74
		Week 52	67	0.73 (0.09)	0.71, 0.76	55	0.72 (0.08)	0.70, 0.74
		% change from BL (week 52)	67	**0.65** (5.70)	-0.74, 2.04	55	**-0.08** (3.99)	-1.15, 1.00
TOTAL HIP	T-score at baseline ≥ -1.0: Normal	Baseline	129	0.99 (0.11)	0.97, 1.00	135	0.99 (0.10)	0.97, 1.01
		Week 52	104	0.98 (0.12)	0.96, 1.00	120	0.98 (0.10)	0.96, 1.00
		% change from BL (week 52)	104	**-1.15** (2.76)	-1.69, -0.61	120	**-1.45** (2.90)	-1.98, -0.93
	T-score at baseline < -1.0: Low bone mass	Baseline	43	0.79 (0.05)	0.78, 0.81	30	0.78 (0.06)	0.76, 0.80
		Week 52	38	0.79 (0.07)	0.77, 0.82	26	0.78 (0.05)	0.76, 0.80
		% change from BL (week 52)	38	**0.52** (6.52)	-1.63, 2.66	26	**-0.96** (3.53)	-2.39, 0.47
LUMBAR SPINE	T-score at baseline ≥ -1.0: Normal	Baseline	109	1.16 (0.15)	1.13, 1.19	119	1.14 (0.12)	1.12, 1.17
		Week 52	91	1.16 (0.17)	1.13, 1.20	105	1.14 (0.13)	1.11, 1.16
		% change from BL (week 52)	91	**-0.40** (2.91)	-1.00, 0.21	105	**-1.29** (3.27)	-1.93, -0.66
	T-score at baseline < -1.0: Low bone mass	Baseline	59	0.90 (0.09)	0.88, 0.93	49	0.89 (0.09)	0.86, 0.91
		Week 52	48	0.90 (0.10)	0.87, 0.93	44	0.88 (0.09)	0.85, 0.91
		% change from BL (week 52)	48	**-0.90** (4.03)	-2.07, 0.27	44	**-1.04** (2.60)	-1.83, -0.24

Table 2. BMD at week 52 categorized by T-score, mean (SD) values, and % change from baseline. % BMD loss from baseline was less with elinzanetant vs placebo regardless of T-score at baseline. BL, baseline; BMD, bone mineral density; CI, confidence interval; SD, standard deviation.

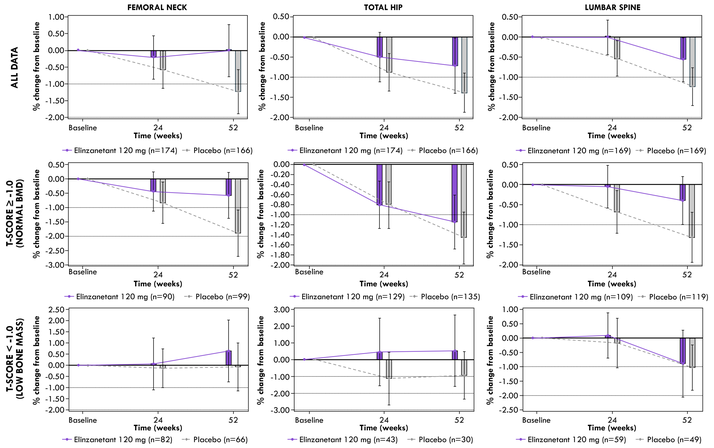

Figure 1. % change in BMD ± 95% CI at weeks 24 and 52 in femoral neck, total hip, and lumbar spine, measured by DXA, categorized by T-score at baseline. % BMD loss from baseline was less with elinzanetant vs placebo, regardless of T-score at baseline. All data (top row), T-score ≥ -1.0 (middle row), and T-score < -1.0 (bottom row). BMD, bone mineral density; CI, confidence interval; DXA, dual-energy X-ray absorptiometry.

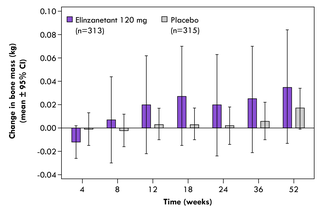

Figure 2. Mean change in bone mass (kg) from baseline up to 52 weeks of treatment, determined indirectly by bioelectrical impedance assessment. Greater preservation of bone mass (kg) was observed in the elinzanetant group compared with placebo. CI, confidence interval.

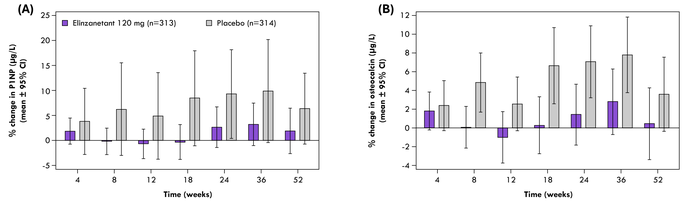

Figure 3. % change in bone turnover markers from baseline up to week 52: (A) P1NP (µg/L) and (B) osteocalcin (µg/L). Bone turnover markers P1NP and osteocalcin were lower with elinzanetant vs placebo over 52 weeks of treatment. CI, confidence interval; P1NP, procollagen 1N-terminal propeptide.

CONCLUSIONS

Data from exploratory endpoints of the long-term safety Phase III OASIS-3 study expand the safety profile of elinzanetant, and suggest potential beneficial effects on skeletal health in postmenopausal women through the potential deceleration of bone loss

This analysis suggests preliminary but novel signals that a dual NK1 and NK3 receptor antagonist may offer benefits in bone health in postmenopausal women

Further research is warranted to provide conclusive evidence of the benefits of elinzanetant specifically in postmenopausal women with normal or low bone mass

REFERENCES

1. Liu D, et al. *Neuropeptides*. 2007;41(5):271-283.
2. Li F-X-Z, et al. *Front Endocrinol (Lausanne)*. 2020;11:77.
3. Lynkuet. Prescribing information. Whippany, NJ: Bayer Healthcare Pharmaceuticals Inc.; 2025.
4. Pinkerton J, et al. *JAMA*. 2024;332(16):1343-1354.

ACKNOWLEDGMENTS

This study was sponsored by Bayer U.S. (Whippany, NJ, USA). Medical writing assistance was provided by Sara Edwards, MSc, of Envision Catalyst, an Envision Medical Communications agency, a part of Envision Pharma Group, funded by Bayer.

DISCLOSURES

E. Michael Lewiecki: consultant and/or speaker for Amgen, Angitia, Ascendis, Kyowa Kirin, Radius, and Ultragenyx. Andrea Singer: consultant and/or speaker for Amgen, Astellas, Bayer, Radius Health, and UCB. Sandra Hurtado: consultant/speaker for Bayer U.S. and 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. Ioanna Gkioni: employee of Bayer Hellas AG (Athens, Greece).

Presented at the American College of Obstetricians and Gynecologists (ACOG) 2026 Annual Clinical & Scientific Meeting; May 1–3, 2026; Washington, DC, USA. Some data previously presented at the Endocrine Society Annual Meeting (ENDO); July 12–15, 2025; San Francisco, CA, USA