OASIS 4 study design: a Phase 3 trial assessing the efficacy and safety of elinzanetant in the treatment of vasomotor symptoms caused by adjuvant endocrine therapy for breast cancer

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INTRODUCTION

Vasomotor symptoms (VMS) are common side-effects experienced by women receiving adjuvant endocrine therapy for hormone receptor-positive (HR+) breast cancer that can have a substantial impact on quality of life and may lead to the discontinuation of therapy.[1,2]

Hormone therapy is contraindicated in women with HR+ breast cancer, and there is an unmet need for well-tolerated and effective nonhormonal treatments to safely address VMS in this population.[3]

Elinzanetant is a selective neurokinin-1,3 receptor antagonist currently being evaluated for the treatment of VMS associated with menopause in the Phase 3 OASIS program.

The objectives of this Phase 3 study are to assess the efficacy and safety of elinzanetant for the treatment of VMS caused by adjuvant endocrine therapy in women with, or at a high risk for developing HR+ breast cancer.

DESIGN

OASIS 4 (clinicaltrials.gov identifier: NCT05587296) is an ongoing, multicentre, multicountry, double-blind, randomized, placebo-controlled, Phase 3 study evaluating the efficacy and safety of elinzanetant 120 mg in women receiving adjuvant endocrine therapy for HR+ breast cancer and experiencing VMS (**Figure 1**).

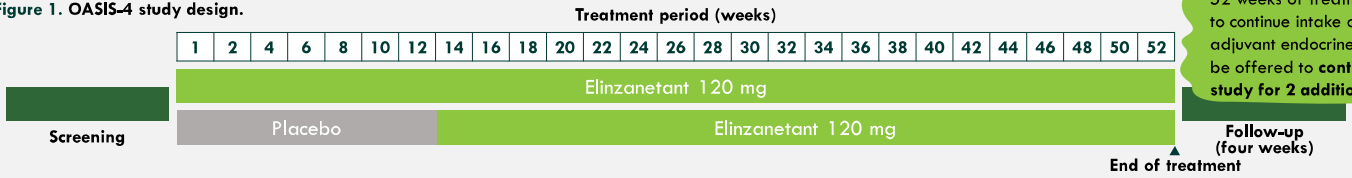
Following a screening period, approximately 405 eligible participants (see **Table 1** for eligibility criteria) will be randomized to receive either:

- once-daily elinzanetant 120 mg for 52 weeks, or
- matching placebo for 12 weeks, followed by elinzanetant 120 mg for 40 weeks.

After treatment, participants will undergo a four-week follow-up period.

Participants who have completed 52 weeks of treatment and need to continue intake of their adjuvant endocrine therapy will be offered to **continue with the study for 2 additional years**

Figure 1. OASIS-4 study design.



OUTCOMES

Patient-reported outcomes (**Table 2**) will be collected using an electronic handheld device. Patient-reported outcomes include the hot flash daily diary (HFDD), Patient-Reported Outcomes Measurement Information System Sleep Disturbance Short Form (PROMIS SD SF) 8b and Menopause-specific Quality-Of-Life questionnaire (MENQOL).

The **HFDD** will assess the number of mild, moderate, and severe VMS experienced each day.

Table 1. Eligibility criteria

Key inclusion criteria*
• Females aged 18 to 70 years, inclusive, at signing of informed consent.
• Women experiencing VMS caused by adjuvant endocrine therapy that they are expected to use for the duration of the study: – Tamoxifen with or without the use of GnRH analogues or – Aromatase inhibitors with or without the use of GnRH analogues.
• Women must have: – a personal history of HR+ breast cancer or – a high risk for developing breast cancer.
• Participant has completed HFDD for at least 11 days during the two weeks preceding baseline visit, and participant has recorded at least 35 moderate to severe HFs (including night-time HFs) over the last seven days that the HFDD was completed (assessed at the Baseline Visit).
• Contraceptive use (where applicable) should be consistent with local regulations regarding the methods of contraception for those participating in clinical studies
Key exclusion criteria*
• Initial diagnosis of metastatic HR+ breast cancer (stage IV) or recurrence under adjuvant endocrine therapy of hormone-receptor positive breast cancer.
• Current or previous history of any malignancy, except for HR+ breast cancer (Stage 0-III), basal and squamous cell skin tumours.
• Surgical or non-surgical (e.g., chemotherapy, radiotherapy, immunotherapy) treatment for breast cancer within the last 3 months (except use of tamoxifen, aromatase inhibitors, GnRH analogues).
• Relevant or clinically significant medical condition (either current or historic) that may impact participant outcomes, safety or compliance with study protocol (e.g. arrhythmias, unexplained vaginal bleeding, endometrial hyperplasia).

*List is not exhaustive. BMI, body mass index; GnRH, gonadotropin-releasing hormone; HFDD, hot flash daily diary; HR+, hormone receptor positive; VMS, vasomotor symptoms.

VMS are defined as:

- Mild – sensation of heat without sweating
- Moderate – sensation of heat with sweating, but able to continue activity
- Severe – sensation of heat with sweating, causing cessation (stopping) of activity

The **PROMIS SD SF** 8b includes 8 items assessing sleep disturbance over the past 7 days.[4]

- Items assess self-reported sleep quality, sleep depth and restoration associated with sleep, perceived difficulties with getting to sleep or staying asleep and perceptions of the adequacy of and satisfaction with sleep.

The **MENQOL** questionnaire is comprised of 29 items assessing the presence and impact of menopausal symptoms over the past week.[5]

- The items assess four domains of symptoms and functioning: VMS, psychosocial functioning, physical functioning, and sexual functioning.

Primary and key secondary endpoints will be analysed using a mixed model with repeated measures.

Safety will be assessed using adverse event reporting throughout the duration of the study as well as other routine assessments.

Table 2. Primary and secondary endpoints

Primary endpoints
• Mean change in frequency of moderate or severe VMS from baseline to Week 4
• Mean change in frequency of moderate or severe VMS from baseline to Week 12
Key secondary endpoints
• Mean change in PROMIS SD SF 8b total score from baseline to Week 12
• Mean change in MENQOL total score from baseline to Week 12
Secondary endpoints
• Mean change in severity of moderate or severe VMS from baseline to Week 4
• Mean change in severity of moderate or severe VMS from baseline to Week 12
• Mean change in frequency of moderate or severe VMS from baseline to Week 1
• Mean change in frequency of moderate or severe VMS from baseline over time

MENQOL, Menopause-specific Quality-Of-Life questionnaire; PROMIS SD SF 8b, Patient-Reported Outcomes Measurement Information System Sleep Disturbance Short Form 8b; VMS, vasomotor symptoms.

CONCLUSION

OASIS-1, -2, and -3 are currently evaluating the efficacy and safety of elinzanetant in women with VMS following a natural or surgically induced menopause.

OASIS-4 will aim to demonstrate the efficacy and safety of **elinzanetant** in a population with **a significant unmet need:**

Women receiving adjuvant endocrine therapy for breast cancer and experiencing bothersome VMS.

REFERENCES

1. Moon Z, et al. J Psychosom Obstet Gynaecol. 2017;38(3):226–235
2. Smith KL, et al. npj Breast Cancer 2022;8:53
3. Biglia N, et al. ecancer 2019;13:909
4. Yu L, et al. Behav Sleep Med 2011;10(1):6–24
5. Hilditch JR, et al. Maturitas 2008;61(1-2):107–21

DISCLOSURES

Fatima Cardoso has personal financial interest in form of consultancy role for: Amgen, Astellas/Medivation, AstraZeneca, 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. Lineke Zuurman and Cecilia Caetano are employees of Bayer CC AG. Christian Seitz and Susanne Parke are employees of Bayer AG. Kaisa Laapas is an employee of Bayer Oy. Leonor Matos has no conflicts of interest to declare.

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