

Trial in Progress: HIGHLIGHT 1 – a study of fezolinetant in treatment-induced VMS

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Objectives

- To assess the efficacy and safety of fezolinetant 45 mg once daily for treatment of moderate to severe vasomotor symptoms (VMS) in women with stage 0 to 3 hormone receptor-positive (HR+) breast cancer receiving adjuvant endocrine therapy
 - Stage 0: cancer cells have not spread to nearby tissue
 - Stage 3: cancer has spread from breast to lymph nodes near the breast or the chest wall

Conclusions

- HIGHLIGHT 1 will confirm the efficacy and safety of fezolinetant (45 mg once daily) in the treatment of women with moderate to severe VMS associated with tamoxifen or aromatase inhibitors for stage 0 to 3 HR+ breast cancer**
- HIGHLIGHT 1 will also explore the effect of fezolinetant on patient-reported QoL and sleep disturbance since VMS can adversely affect QoL and sleeping patterns**

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Introduction

- Breast cancer is the most common cause of death due to malignant neoplasms in women globally, with approximately 2.3 million new cases in 2022¹
- Vasomotor symptoms (VMS) – hot flushes and night sweats – are a prominent side effect of adjuvant endocrine therapies (e.g., tamoxifen and aromatase inhibitors) used for treatment of breast cancer² and can adversely affect patients' quality of life (QoL) and treatment compliance^{3,4}
- The pathophysiology of VMS in women undergoing cancer treatment is not fully elucidated but is hypothesised to have similar aetiology to VMS associated with menopause, i.e., rapid decline of oestrogen⁵
- Fezolinetant, an oral, nonhormonal, neurokinin 3 receptor antagonist, has demonstrated reductions in the frequency and severity of VMS associated with menopause,^{6,7} and has been approved in many regions, including North America, Europe, Asia, and Australia at a dose of 45 mg once daily⁸⁻¹³
- Fezolinetant works by blocking neurokinin B binding on the kisspeptin/neurokinin/dynorphin neuron, to restore normal sensitivity of the thermoregulatory centre in the hypothalamus to reduce the number and intensity of hot flashes and night sweats^{6,7}

Results

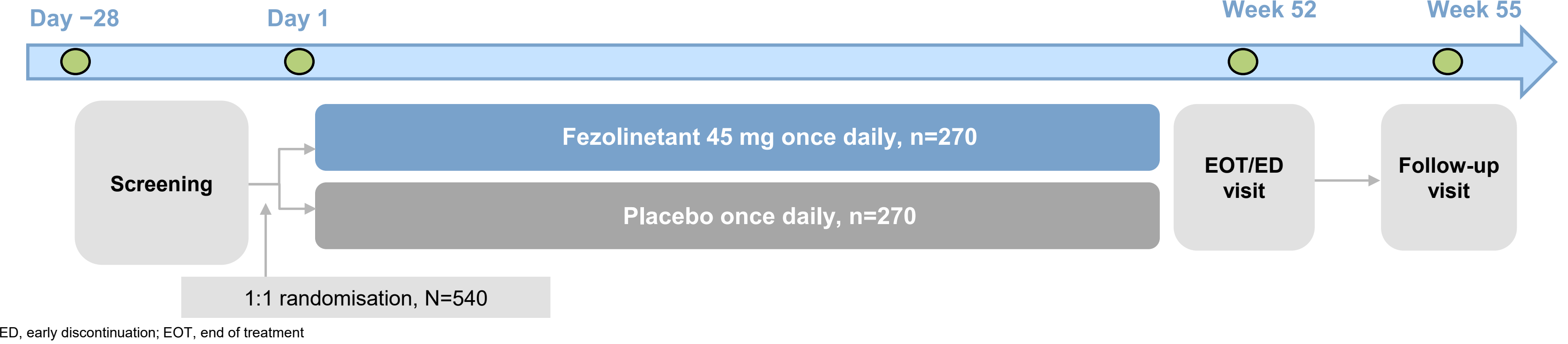
- Efficacy will be monitored over the 52-week study period using an electronic VMS daily diary
- Patient-reported outcomes will be recorded on an electronic device in the local language
 - The menopause-specific Quality of Life Questionnaire (MENQOL) assesses QoL related to menopause symptoms
 - The patient-reported outcomes measurement information system (PROMIS SD SF 8b) assesses sleep disturbance
- Treatment-emergent adverse events will be collected over 55 weeks, from the start of study intervention and are defined as adverse events that occurred after the first dose of study intervention and up to 21 days after the last dose

Table 1. HIGHLIGHT 1 primary and secondary objective and endpoints

Primary objective	Co-primary endpoints
Evaluate the efficacy of fezolinetant on frequency and severity of VMS in women experiencing VMS due to adjuvant endocrine therapy for stage 0 to 3 HR+ breast cancer	Mean change from baseline to weeks 4 and 12 in frequency and severity of moderate to severe VMS
Secondary objectives	Secondary endpoints
Key: explore the effect of fezolinetant on patient-reported QoL and sleep disturbance Other objectives include evaluation of the safety of fezolinetant in women experiencing VMS due to adjuvant endocrine therapy for stage 0 to 3 HR+ breast cancer, as well as the persistence of effect of fezolinetant through 24 weeks	- Mean change from baseline to week 12 in MENQOL VMS domain score and PROMIS Total Score Sleep Disturbance–Short Form 8b - Treatment-emergent adverse events to assess fezolinetant safety and tolerability - Mean change from baseline to week 24 in frequency and severity of moderate to severe VMS
Exploratory objectives	Exploratory endpoints
Exploratory endpoints included evaluation of the effect of fezolinetant on patient-reported QoL and work productivity	- Change in WPAI-VMS domain scores from baseline to weeks 4, 8, 12, and 24 - Change in EQ-5D-5L VAS from baseline to weeks 4, 8, 12, and 24

EQ-5D-5L, EuroQol 5 Dimension 5 Level; MENQOL, menopause-specific Quality of Life Questionnaire; PROMIS, Patient-Reported Outcomes Measurement Information System; QoL, quality of life; WPAI-VMS, Work Productivity and Activity Impairment for Vasomotor Symptoms; VAS, visual analogue scale; VMS, vasomotor symptoms

Figure 1. HIGHLIGHT 1 study design



Key inclusion criteria

- Women aged ≥18 years
- History of stage 0 to 3 HR+ breast cancer
- Average of ≥7 moderate to severe VMS episodes/day recorded in the electronic daily diary
- Receiving adjuvant endocrine therapy, e.g., tamoxifen or aromatase inhibitors, with or without gonadotropin-releasing hormone agonists/antagonists, for a minimum of 4 months

Key exclusion criteria

- History of or current malignancy other than HR+ breast cancer (stage 0 to 3) or basal cell carcinoma
- Had surgery or nonsurgical treatment for breast cancer within 3 months
- Active liver disease, jaundice, or elevated liver aminotransferases, elevated total bilirubin or direct bilirubin, or elevated alkaline phosphatase at screening
- Creatinine >1.5× upper limit of normal; or estimated glomerular filtration rate using the Modification of Diet in Renal Disease formula <30 ml/min/1.73 m²

Figure 2. HIGHLIGHT 1 study sites

More detailed information about the sites with enrolled participants, as of 15 May 2025, has been provided here:

Canada

United Kingdom

Germany

France

Spain

Italy

Denmark

Netherlands

Poland

Czech Republic

Hungary

ACTIVATED SITES					
Country and city	DENMARK	GERMANY	ITALY	POLAND	SPAIN
CANADA	Esbjerg	Moenchengladbach	Milano	Warszawa	Murcia
Quebec	Sonderborg	Botrop	Terni	Skzewo	Girona
Montreal	Aalborg	Leipzig	Tricase	Swidnik	Granada
Sherbrooke				Jaeen	Katowice
Trois Rivières				Bialystok	Elche
	FRANCE	HUNGARY	NETHERLANDS	Rotterdam	El Palmar Murcia
Bayonne	Kecskemet		Haarlem	Szczecin	Majadahonda Madrid
Saint Herblain Cedex	Székesfehérvár		Dijkssland	Poznan	Madrid
Angers Cedex 02	Budapest		Terneuzen	Lodz	Sevilla
Bordeaux	Eger		Breda	Szczecin	Barcelona
Montpellier Cedex 5	Salgotarjan			Krakow	Leon
Lyon, France				Pila	
CZECHIA					
Olomouc					
Angers Cedex 02					
Tabor					
Ceske Budejovice 4					
Novy Jicin					
Horovice					

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