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Pharmacokinetics, compliance, and oestradiol levels in women with breast cancer receiving elinzanetant for the treatment of endocrine therapy-associated vasomotor symptoms

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INTRODUCTION

In the Phase III OASIS-4 study, elinzanetant significantly reduced vasomotor symptoms (VMS) associated with endocrine therapy (ET) for hormone receptor-positive breast cancer.[1] This analysis evaluated elinzanetant and ET pharmacokinetics (PK), ET compliance, and oestradiol (E2) levels.

METHODS

OASIS-4 (NCT05587296) included women aged 18–70 years experiencing ≥35 moderate-to-severe VMS per week while receiving ET for the treatment or prevention of hormone receptor-positive breast cancer.[1] Women were randomised 2:1 to receive elinzanetant 120 mg for 52 weeks or placebo for 12 weeks followed by elinzanetant for 40 weeks.

Outcomes

Serial plasma samples were collected during 52 weeks of elinzanetant exposure to:

- assess the ability of the existing **population PK models for elinzanetant to describe observed plasma concentrations** in OASIS-4.
- assess **plasma concentrations of tamoxifen (and its metabolites) and anastrozole** when coadministered with elinzanetant compared to baseline steady state concentrations.

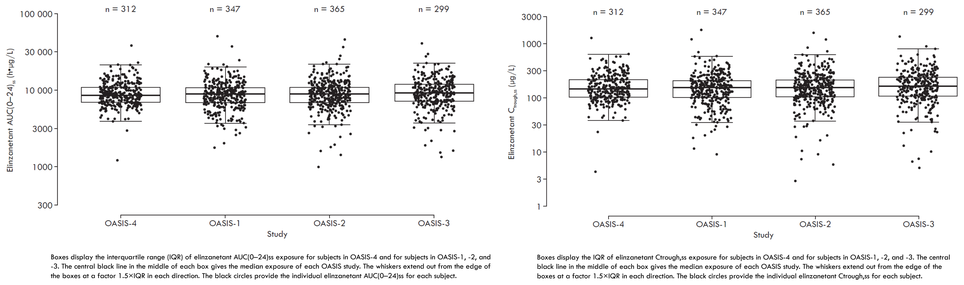
ET compliance estimated via eDiary:

$$100 \times \frac{\text{\# days the medication was taken}}{\text{\# days with eDiary ET intake data during treatment} \times \text{daily dosage during baseline}}$$

E2 serum levels from baseline to week 12 analysed by ET subgroup (tamoxifen, aromatase inhibitors, ovarian function suppression [OFS], no OFS).

RESULTS

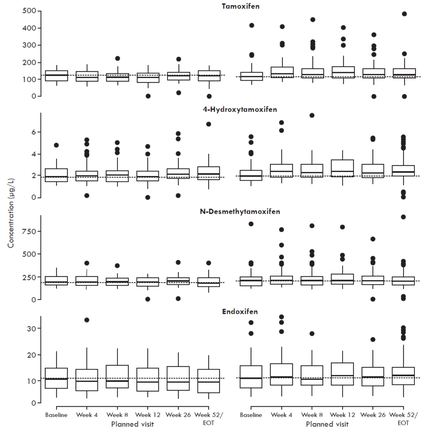
Figure 1. Population PK model-based assessment of elinzanetant plasma concentrations



Boxes display the interquartile range (IQR) of elinzanetant AUC(0–24)ss exposure for subjects in OASIS-4 and for subjects in OASIS-1, -2, and -3. The central black line in the middle of each box gives the median exposure of each OASIS study. The whiskers extend out from the edge of the boxes at a factor 1.5×IQR in each direction. The black circles provide the individual elinzanetant AUC(0–24)ss for each subject.

Boxes display the IQR of elinzanetant Ctrough,ss exposure for subjects in OASIS-4 and for subjects in OASIS-1, -2, and -3. The central black line in the middle of each box gives the median exposure of each OASIS study. The whiskers extend out from the edge of the boxes at a factor 1.5×IQR in each direction. The black circles provide the individual elinzanetant Ctrough,ss for each subject.

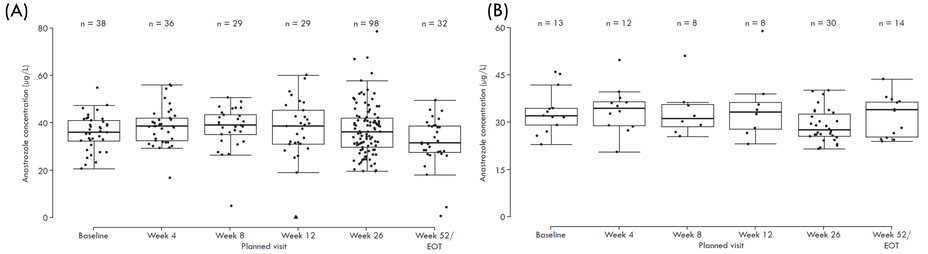
Figure 2. Plasma concentrations of tamoxifen and its metabolites over 52 weeks



The whiskers, box, and line depict the 5th, 25th, 50th, 75th, and 95th percentile of the data. The continuous horizontal line represents the compound and treatment group-specific median of the baseline visit. Points depict outliers.

- PopPK assessment showed **no change in elinzanetant PK parameters** compared with the OASIS-1, -2, and -3 studies in postmenopausal women (Figure 1).
  - OASIS-1, -2, -3: AUC(0–24)ss of 8650 h·µg/L and Ctrough,ss of 146.6 µg/L.
  - OASIS-4: 8572 h·µg/L and 143.5 µg/L, respectively.
- **ET had no effect on elinzanetant plasma concentrations, and elinzanetant did not affect plasma concentrations of tamoxifen,** its metabolites, **or anastrozole** (Figures 2 and 3) throughout 52 weeks.

Figure 3. Plasma concentrations of anastrozole over 52 weeks for the elinzanetant (A) and placebo-elinzanetant (B) treatment arms



Boxes display the IQR of anastrozole observations stratified by the study visit week. The first dose of elinzanetant was taken after the baseline observations by the elinzanetant subjects. The central black line in the middle of each box gives the median anastrozole concentration of that study visit. The whiskers extend out from the edge of the boxes at a factor 1.5×IQR in each direction. The black circles provide the individual anastrozole observations > LLOQ for the elinzanetant arm. The black triangles provide the individual anastrozole observations < LLOQ for the elinzanetant arm within that period. The total number of anastrozole observations during each study visit is listed above.

Boxes display the IQR of anastrozole observations stratified by the study visit week. The first dose of elinzanetant was taken after the Week 12 visit observations by the placebo + elinzanetant subjects. The central black line in the middle of each box gives the median anastrozole concentration of that study visit. The whiskers extend out from the edge of the boxes at a factor 1.5×IQR in each direction. The black circles provide the individual anastrozole observations > LLOQ for the elinzanetant arm. The total number of anastrozole observations during each study visit is listed above.

- Median **self-reported ET compliance over 52 weeks was 100%.**
- **High variability was seen in E2 levels** at baseline and throughout treatment (Table 1).
- There was a trend towards **higher mean baseline serum E2 levels in the tamoxifen group.**

Table 1. E2 levels by type of background endocrine therapy

	Tamoxifen		Aromatase inhibitors		OFS		No OFS	
	EZN (n=175)	PBO (n=90)	EZN (n=141)	PBO (n=68)	EZN (n=88)	PBO (n=48)	EZN (n=228)	PBO (n=110)
Mean (95% CI) baseline serum E2 levels (pg/mL)	20.24 (11.33, 29.14)	36.23 (1.36, 71.09)	7.48 (5.15, 9.82)	6.11 (4.77, 7.46)	9.24 (6.55, 11.94)	15.96 (0.62, 31.30)	16.62 (9.67, 23.58)	26.36 (-1.42, 54.15)
Mean (95% CI) change in serum E2 levels from baseline to week 12 (pg/mL)	-3.43 (-14.28, 7.42)	-0.36 (-18.46, 17.74)	0.64 (-1.79, 3.08)	2.00 (-0.55, 4.54)	-0.34 (-4.42, 3.74)	6.33 (-19.02, 31.68)	-2.12 (-10.49, 6.24)	-2.02 (-12.23, 8.18)

CI, confidence interval; E2, oestradiol; EZN, elinzanetant; OFS, ovarian function suppression; PBO, placebo.

CONCLUSIONS

Overall, no clinically relevant PK interactions are expected with coadministration of elinzanetant with either tamoxifen or anastrozole.

Self-reported compliance with ET was high.

As expected, there was a trend towards higher baseline serum E2 levels in the tamoxifen group.

ACKNOWLEDGEMENTS

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REFERENCES

1. Cardoso F, et al. New England J Med 2025;393:752–63.

DISCLOSURES

Fatima Cardoso declares paid consultancy for: Amgen, Astellas/Medivation, AstraZeneca, Bayer, Celgene, Daiichi-Sankyo, Eisai, GE Oncology, Genentech, Gilead, GlaxoSmithKline, Iqvia, Macrogenics, Medscape, Merck-Sharp, Merus BV, Mylan, Mundipharma, Novartis, Pfizer, Pierre-Fabre, prIME Oncology, Roche, Sanofi, Samsung Bioepis, Seagen, Teva, Touchime.