Efficacy of elinzanetant for the treatment of vasomotor symptoms in women with breast cancer: subgroup analysis of the OASIS-4 trial by type of endocrine therapy

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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, Mylan, Mundipharma, Novartis, Pfizer, Pierre Fabre, prIME Oncology, Roche, Sanofi, Samsung Bioepis, Seagen, Teva, touchIME.

Donal J Brennan has acted in an advisory capacity for Merck, GSK, AstraZeneca, Bayer, Astellas; received research funding from Pfizer, GSK, AstraZeneca, Bayer; and received Honoraria from Bayer, Medtronic, Olympus, MSD, RAND Biotech.

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Lauren Wahyudi is an employee of Bayer CC AG.

Christian Seitz is an employee of Bayer AG.

Kaisa Laapas is an employee of Bayer Oy.

Introduction

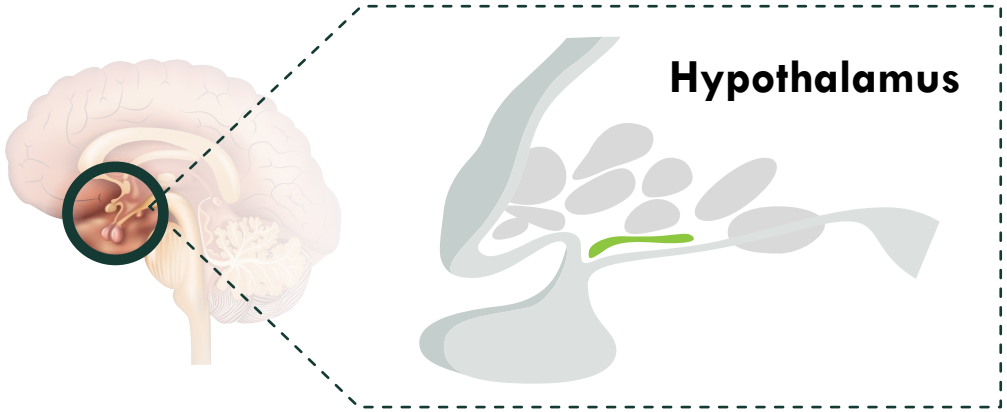
Elinzanetant is the first and only non-hormonal, dual-targeted therapy (NK-1 and NK-3 receptor antagonist) approved for the treatment of VMS associated with menopause or endocrine therapy for breast cancer

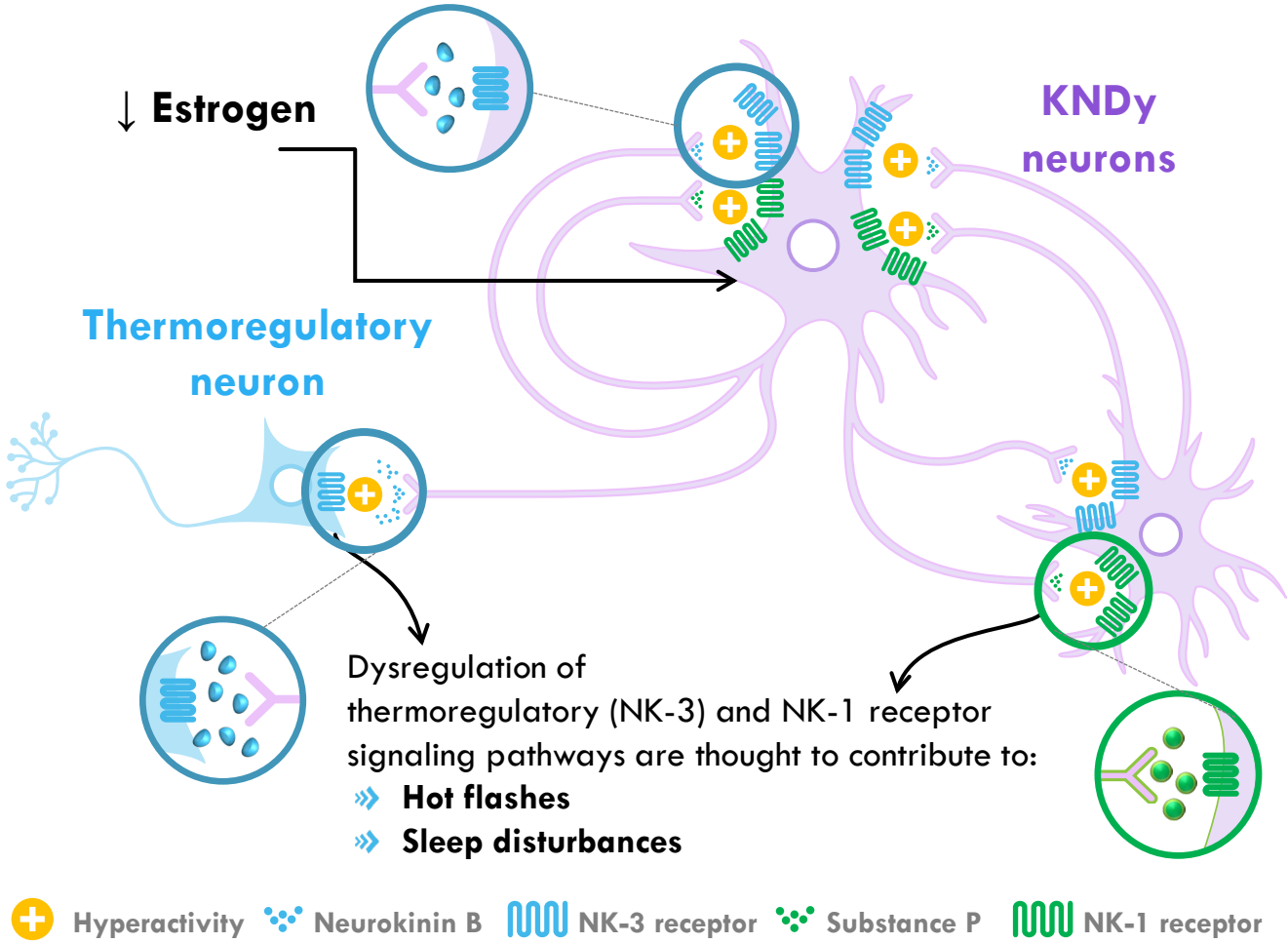
In the Phase III OASIS-4 trial, elinzanetant demonstrated significant improvements in VMS, sleep disturbances, and menopause-related quality of life in women taking endocrine therapy for breast cancer

This subgroup analysis evaluated the effect of elinzanetant on VMS frequency and severity by type of endocrine therapy in OASIS-4

NK, neurokinin; VMS, vasomotor symptoms.

Background: what may be the link between menopause, thermoregulation, and sleep?[1-8]





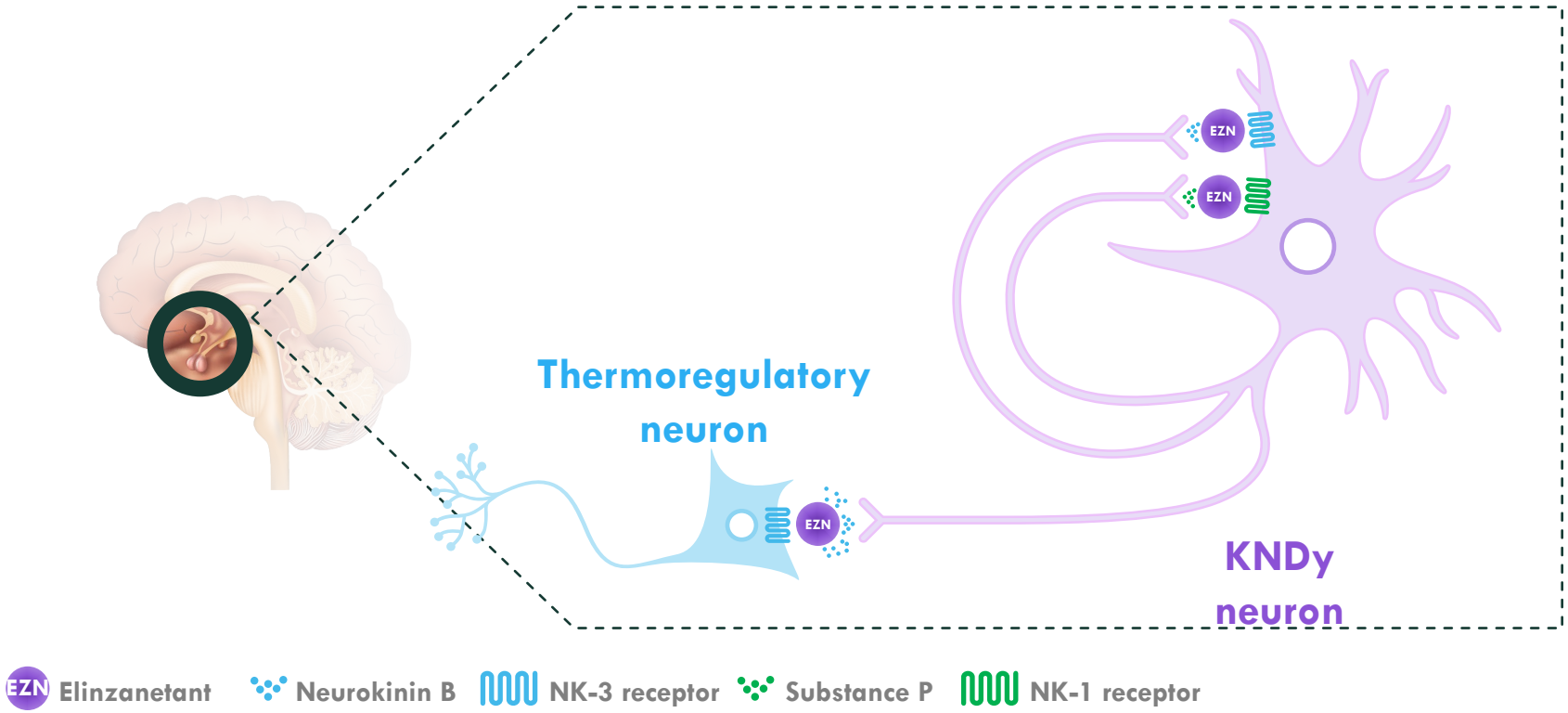
- **KNDy** neurons express **estrogen receptors,** and their hyperactivity occurs due to a **decline** in **estrogenic activity** as a result of natural or surgical menopause or endocrine therapy

KNDy, kisspeptin/neurokinin B/dynorphin; NK, neurokinin; VMS, vasomotor symptoms.

1. Rance NE, et al. Front Neuroendocrinol 2013;34:211–27; 2. Modi M, et al. Semin Reprod Med 2019;37:125–30; 3. Navarro VM, et al. Endocrinology 2015;156:627–37; 4. Padilla SL, et al. Curr Biol 2019;29:592–604.e4; 5. Sergeeva OA, et al. Peptides 2022;150:170729. 6. Pillay OC, Manyonda I. Best Pract Res Clin Obstet Gynaecol 2022;81:111–8; 7. Shifren JL, et al. Menopause 2014;21:1038–62; 8. Zhang Z, et al. Elife 2021;10:e63333.

Background: elinzanetant's mode of action

It is thought that by targeting **NK-1** and **NK-3** receptors found centrally in the **hypothalamus,** as well as **NK-1** receptors in the **skin,** elinzanetant may contribute to restoring temperature regulation and sleep[1–5]

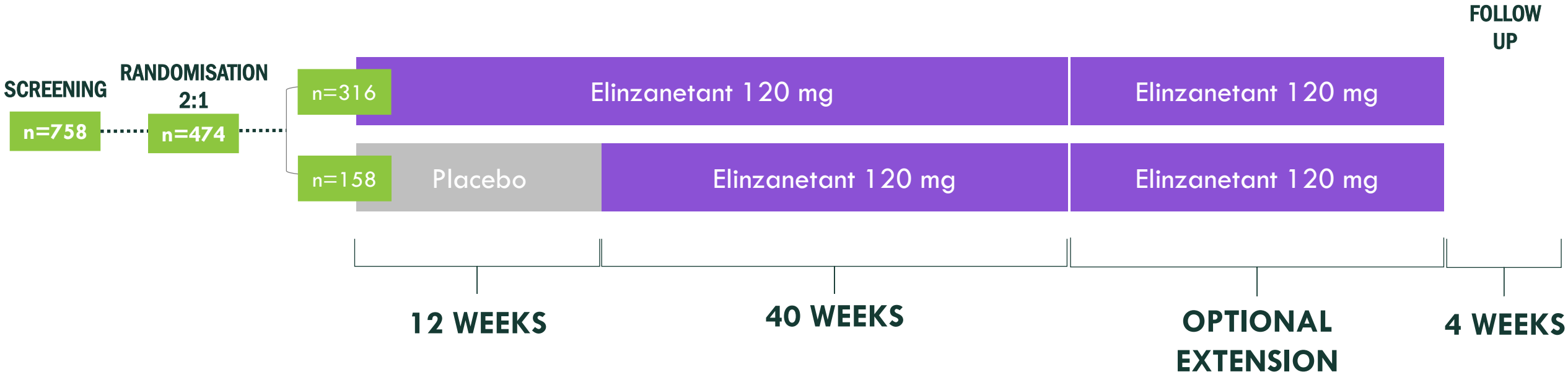


EZN, elinzanetant; KNDy, kisspeptin/neurokinin B/dynorphin; NK, neurokinin.

1. Pinkerton JV, et al. JAMA 2024;332:1343–54; 2. Simon JA, et al. Menopause 2023;30:239–46; 3. Cardoso F, et al. N Engl J Med 2025;393:753–63; 4. Panay N, et al. JAMA Intern Med 2025;185(11):1319–27; 5. Wong BJ, Minson CT. J Physiol 2006;577:1043–51.

Study design

OASIS-4 (NCT05587296) was a **multicentre, randomised, double-blind, placebo-controlled** Phase III trial evaluating elinzanetant 120 mg for the treatment of **VMS associated with endocrine therapy in women with or at high risk of hormone receptor-positive breast cancer**



Women who completed 52 weeks of treatment were able to participate in an ongoing extension for up to 2.5 years

VMS, vasomotor symptoms.

Study design

Key inclusion criteria

- Women aged 18–70 years
- Taking endocrine therapy (tamoxifen or aromatase inhibitors with or without GnRH analogues) for HR+ breast cancer
- Experiencing **≥35 moderate-to-severe hot flashes per week**

Mild hot flashes include a **sensation of heat** without sweating

Moderate hot flashes include **sweating** in addition to the sensation of heat

Severe hot flashes feature a **sensation of heat with sweating** that forces a woman to **stop her daily activities**

Endpoints

Mean change from baseline in:

- Daily **moderate-to-severe VMS frequency** to weeks 1, 4, and 12
- Daily **moderate-to-severe VMS severity** to weeks 4 and 12

Analysis

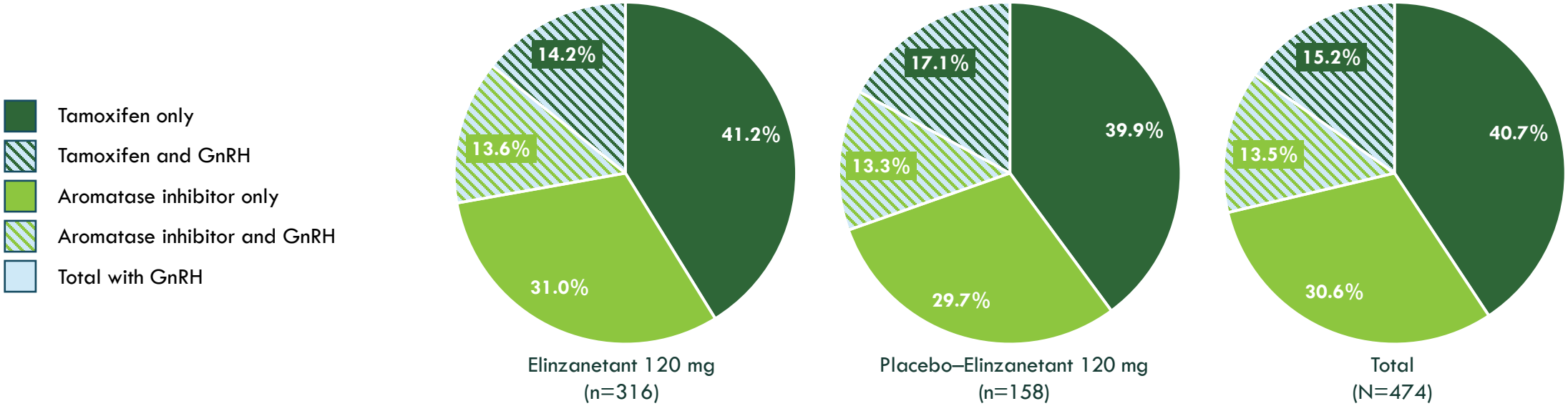
Endpoints were analysed descriptively by type of **endocrine therapy** at baseline:

- Tamoxifen
- Aromatase inhibitors
- With GnRH
- Without GnRH

GnRH, gonadotrophin-releasing hormone; HR+, hormone receptor-positive; VMS, vasomotor symptoms.

Prior adjuvant endocrine therapy* (FAS)

Drug / drug class	Elinzanetant 120 mg (n=316)	Placebo–Elinzanetant 120 mg (n=158)	Total (N=474)
Number (%) of subjects	**316 (100.0%)**	**158 (100.0%)**	**474 (100.0%)**
Duration of adjuvant endocrine therapy (years), mean (SD)	2.0 (1.5)	1.8 (1.5)	1.9 (1.5)
Tamoxifen	**175 (55.4%)**	**90 (57.0%)**	**265 (55.9%)**
Tamoxifen with GnRH	45 (14.2%)	27 (17.1%)	72 (15.2%)
Aromatase inhibitors	**141 (44.6%)**	**68 (43.0%)**	**209 (44.1%)**
Aromatase inhibitors with GnRH	43 (13.6%)	21 (13.3%)	64 (13.5%)
Total with GnRH	**88 (27.8%)**	**48 (30.4%)**	**136 (28.7%)**



*Medications taken before the start of study drug (regardless of when they ended).
FAS, full analysis set; GnRH, gonadotropin-releasing hormone; SD, standard deviation.

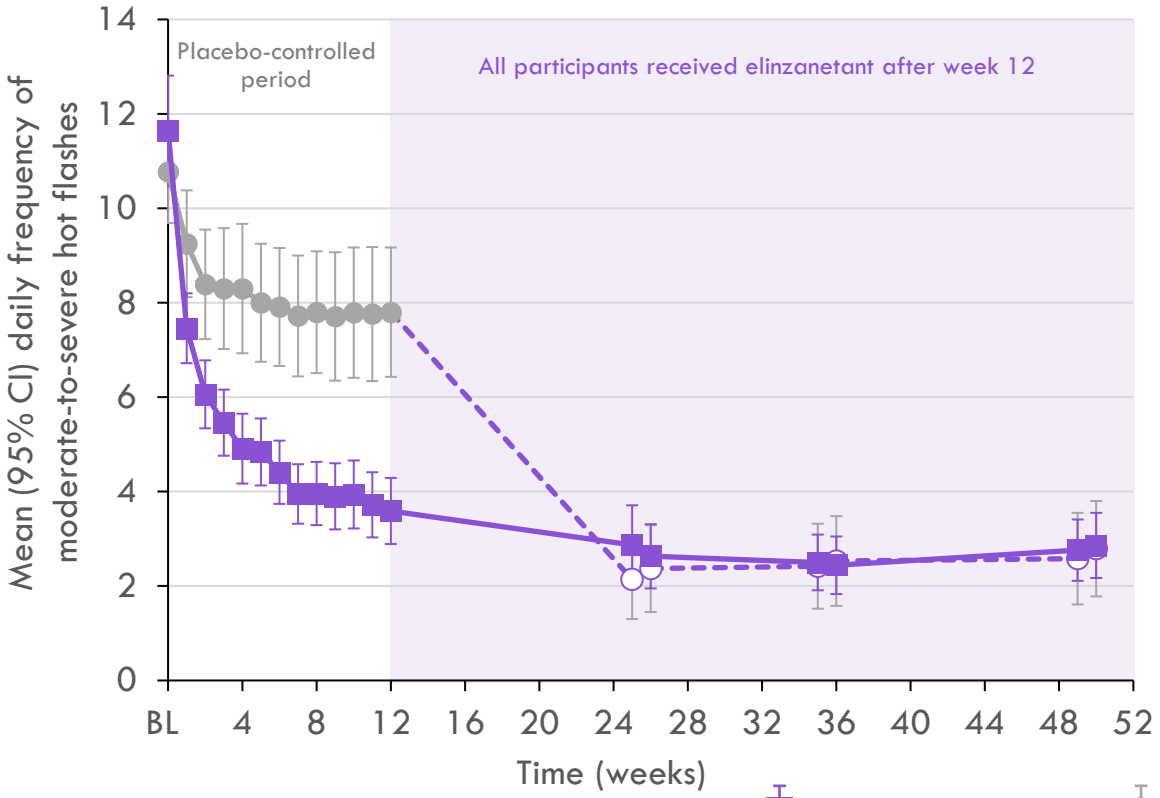
Participant demographics (FAS)

Characteristic	Tamoxifen (n=265)	Aromatase inhibitors (n=209)	GnRH (n=136)	No GnRH (n=338)
Age (years), mean (SD)	50.4 (6.8)	51.9 (7.7)	45.2 (5.7)	53.4 (6.4)
Duration of endocrine therapy (years), mean (SD)	2.1 (1.6)	1.8 (1.3)	1.7 (1.3)	2.0 (1.5)
Race, n (%)				
White	231 (87.2%)	187 (89.5%)	129 (94.9%)	289 (85.5%)
Black/African American	4 (1.5%)	3 (1.4%)	1 (0.7%)	6 (1.8%)
Hispanic/Latino, n (%)	6 (2.3%)	6 (2.9%)	2 (1.5%)	10 (3.0%)
Weight (kg), mean (SD)	71.0 (12.8)	72.9 (13.1)	69.5 (12.4)	72.8 (13.1)
BMI (kg/m^2), mean (SD)	25.9 (4.3)	26.9 (4.9)	25.4 (4.7)	26.7 (4.5)
Smoking history, n (%)				
Never	174 (65.7%)	135 (64.6%)	90 (66.2%)	219 (64.8%)
Former	58 (21.9%)	46 (22.0%)	25 (18.4%)	79 (23.4%)
Current	33 (12.5%)	28 (13.4%)	21 (15.4%)	40 (11.8%)

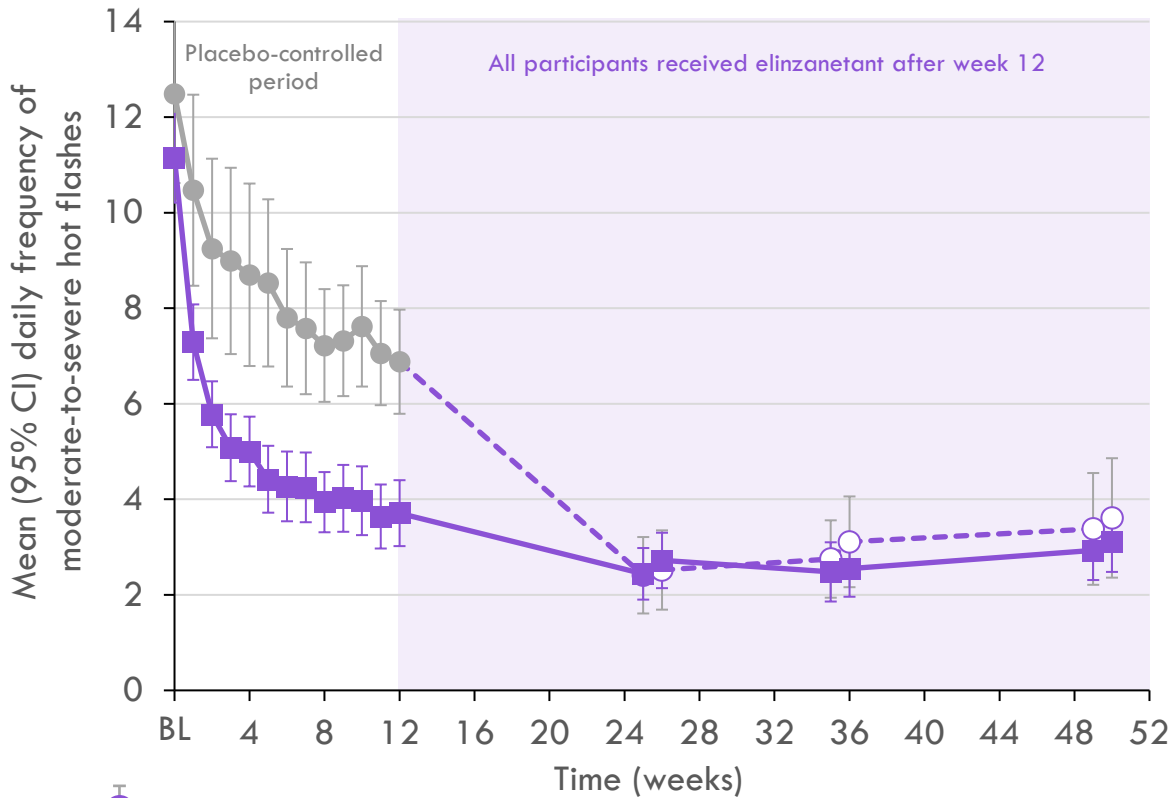
BMI, body mass index; FAS, full analysis set; GnRH, gonadotropin-releasing hormone; SD, standard deviation.

Daily frequency of moderate-to-severe VMS over time

Tamoxifen



Aromatase inhibitors



Elinzanetant 120 mg — Placebo — Placebo–Elinzanetant 120 mg

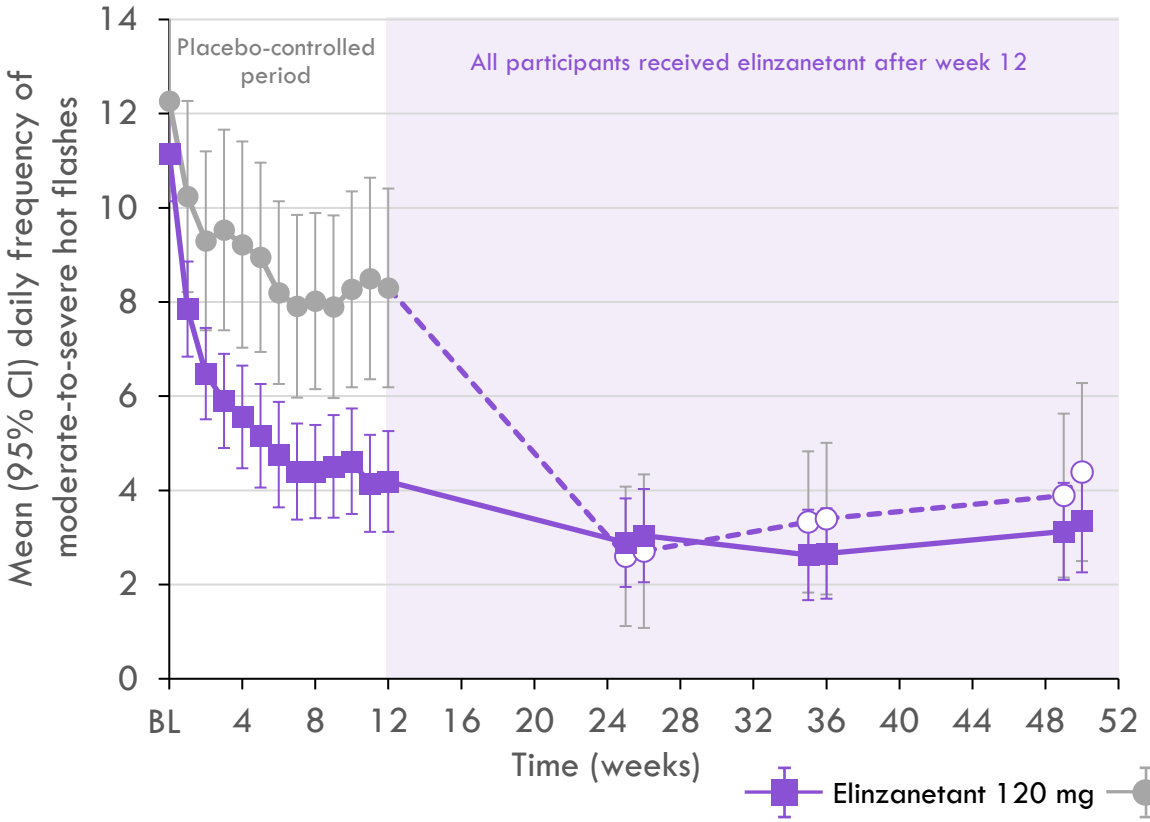
	Baseline, mean (95% CI)	Mean (95% CI) change from baseline		
		Week 1	Week 4	Week 12
Elinzanetant (N=175)	11.6 (10.5, 12.8)	-4.2 (-5.2, -3.3)	-6.8 (-8.0, -5.7)	-8.1 (-9.2, -7.0)
Placebo (N=90)	10.8 (9.7, 11.9)	-1.6 (-2.2, -0.9)	-2.5 (-3.5, -1.6)	-3.0 (-4.1, -2.0)

	Baseline, mean (95% CI)	Mean (95% CI) change from baseline		
		Week 1	Week 4	Week 12
Elinzanetant (N=141)	11.1 (10.2, 12.1)	-3.8 (-4.4, -3.3)	-6.1 (-6.8, -5.4)	-7.4 (-8.2, -6.6)
Placebo (N=68)	12.5 (10.6, 14.4)	-2.0 (-3.2, -0.9)	-3.7 (-5.2, -2.3)	-5.8 (-7.6, -4.0)

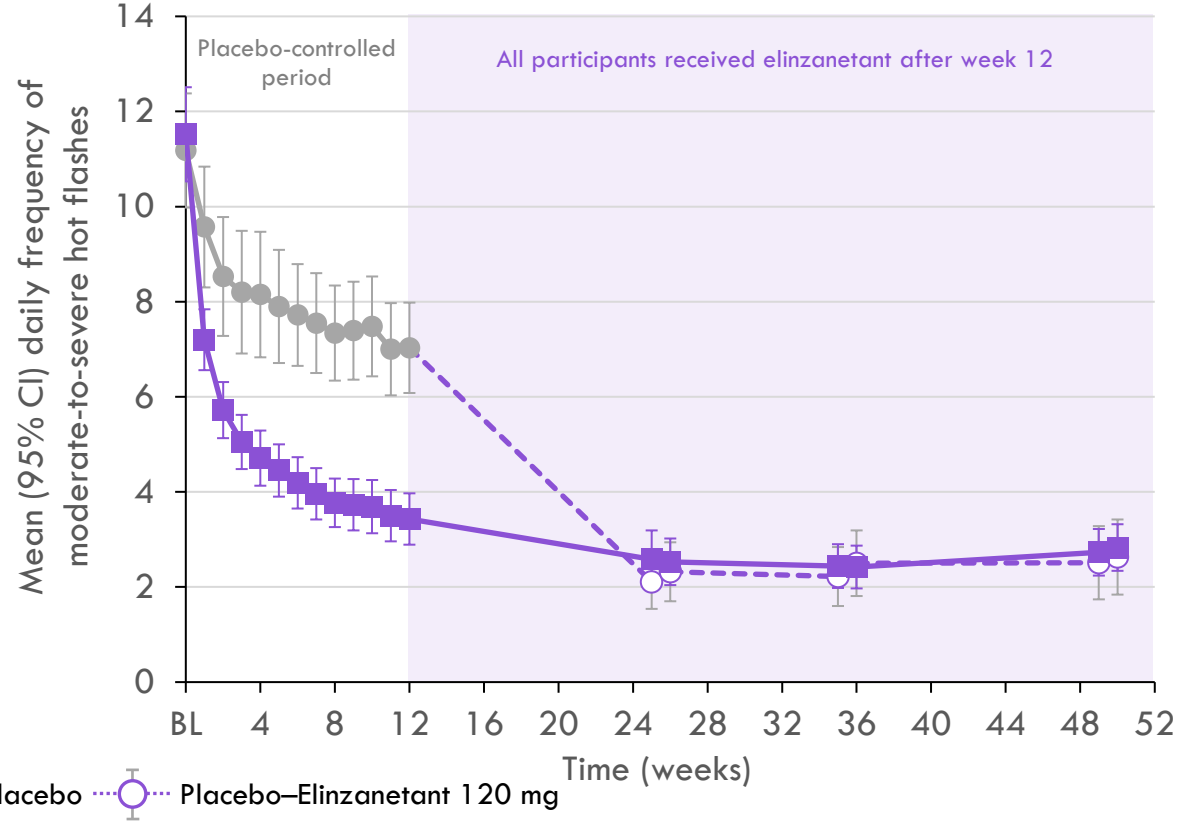
BL, baseline; CI, confidence interval; VMS, vasomotor symptoms.

Daily frequency of moderate-to-severe VMS over time

With GnRH



Without GnRH



Elinzanetant 120 mg — Placebo — Placebo–Elinzanetant 120 mg

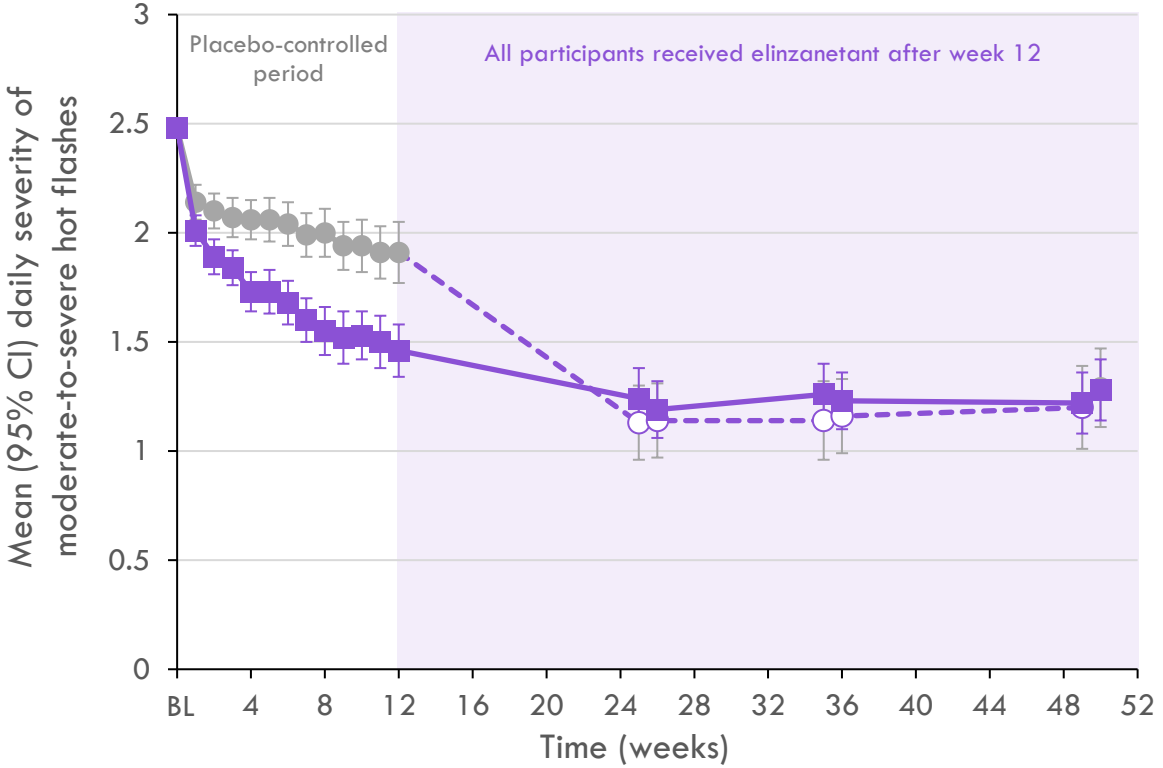
	Baseline, mean (95% CI)	Mean (95% CI) change from baseline		
		Week 1	Week 4	Week 12
Elinzanetant (N=88)	11.1 (10.1, 12.2)	-3.3 (-3.9, -2.7)	-5.6 (-6.4, -4.8)	-6.9 (-7.8, -6.0)
Placebo (N=48)	12.3 (10.4, 14.2)	-2.1 (-3.0, -1.1)	-3.2 (-4.7, -1.7)	-4.3 (-6.2, -2.4)

	Baseline, mean (95% CI)	Mean (95% CI) change from baseline		
		Week 1	Week 4	Week 12
Elinzanetant (N=228)	11.5 (10.5, 12.5)	-4.3 (-5.1, -3.6)	-6.9 (-7.8, -6.0)	-8.1 (-9.1, -7.2)
Placebo (N=110)	11.2 (10.0, 12.4)	-1.6 (-2.4, -0.9)	-3.0 (-4.0, -2.0)	-4.2 (-5.4, -3.0)

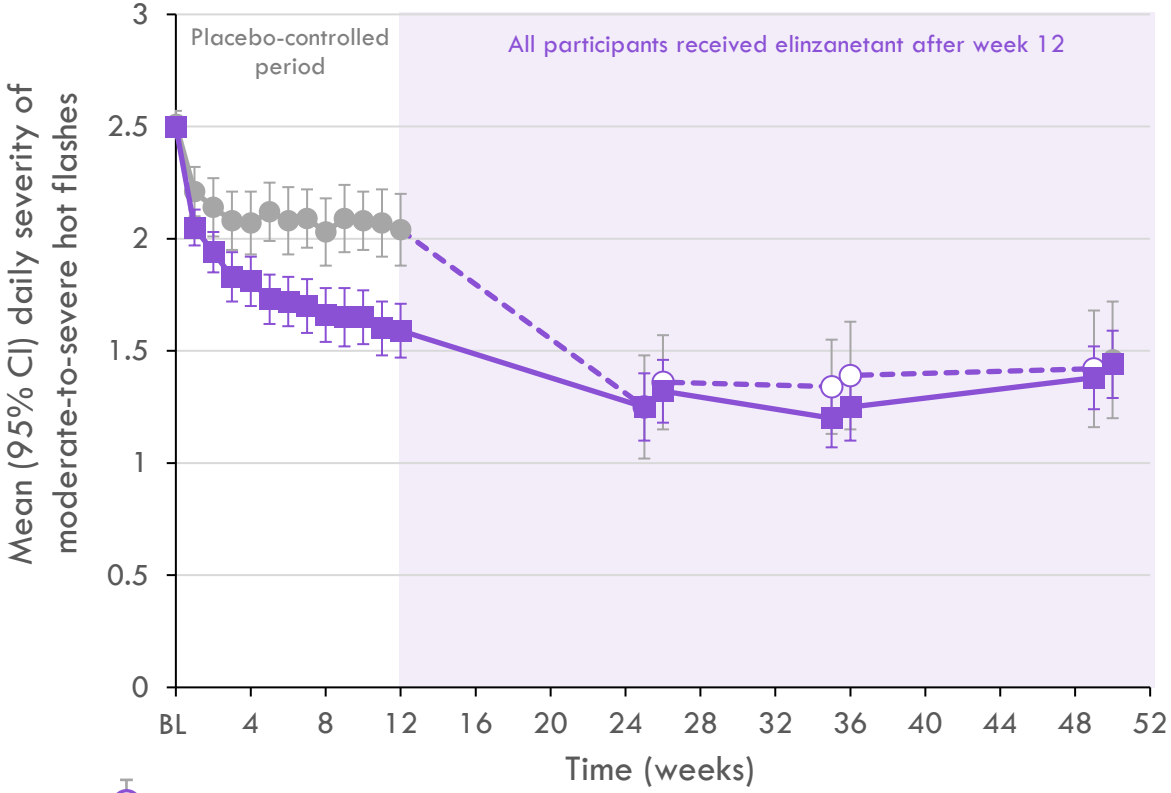
BL, baseline; CI, confidence interval; GnRH, gonadotrophin-releasing hormone; VMS, vasomotor symptoms.

Daily severity of moderate-to-severe VMS over time

Tamoxifen



Aromatase inhibitors



Elinzanetant 120 mg — Placebo — Placebo–Elinzanetant 120 mg

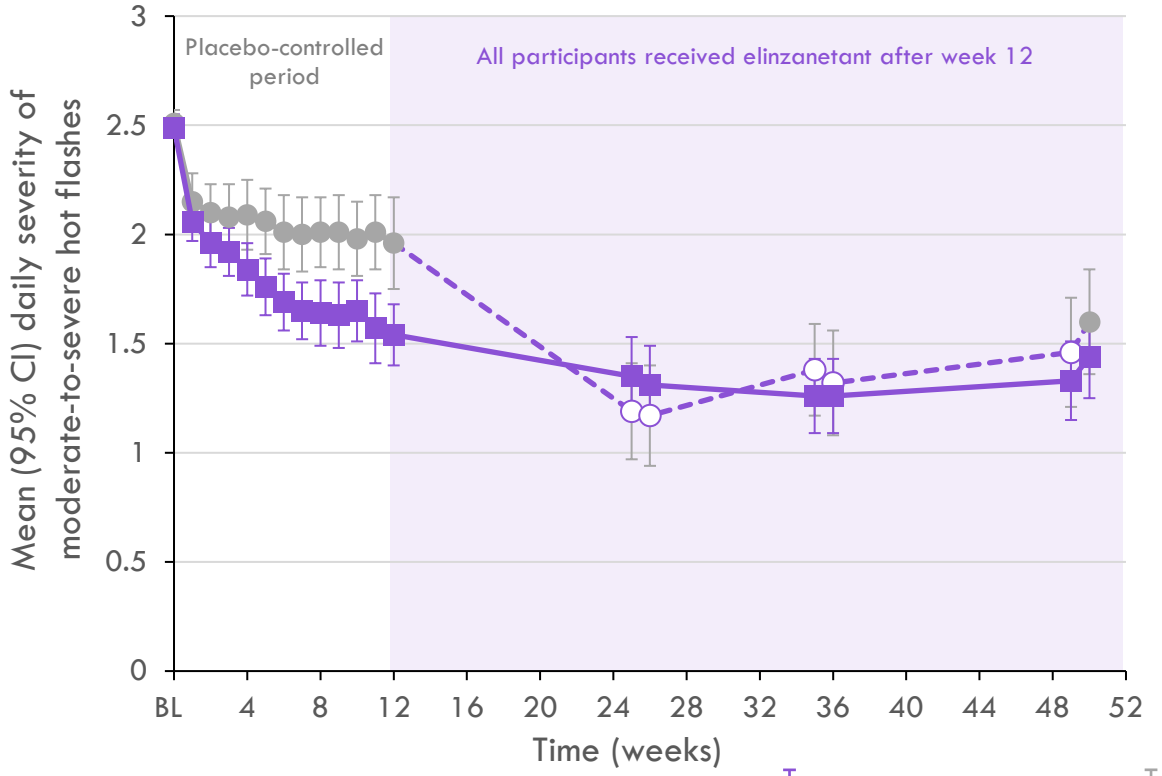
	Baseline, mean (95% CI)	Mean (95% CI) change from baseline Week 4	Week 12
Elinzanetant (N=175)	2.5 (2.4, 2.5)	-0.8 (-0.8, -0.7)	-1.0 (-1.2, -0.9)
Placebo (N=90)	2.5 (2.4, 2.5)	-0.4 (-0.5, -0.3)	-0.6 (-0.7, -0.4)

	Baseline, mean (95% CI)	Mean (95% CI) change from baseline Week 4	Week 12
Elinzanetant (N=141)	2.5 (2.5, 2.5)	-0.7 (-0.8, -0.6)	-0.9 (-1.0, -0.8)
Placebo (N=68)	2.5 (2.5, 2.6)	-0.4 (-0.6, -0.3)	-0.5 (-0.6, -0.4)

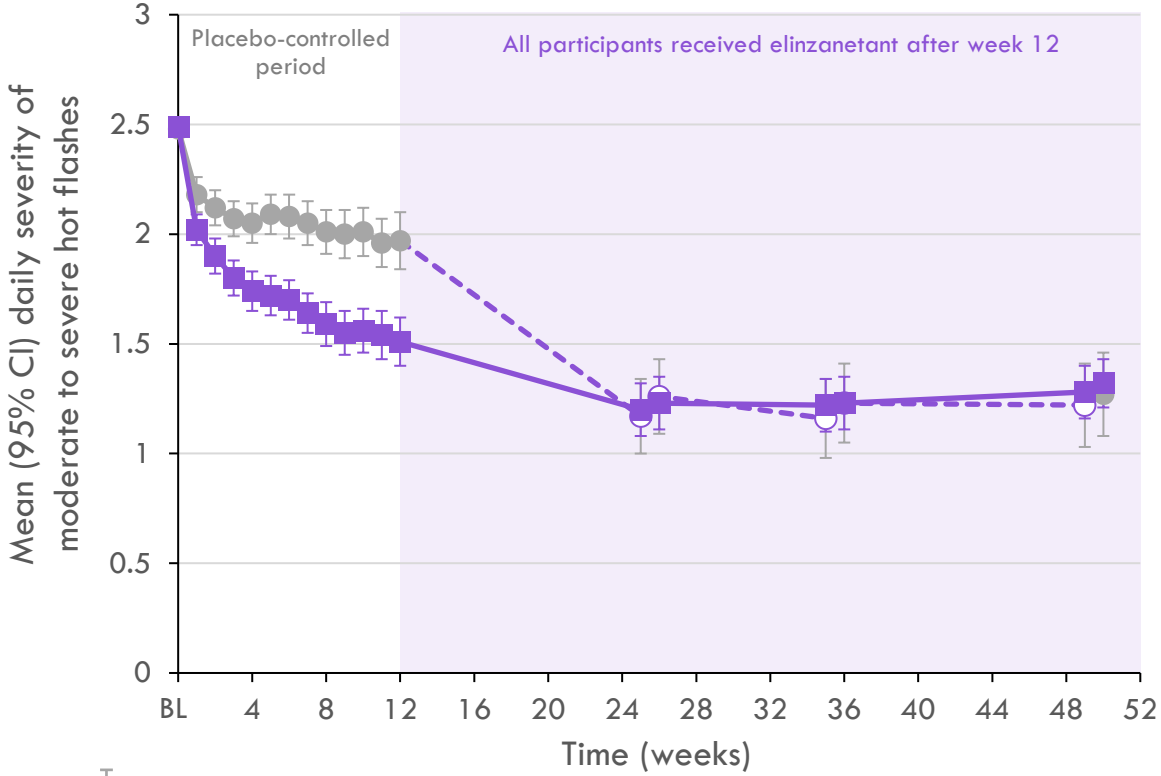
BL, baseline; CI, confidence interval; VMS, vasomotor symptoms.

Daily severity of moderate-to-severe VMS over time

With GnRH



Without GnRH



Elinzanetant 120 mg — Placebo — Placebo–Elinzanetant 120 mg

	Baseline, mean (95% CI)	Mean (95% CI) change from baseline Week 4	Week 12
Elinzanetant (N=88)	2.5 (2.4, 2.5)	-0.6 (-0.8, -0.5)	-0.9 (-1.1, -0.8)
Placebo (N=48)	2.5 (2.5, 2.6)	-0.4 (-0.5, -0.3)	-0.6 (-0.8, -0.4)

	Baseline, mean (95% CI)	Mean (95% CI) change from baseline Week 4	Week 12
Elinzanetant (N=228)	2.5 (2.5, 2.5)	-0.8 (-0.8, -0.7)	-1.0 (-1.1, -0.9)
Placebo (N=110)	2.5 (2.4, 2.5)	-0.4 (-0.5, -0.3)	-0.5 (-0.6, -0.4)

BL, baseline; CI, confidence interval; GnRH, gonadotrophin-releasing hormone; VMS, vasomotor symptoms.

Conclusions

Elinzanetant demonstrated greater reductions in VMS frequency and severity than placebo irrespective of the type of endocrine therapy

The effect of elinzanetant in reducing VMS frequency was seen by week 1 and sustained over 52 weeks

Results are consistent with those of the overall population in OASIS-4 and support the potential for elinzanetant to rapidly relieve VMS in women taking any type of background endocrine therapy for breast cancer

VMS, vasomotor symptoms.

Thank you