Accepted: 14 January 2024

DOI: 10.1111/1471-0528.17773

BJOG An International Journal of Obstetrics and Gynaecology

RESEARCH ARTICLE

Fezolinetant impact on health-related quality of life for vasomotor symptoms due to the menopause: Pooled data from SKYLIGHT 1 and SKYLIGHT 2 randomised controlled trials

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Funding information
Astellas Pharma Inc.

Abstract

Objective: To assess the effect of fezolinetant treatment on health-related quality of life using pooled data from SKYLIGHT 1 and 2 studies.

Design: Prespecified pooled analysis.

Setting: USA, Canada, Europe; 2019–2021.

Population: 1022 women aged ≥40 to ≤65 years with moderate-to-severe vasomotor symptoms (VMS; minimum average seven hot flushes/day), seeking treatment for VMS.

Methods: Women were randomised to 12-week double-blind treatment with once-daily placebo or fezolinetant 30 or 45 mg. Completers entered a 40-week, active extension (those receiving fezolinetant continued that dose; those receiving placebo re-randomised to fezolinetant received 30 or 45 mg).

Main outcome measures: Mean changes from baseline to weeks 4 and 12 on Menopause-Specific Quality of Life (MENQoL) total and domain scores, Work Productivity and Activity Impairment questionnaire specific to VMS (WPAI-VMS) domain scores, Patient Global Impression of Change in VMS (PGI-C VMS); percentages achieving PGI-C VMS of 'much better' (PGI-C VMS responders). Mean reduction was estimated using mixed model repeated measures analysis of covariance.

Results: Fezolinetant 45 mg mean reduction over placebo in MENQoL total score was −0.57 (95% confidence interval [CI] −0.75 to −0.39) at week 4 and −0.47 (95% CI −0.66 to −0.28) at week 12. Reductions were similar for 30 mg. MENQoL domain scores were also reduced and WPAI-VMS scores improved. Twice as many women receiving fezolinetant reported VMS were 'much better' than placebo based on PGI-C VMS assessment.

Conclusions: Fezolinetant treatment was associated with improvement in overall QoL, measured by MENQoL, and work productivity, measured by WPAI-VMS. A high proportion receiving fezolinetant felt VMS were 'much better' based on PGI-C VMS responder analysis.

KEYWORDS
fezolinetant, health-related quality of life, neurokinin 3 receptor antagonist, patient-reported outcomes, vasomotor symptoms

Clinical Trial Registration: SKYLIGHT 1, ClinicalTrials.gov NCT04003155, https://clinicaltrials.gov/ct2/show/NCT04003155; SKYLIGHT 2, ClinicalTrials.gov NCT04003142, https://clinicaltrials.gov/ct2/show/NCT04003142.

1 | INTRODUCTION

Up to 80% of women report hot flushes and night sweats (vasomotor symptoms [VMS]) during menopausal transition.[1–3] Moderate-to-severe VMS are associated with sleep disruption, anxiety, mood disturbances, fatigue, cognitive impairment and cardiovascular disease, which can negatively affect health-related quality of life (HRQoL).[4–15] Additionally, greater severity of VMS is associated with lower health status and work productivity and greater healthcare resource use,[4,16] which may result in increased absenteeism and presenteeism.[4] Because frequent VMS may persist for years,[17] and because most women spend a significant portion of their lives as postmenopausal, maintaining functional ability and good QoL is important.

Hormone therapy (HT) remains the principal treatment for VMS associated with menopause.[18–20] However, HT may not be appropriate for all women, depending on underlying medical conditions, risk factors, age and time since menopause.[18] Non-hormonal alternatives have been tested in a number of randomised trial, but are not always well tolerated and are only partially effective versus HT. Moreover, until recently, only paroxetine was approved by the U.S. Food and Drug Administration (FDA) for treatment of VMS.[21] Additionally, many women try complementary and alternative medicine options to alleviate VMS and improve HRQoL, including cognitive behavioural therapy, nutritional, physical and herbal remedies; however, evidence concerning their efficacy is conflicting.[22,23] There is therefore a clinical need to identify additional effective pharmacological approaches to treat VMS.

Fezolinetant is a novel selective non-hormonal neurokinin 3 receptor antagonist approved, at a once-daily 45 mg dose, by the FDA for treatment of VMS due to menopause and by the European Medicines Agency for treatment of VMS associated with menopause.[24] The thermoregulatory centre in the hypothalamus is innervated by kisspeptin-neurokinin B-dynorphin (KNDy) neurones, whose action is inhibited by oestrogen and stimulated by neurokinin B (NKB) via NK3R.[25] With declining oestrogen levels during menopause, NK3R-mediated activation is unopposed, leading to hypertrophy of KNDy neurones; this increases heat dissipation mechanisms, leading to hot flushes and night sweats. Fezolinetant blocks NKB binding on KNDy neurones, thereby reducing the frequency and severity of VMS associated with menopause.[26]

SKYLIGHT 1 (NCT04003155) and SKYLIGHT 2 (NCT04003142) were identical, double-blind, placebo-controlled phase 3 studies evaluating the safety and efficacy of fezolinetant versus placebo on the frequency and severity of VMS associated with menopause. Fezolinetant was efficacious and well tolerated,[27,28] with a favourable safety profile confirmed by SKYLIGHT 4 (NCT04003389).[29] The objective of this prespecified analysis was to assess the effect of fezolinetant treatment on HRQoL using pooled data from SKYLIGHT 1 and 2 via three patient-reported outcome measures (PROMs).

2 | METHODS

2.1 | Study design

SKYLIGHT 1 and 2 were conducted at multiple sites throughout North America (USA and Canada) and Europe (Poland, Czech Republic, Spain, UK; Hungary [SKYLIGHT 1 only] and Latvia [SKYLIGHT 2 only]). Study dates were July 2019 to August 2021 (SKYLIGHT 1) and July 2019 to April 2021 (SKYLIGHT 2). Detailed methodology for these studies has been published previously.[27,28] Astellas Pharma Inc. provided study funding.

Both studies were conducted in accordance with the Declaration of Helsinki, Good Clinical Practice and International Council for Harmonisation guidelines. An independent ethics committee or institutional review board reviewed the ethical, scientific and medical appropriateness of the studies at each site before data collection. Written informed consent was obtained from all participants before any study-related procedures were performed.

2.2 | Patient involvement

In brief, the study population comprised individuals aged ≥40 to ≤65 years who were genetically female at birth, had moderate-to-severe VMS (minimum average of seven hot flushes per day) and were seeking treatment or relief for VMS. Eligible women had a body mass index of ≥18 to ≤38 kg/m^2 and confirmed postmenopausal status, defined as spontaneous amenorrhoea for ≥12 consecutive months, spontaneous amenorrhoea for ≥6 months with biochemical confirmation of menopause or a bilateral oophorectomy ≥6 weeks prior to the screening visit. Exclusion criteria included the presence of previous or current malignant tumours; a current diagnosis of hypertension, active liver disease, jaundice or elevated liver aminotransferases or alkaline phosphatase more than 1.5 times the upper limit of normal; elevated total or direct bilirubin; elevated international normalised ratio; use of a prohibited therapy for VMS (e.g. strong or moderate cytochrome P450 1A2 inhibitors, HT, hormonal contraceptive); or current or prior participation in a fezolinetant clinical trial.

In both studies, women were randomised to receive once-daily doses of placebo, fezolinetant 30 mg or fezolinetant 45 mg (1:1:1 ratio) during a 12-week double-blind treatment period (Figure 1). Women who completed this treatment period were re-randomised and entered a 40-week active treatment extension period in which those who were treated with fezolinetant continued to receive their current dose and those who received placebo were re-randomised to receive fezolinetant 30 or 45 mg.

2.3 | HRQoL assessments

In both studies, PROMs used to assess HRQoL during the 12-week double-blind treatment period included the

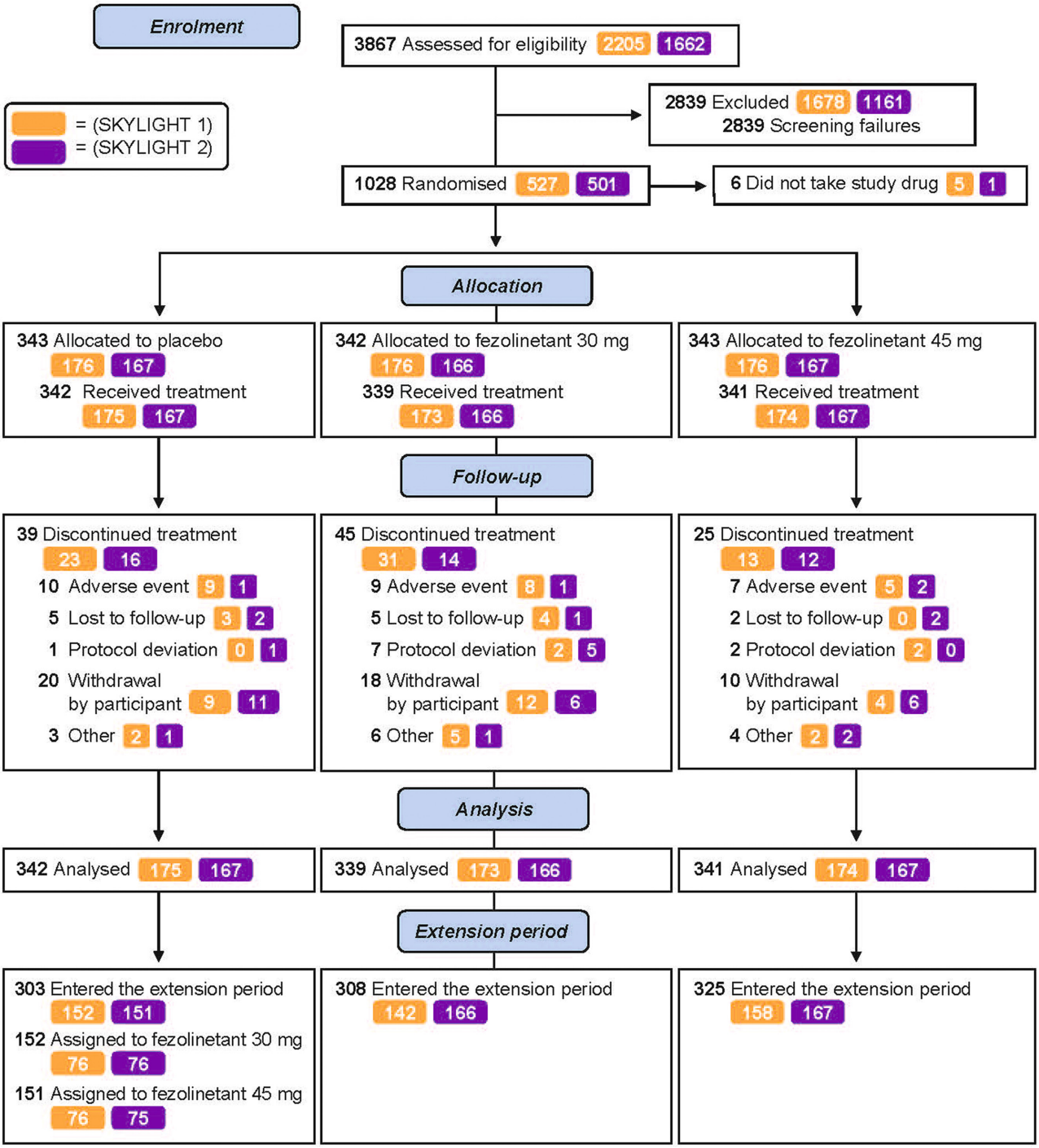

FIGURE 1 Flow diagram.

following: mean changes from baseline to weeks 4 and 12 on the Menopause-Specific Quality of Life (MENQoL) total and domain scores; mean changes from baseline to weeks 4 and 12 on Work Productivity and Activity Impairment questionnaire specific to VMS (WPAI-VMS) domain scores; changes from baseline to weeks 4 and 12 in the Patient Global Impression of Change in VMS (PGI-C VMS); and the percentage of women achieving a PGI-C VMS response of 'much better' (PGI-C VMS responders) – the highest response category possible in the PGI-C VMS toolbox.

The MENQoL is a validated, menopause-specific, self-administered questionnaire that consists of 29 items assessing the impact of four domains of menopausal symptoms over the last week (vasomotor, psychosocial, physical and sexual).[30,31] The vasomotor domain evaluates hot flushes, night sweats and sweating. The psychosocial domain evaluates the psychological wellbeing of the individual by including items regarding anxiousness, memory and feeling 'blue'. The physical domain assesses items such as flatulence, bloating, pain, tiredness, sleeping, energy and

weight gain. The sexual domain comprises questions about changes in sexual desire, vaginal dryness and intimacy. Specific symptoms are rated as present or not present and, if present, are rated on a scale of 0 (not bothersome) to 6 (extremely bothersome). Mean change on the MENQoL total score and on the individual domains was captured.

The WPAI-VMS is a six-item measure that examines VMS-related work productivity and activity in the preceding 7 days.[32,33] It consists of four domains: absenteeism (the percentage of work time missed because of VMS in the past 7 days), presenteeism (the percentage of impairment experienced while at work in the past 7 days because of VMS), overall work productivity loss (overall work impairment measured by combining absenteeism and presenteeism to determine the total percentage of missed time) and activity impairment (the percentage of impairment of daily activities because of VMS in the past 7 days). WPAI-VMS outcomes are expressed as impairment percentages, with higher numbers indicating greater impairment and reduced productivity (i.e. worse outcomes).

Participants completed HRQoL assessments electronically using a tablet during the study site visits. The MENQoL and WPAI-VMS questionnaires were also completed at randomisation.

2.4 | Statistical analyses

All data are shown for the full analysis set, comprising all participants who were randomised and received at least one dose of study intervention. Demographic data (including race, ethnicity, age, height, weight and menopausal symptoms) were collected at screening and summarised using descriptive statistics. MENQoL and WPAI-VMS total scores were assessed using a mixed models repeated measures analysis of covariance model. Treatment group, week, smoking status (current versus former/never) and study were factors. Covariates were baseline weight and baseline measurement, as well as an interaction of treatment by week and an interaction of baseline measurement by week. An unstructured covariance structure shared across treatment groups was used to model the within-patient errors. The Kenward–Roger approximation was used to estimate denominator degrees of freedom and adjust standard errors [SEs].

SKYLIGHT 1 and SKYLIGHT 2 were designed so that the family-wise type I error rate was controlled for all the comparisons of active dose groups with placebo for the co-primary efficacy endpoints, namely, mean change from baseline to weeks 4 and 12 in frequency and severity of moderate-to-severe VMS. The current pooled analyses do not control the type I error rate, i.e. without multiplicity adjustment, so *P*-values do not confer statistical significance. Rather, the *P*-values have been used for the purposes of hypothesis generation.

3 | RESULTS

A total of 1022 women were randomised and received at least one dose of study drug across both studies (placebo, $n = 342$; fezolinetant 30 mg, $n = 339$; fezolinetant 45 mg, $n = 341$) (Table 1). Mean (SD) age was 54.3 (5.0) years and the majority of the women were white (828, 81.1%). Demographic data were largely balanced across groups, although mean (range) time since onset of VMS was slightly longer in the placebo group (81.9 [2–422] months) than in the 30 mg (76.7 [3–370] months) and 45 mg fezolinetant groups (76.9 [1–396]) groups.

Improvements in MENQoL total score, as indicated by decreases from baseline, were observed in the fezolinetant and placebo groups at weeks 4 and 12 (Figure 2A). The reduction in MENQoL total score was greater with fezolinetant 45 mg than with placebo at all time points. Least squares mean reduction over placebo (SE) for fezolinetant 45 mg at week 4 was −0.57 (0.09; 95% CI −0.75 to −0.39) and at week 12 was −0.47 (0.10; 95% CI −0.66 to −0.28). Within-treatment percentage changes from baseline to week 4 were −29.7% for fezolinetant 45 mg and −17.1% for placebo. Within-treatment percentage changes from baseline to week 12 were −31.1% for fezolinetant 45 mg and −20.5% for placebo. MENQoL domain scores were also reduced (Figure 2B; Table S1). The greatest reductions were in the MENQoL vasomotor domain total score: least squares mean reduction over placebo (SE) for fezolinetant 45 mg at week 4 was −1.01 (0.15; 95% CI −1.30 to −0.73) and at week 12 was −0.86 (0.16; 95% CI −1.17 to −0.56). For the other domains at week 12, the values were −0.35 (0.10) for the physical domain, −0.41 (0.11) for the psychosocial domain and −0.25 (0.15) for the sexual domain.

Greater improvements in WPAI activity impairment, overall work productivity loss and presenteeism were seen with fezolinetant at both doses compared with placebo (Figure 3). Absenteeism was improved in all treatment groups at week 4, but only in the fezolinetant 45 mg group at week 12, whereas mean scores worsened in the placebo group.

Improvements in PGI-C VMS were larger for fezolinetant 45 mg versus placebo, including both 'moderately better' and 'much better' responses (Figure 4). The number of PGI-C VMS responders (those indicating they felt 'much better', the highest response category) was greater for fezolinetant than for placebo. At week 4, the number of PGI-C VMS responders was 140 of 319 (43.9%) in the fezolinetant 45 mg group and 57 of 311 (18.3%) for placebo. At week 12, 47.5% (144/303 women) in the fezolinetant 45 mg group were responders compared with 23.9% (70/293 women) in the placebo group.

Improvements in overall mean MENQoL score were similar for the 30-mg dose: −0.46 (0.09; 95% CI −0.64 to −0.27) at week 4 and −0.32 (0.10; 95% CI −0.51 to −0.12) at week 12 (Figure 2A). Within-treatment percentage changes from baseline for the 30 mg dose were also similar to values for the 45-mg dose: −26.2% at week 4 and −27.9% at week 12. MENQoL domain scores were reduced for fezolinetant 30 mg, although to a slightly lesser extent than for fezolinetant 45 mg for the total, physical, psychosocial and vasomotor domains (Figure 2B; Table S1). WPAI absenteeism was improved in the fezolinetant 30 mg at week 4 but not at week 12, whereas mean scores worsened (Figure 3). The number of PGI-C VMS responders for fezolinetant 30 mg was 111 of

TABLE 1 Key participant demographics and baseline characteristics (FAS).

Parameter	Placebo ($n = 342$)	Fezolinetant 45 mg ($n = 341$)	Fezolinetant 30 mg ($n = 339$)	Total ($N = 1022$)
Ethnicity[a], *n* (%)				
Hispanic or Latina	78 (22.9)	89 (26.1)	76 (22.4)	243 (23.8)
Not Hispanic or Latina	262 (77.1)	252 (73.9)	263 (77.6)	777 (76.2)
Race[b], *n* (%)				
American Indian or Alaska Native, Asian, Other[c]	7 (2.0)	8 (2.3)	4 (1.2)	19 (1.9)
Black or African American	59 (17.3)	59 (17.3)	56 (16.6)	174 (17.0)
White	276 (80.7)	274 (80.4)	278 (82.2)	828 (81.1)
Age, mean (SD), years	54.7 (4.7)	54.3 (5.3)	54.0 (4.9)	54.3 (5.0)
Weight, mean (range), kg	74.5 (46.2–125.0)	75.2 (45.0–110.6)	75.2 (42.0–121.2)	75.0 (42.0–125.0)
BMI[d], mean (range), kg/m^2	28.2 (18.6–38.0)	28.1 (18.0–37.9)	28.0 (18.0–37.8)	28.1 (18.0–38.0)
Current smoker, *n* (%)	57 (16.7)	57 (16.7)	55 (16.2)	169 (16.5)
Time since onset of VMS, mean (range), months	81.9 (2–422)	76.9 (1–396)	76.7 (3–370)	78.5 (1–422)
Amenorrhoea, *n* (%)				
No	13 (3.8)	7 (2.1)	7 (2.1)	27 (2.6)
Yes	329 (96.2)	334 (97.9)	332 (97.9)	995 (97.4)
Hysterectomy, *n* (%)				
No	240 (70.2)	228 (66.9)	226 (66.7)	694 (67.9)
Yes	102 (29.8)	113 (33.1)	113 (33.3)	328 (32.1)
Oophorectomy, *n* (%)				
No	267 (78.1)	265 (77.7)	269 (79.4)	801 (78.4)
Yes	75 (21.9)	76 (22.3)	70 (20.6)	221 (21.6)

Note: Data shown for FAS (all participants who were randomised and received at least one dose of study intervention).

Abbreviations: BMI, body mass index; FAS, full analysis set; VMS, vasomotor symptoms.

[a]Data on ethnicity were missing for two participants in the placebo (and total) group.

[b]Data on race were missing for one participant in the fezolinetant 30 mg (and total) group.

[c]More than one race.

[d]Data on BMI were missing for one participant in the fezolinetant 45 mg (and total) group.

305 (36.4%) at week 4 and 117 of 275 (42.5%) at week 12, slightly lower percentages compared with the 45-mg group (Figure 4).

4 | DISCUSSION

4.1 | Main findings

Pooled data from SKYLIGHT 1 and 2 were analysed for this HRQoL analysis, including 1022 participants in the full analysis set. MENQoL total and domain scores improved with fezolinetant at weeks 4 and 12 compared with placebo. The greatest improvement was seen in the relevant VMS domain of the MENQoL. Fezolinetant treatment demonstrated consistent improvements in work productivity and activity as measured by WPAI scores versus placebo, likely owing to effective treatment of VMS and highlighting that improvement in VMS could have a positive impact on productivity in the workplace. According to the PGI-C VMS, approximately twice as many women receiving fezolinetant felt their VMS were 'much better' (responders; the highest response possible in the PGI-C VMS) at week 12 compared with women receiving placebo.

4.2 | Strengths and limitations

A strength of the analysis is the inclusion of three independent PROMs (the validated MENQoL, the WPAI and the PGI-C VMS) that quantify different aspects of the impact of VMS on women's lives. The MENQoL and WPAI questionnaires were also chosen to evaluate the burden associated with menopausal symptoms in a large global screening survey involving 3460 postmenopausal women in Europe, the USA and Japan.[34] According to the MENQoL, the most commonly reported menopausal symptom in the past week was feeling tired or worn out (74% in Europe and 75% in both the USA and Japan). In Japan, decrease in physical strength was reported by 74%, sweating by 72% and decrease in stamina by 70%. Other symptoms reported by a high proportion of women were aching in muscles and joints (69% in Europe, 68% in the USA and 61% in Japan), difficulty sleeping (69% in Europe, 66% in the USA and 60% in Japan), hot

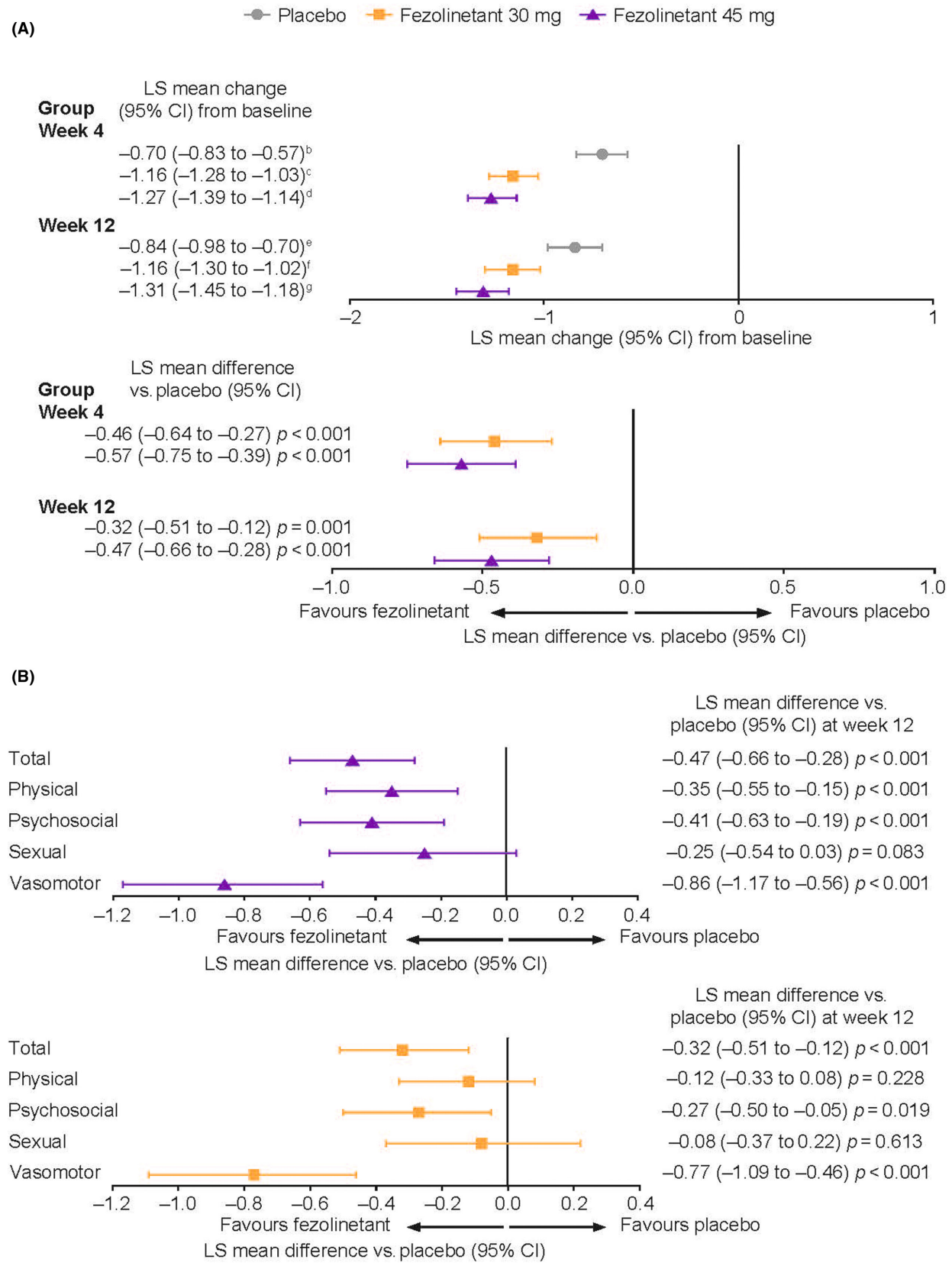

FIGURE 2 Change from baseline in (A) Menopause-Specific Quality of Life total score[a] and (B) domain scores during the 12-week double-blind period (full analysis set). [a]Comprises all four domains and 29 items. Negative change indicates improvement from baseline. [b]$n = 310$ for LS change from baseline. [c]$n = 304$ for LS change from baseline. [d]$n = 318$ for LS change from baseline. [e]$n = 291$ for LS change from baseline. [f]$n = 273$ for LS change from baseline. [g]$n = 303$ for LS change from baseline. LS means, SEs, CIs and *P*-values come from a mixed model repeated measures analysis of covariance model, with change from baseline as the dependent variable and treatment group, week, smoking status (current versus former/never) and study as factors, with baseline measurement and baseline weight as covariates, as well as an interaction of treatment by week and an interaction of baseline measurement by week. LS, least squares.

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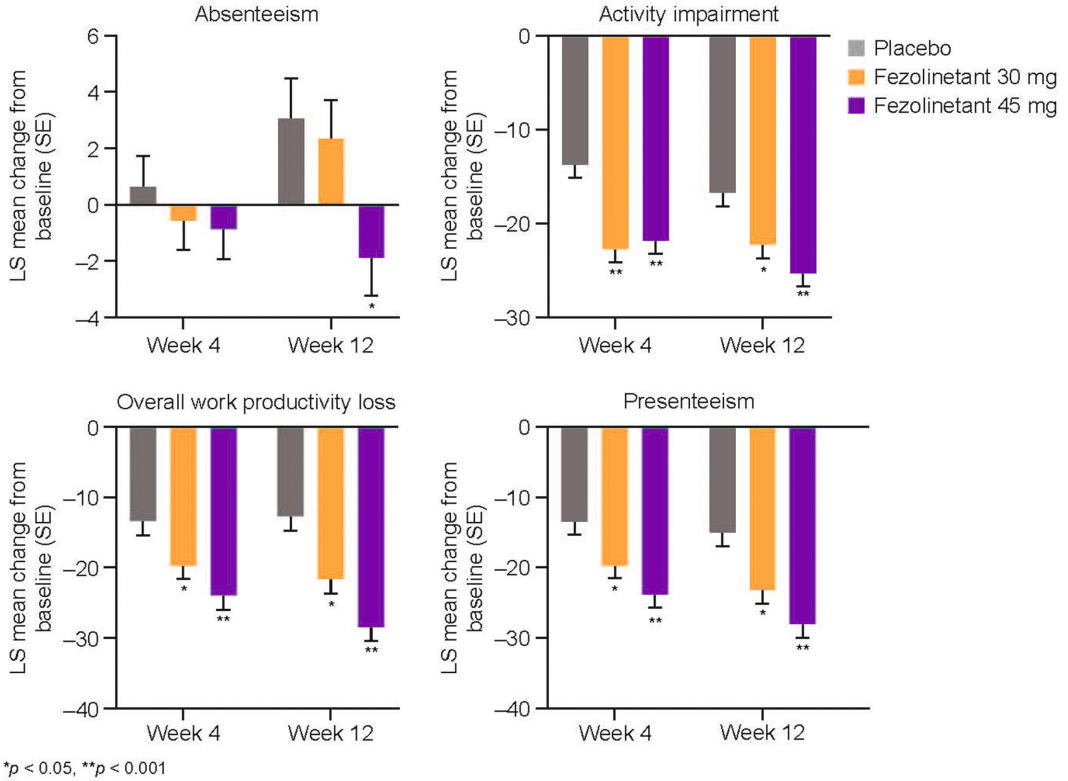

FIGURE 3 Mean change from baseline in Work Productivity and Activity Impairment questionnaire specific to vasomotor symptoms domain scores during the 12-week double-blind period (full analysis set). LS, least squares. LS means, SEs, CIs and *P*-values come from a mixed model repeated measures analysis of covariance model, with change from baseline as the dependent variable and treatment group, study protocol, week, smoking status (current versus former/never) and study as factors, with baseline measurement and baseline weight as covariates, as well as an interaction of treatment by week and an interaction of baseline measurement by week.

flushes (67% in Europe, 68% in the USA and 62% in Japan) and night sweats (68% in Europe, 67% in the USA and 52% in Japan). According to WPAI findings, hot flushes and night sweats had a greater impact on daily activities (e.g. work around the house, shopping, childcare, exercising, studying) than on working activities.

Another strength of the current analysis was that we identified patient-centric treatment outcomes that an individual patient would identify as important and beneficial. This was measured by the percentage of women achieving a PGI-C VMS response of 'much better' (PGI-C VMS responders). 'Much better' is the highest possible response category in the PGI-C VMS toolbox. Furthermore, the percentage of women who reported combined responses of 'a little better', 'moderately better' and 'much better' in the PGI-C VMS was also higher for fezolinetant than for placebo (Figure 4). An additional strength of the study was the racial diversity of the population, with 17% of women self-identifying as black or African American and 81% as white, which is reflective of the North American population and relevant to several countries in Europe. A limitation of the current study, along with other studies of this type, is that it was not powered for the secondary and exploratory outcomes. Although approximately 30% of participants were obese, the body mass index inclusion criterion of ≤38.0 kg/m^2 prevented enrolment of participants with class III obesity (formerly known as morbid obesity). Finally, the SKYLIGHT programme relied on PROMs to capture patient-relevant outcomes, whereas wearable monitors are being introduced in some other VMS studies and clinical studies involving other medical conditions. It must be noted, however, that although wearable monitors can accurately capture sleep quantity, their validity in capturing other sleep outcomes is still under question.[35]

4.3 | Interpretation

Although it is important to reduce the frequency and severity of VMS due to menopause, it is equally important that improvements in VMS translate into HRQoL benefits for women. Because HT is not appropriate for all women, there is a need for effective medicine options to alleviate VMS and improve HRQoL. The objective of the current analysis was to assess the effect of a novel non-hormonal treatment, fezolinetant, on HRQoL using pooled data from SKYLIGHT 1 and 2. Data from the individual SKYLIGHT 1 and 2 studies showed a statistically significant benefit of fezolinetant over placebo in VMS frequency and severity.[27,28]

These analyses demonstrate that fezolinetant improves women's HRQoL, through a range of PROMs with direct applicability to menopause, providing further evidence of the beneficial effect of fezolinetant, particularly in participants

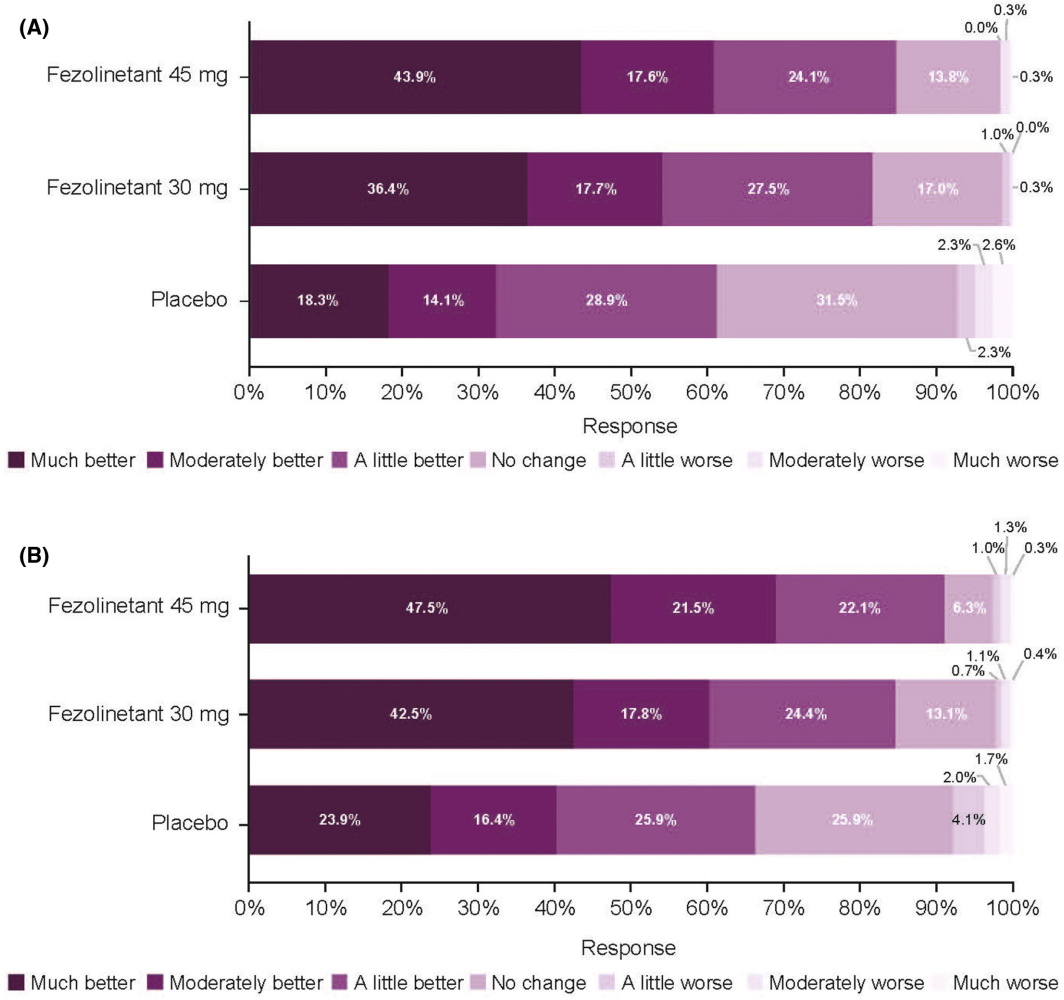

FIGURE 4 Distribution of Patient Global Impression of Change in vasomotor symptoms at (A) week 4 and (B) week 12. $P < 0.001$ for fezolinetant 30 mg versus placebo and for fezolinetant 45 mg versus placebo at weeks 4 and 12. *P*-values were obtained using Cochran–Mantel–Haenszel test with modified ridit scores.

treated with the 45-mg dose and in concordance with the improvements observed for the changes in VMS frequency and severity.[27,28] Fezolinetant treatment demonstrated consistent improvements in work productivity and activity as measured by WPAI scores compared with placebo, likely owing to effective treatment of VMS and highlighting that improvement in VMS could have a positive impact on productivity in the workplace. The current results demonstrate that these benefits also translate into improvements in several aspects of HRQoL measured by MENQoL total score and its domains.

In a study using data from the 2005 US National Health and Wellness Survey,[8] women aged 40–64 years who were experiencing menopausal symptoms reported significantly higher presenteeism (17.7% versus 13.6%, $P < 0.05$) and overall work impairment (16.1% versus 12.3%, $P < 0.05$) than women not experiencing menopausal symptoms. Absenteeism (3.7% versus 3.4%, $P = 0.50$) was similar between groups. In the current study, greater improvements in WPAI activity impairment, overall work productivity loss and presenteeism were seen with fezolinetant compared with placebo. Although fezolinetant 45 mg was associated with improvements in the absenteeism domain of the WPAI in the current analysis, fezolinetant 30 mg was not, possibly because this dose was not sufficient to have an impact on this domain.

Data from all three independent PROMs in this prespecified analysis support findings from the pivotal phase 3 studies. Effective treatment of VMS, as shown in the SKYLIGHT studies, has been shown to translate into substantial improvement in HRQoL in this analysis.

5 | CONCLUSION

Fezolinetant treatment for moderate-to-severe VMS was associated with improvement in overall QoL, as measured by the MENQoL, and in self-reported work productivity, as measured by the WPAI. Additionally, a high proportion of women treated with fezolinetant felt their VMS were 'much better' (responders), as measured by the PGI-C VMS. Effective treatment of VMS can not only alleviate direct menopausal symptoms such as hot flushes and night sweats but also positively impact the QoL in women

experiencing menopause. More emphasis on the HRQoL benefit experienced with treatment can facilitate meaningful dialogue between clinicians and patients.

AUTHOR CONTRIBUTIONS

MB, MLE, AM, LS and ES made substantial contributions to the study designs. MB, MLE, AM, LS, ES and FDO participated in the acquisition and analysis of study data. AC, REN, NS, PS, MB, MLE, AM, LS, ES and FDO were involved in the interpretation of the study data, provided input into the writing of the paper and approved the final draft for submission.

ACKNOWLEDGEMENTS

This study was sponsored by Astellas Pharma Inc. Medical writing support was provided by Sue Cooper, CMPP, of Excel Scientific Solutions and was funded by Astellas Pharma Inc.

FUNDING INFORMATION

Astellas Pharma Inc.

CONFLICT OF INTEREST STATEMENT

AC reports being a past President of the European Menopause and Andropause Society; a consultant for Astellas, ItalFarmaco and Theramex; and a member of the Fezolinetant Scientific Steering Committee. REN reports past financial relations (lecturer, member of advisory boards and/or consultant) with Boehringer Ingelheim, Eli Lilly, Endoceutics, Exeltis, Novo Nordisk, Palatin Technologies, Pfizer, Procter & Gamble, Teva Women's Health and Zambon; ongoing relations with Abbott, Astellas, Bayer HealthCare, Besins Healthcare, Fidia, Gedeon Richter, HRA Pharma, Merck & Co., Organon, Shionogi, Theramex and Viatris; serving as President elect of the International Menopause Society; and is a member of the Fezolinetant Scientific Steering Committee. NS reports being a study investigator, member of a scientific advisory board and consultant for Astellas; a member of a scientific advisory board for Amazon (Project Ember), MenoGeniX and QUE Oncology; a consultant for Ansh Labs; an Associate Editor for Menopause; and a past President of the Society for Reproductive Investigation. PS reports being a consultant for Astellas; a board member for DMG and EMAS; President of the SGEM; and a member of the Fezolinetant Scientific Steering Committee. MB, MLE, LS and FDO are employees of Astellas Pharma Inc. AM and ES are employees of Astellas Pharma Europe Ltd.

DATA AVAILABILITY STATEMENT

Researchers may request access to anonymised participant-level data, trial-level data and protocols from Astellas sponsored clinical trials at www.clinicalstudydatarequest.com. For the Astellas criteria on data sharing, see: https://clinicalstudydatarequest.com/Study-Sponsors/Study-Sponsors-Astellas.aspx.

ETHICS STATEMENT

The SKYLIGHT 1 and SKYLIGHT 2 studies were conducted in accordance with the Declaration of Helsinki, Good Clinical Practice and International Council for Harmonisation guidelines. An independent ethics committee or institutional review board reviewed the ethical, scientific and medical appropriateness of the studies at each site before data collection. Written informed consent was obtained from all participants before any study-related procedures were performed.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Cano A, Nappi RE, Santoro N, Stute P, Blogg M, English ML, et al. Fezolinetant impact on health-related quality of life for vasomotor symptoms due to the menopause: Pooled data from SKYLIGHT 1 and SKYLIGHT 2 randomised controlled trials. BJOG. 2024;00:1–10. https://doi.org/10.1111/1471-0528.17773