Association Between EQ-5D and Moderate-to-Severe Vasomotor Symptom Response in Menopause: A Post-Hoc Analysis of the OASIS 1/2 Trials

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KEY FINDING

Among women within one year of menopause, those who achieved a ≥50% reduction in moderate-to-severe vasomotor symptoms with elinzanetant was associated with a clinically meaningful improvement in health-related quality-of-life, a 0.052 increase in EQ-5D index value compared with those who did not (95% CI 0.033-0.071; p<0.0001). Importantly, this benefit was more than twice that observed in the overall study population (0.024; 95% CI 0.016-0.031; p<0.0001).[1, 2]

INTRODUCTION

- Menopause associated vasomotor symptoms (VMS) can be frequent, persistent, disruptive and reduce quality-of-life (QoL).
- Scientific advances have increased our understanding of the underlying pathways involved in the development of VMS, leading to neurokinin-targeted therapies that effectively manage VMS.
- In OASIS 1 and 2, elinzanetant significantly reduced the frequency and severity of moderate-to-severe VMS, and the benefit was maintained over the observed 26-week study period. Additionally, elinzanetant improved sleep disturbances and menopause-specific QoL, indicating that VMS relief yields measurable HRQoL gains.[1]

OBJECTIVE

To estimate EQ-5D index values associated with a ≥50% reduction in the frequency of moderate-to-severe VMS in women with moderate-to-severe VMS associated with menopause, overall and in women within one year of amenorrhea, to quantify the utility burden of VMS and the impact of improving VMS.

METHODS

- This post-hoc analysis pooled data from OASIS 1 (NCT05042362) and OASIS 2 (NCT05099159), two phase 3, double-blind, randomised, placebo-controlled trials of elinzanetant 120 mg once daily in postmenopausal women (following surgical or natural menopause) aged 40 to 65 years with moderate-to-severe VMS associated with menopause; elinzanetant was given for 26 weeks, or matching placebo for 12 weeks followed by elinzanetant for 14 weeks.[1]
- EQ-5D-5L was collected at baseline and weeks 1, 2, 3, 4, 8, 12, 16 and 26 and mapped to EQ-5D-3L index values using the United Kingdom (UK) Hernández Alava crosswalk algorithm.[3]
- A clinically meaningful reduction in VMS frequency was defined as a reduction of at least 50% from baseline in the frequency of moderate-to-severe VMS, derived at each visit from the hot flash daily diary, and fitted as a time-dependent covariate.
- Time since menopause was defined as time since amenorrhoea; women within one year of surgical or natural menopause at baseline formed the subgroup of interest.
- A mixed model for repeated measures (MMRM) was fitted with fixed effects for VMS response status, time since menopause ≤1 year, their interaction, and baseline utility, with a compound-symmetry covariance structure, Satterthwaite degrees of freedom and restricted maximum likelihood estimation. Further models were fitted with and without randomised treatment arm as a covariate.
- Both randomised arms were pooled; VMS response, not treatment allocation, was the exposure of interest.

ANALYSIS POPULATION

- Randomised across OASIS 1 and OASIS 2 (full analysis set): n=796 (elinzanetant n=399, placebo-elinzanetant n=397), Table 1.
- Evaluable baseline EQ-5D: n=721 (elinzanetant n=363, placebo-elinzanetant n=358).
- Within one year of amenorrhea at baseline: n=117 (14.8% of randomised); n=106 with an evaluable baseline EQ-5D value.

Table 1. Baseline characteristics

Characteristics	≤1 year since amenorrhea (n=117)	Overall (n=796)
Age, years, mean (SD)	51.3 (3.5)	54.6 (4.8)
Body mass index, kg/m², mean (SD)	27.00 (4.85)	27.79 (4.72)
White, n (%)	106 (90.6%)	640 (80.4%)
Current smoker, n (%)	26 (22.2%)	146 (18.3%)
Time since amenorrhea, years, mean (SD)	0.84 (0.26)	7.12 (6.33)
History of oophorectomy, n (%)	27 (23.1%)	164 (20.6%)
History of hysterectomy, n (%)	29 (24.8%)	309 (38.8%)
Baseline EQ-5D index value, mean (SD)	0.810 (0.162)	0.820 (0.168)
Baseline VMS frequency, episodes/day, mean (SD)	13.76 (8.61)	14.62 (11.02)
Baseline VMS severity, mean (SD)	2.51 (0.26)	2.54 (0.24)

Abbreviations: SD: standard deviation; VMS: vasomotor symptoms.

RESULTS

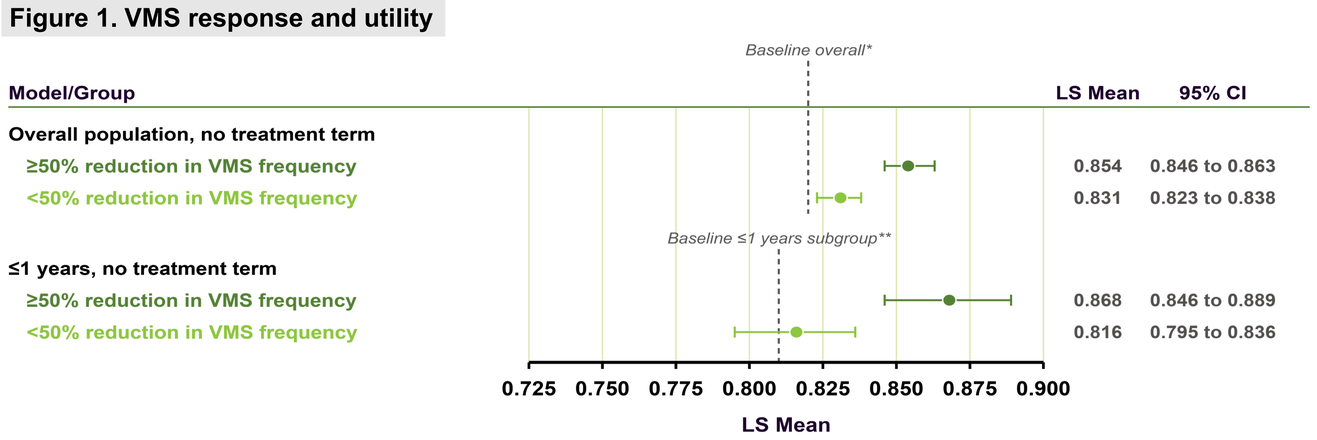
- In the overall population, participants with at least a 50% decrease in VMS frequency had significantly higher EQ-5D index values than those without (p<0.001), Figure 1.
- Participants with a ≥50% reduction in VMS frequency had higher utility than those without in the overall population (difference 0.024, 95% CI 0.016 to 0.031, p<0.0001). The difference was larger among those within 1 year of amenorrhea (0.052, 95% CI 0.033 to 0.071, p<0.0001), Table 2.
- The response × duration interaction was statistically significant (p=0.0017), indicating that utility differences by VMS reduction were greater in women closer to amenorrhea, Table 2.

Table 2. VMS response and utility

Model and subgroup	Difference (≥50% vs <50% reduction)	95% CI	Nominal *p*-Value
Overall population	0.024	0.016 to 0.031	<0.0001
≤1 year since amenorrhea	0.052	0.033 to 0.071	<0.0001
Response × duration* interaction	-	-	0.0017

Abbreviations: CI: confidence interval
*≤1 year since amenorrhea

Figure 1. VMS response and utility



Abbreviations: CI: confidence interval; LS: least square; VMS: vasomotor symptoms.
* Baseline overall population EQ-5D index value, mean (standard deviation): 0.820 (0.168)
** Baseline ≤1 years subgroup EQ-5D index value, mean (standard deviation): 0.810 (0.162)

STRENGTHS & LIMITATIONS

Strengths:

- The analysis used data from two randomised, double-blind, placebo-controlled trials; VMS frequency and severity and EQ-5D were captured prospectively at the same protocol-defined visits. This allows change in health state utility to be observed alongside change in VMS, rather than inferred from cross-sectional or recall-based data.
- The MMRM accounts for the correlation between multiple observations within the same subject rather than treating each visit as independent, adjusts for baseline utility, and uses all available post-baseline observations from all 716 participants.

Limitations:

- This is a post-hoc analysis of trials whose primary objective was to evaluate treatment efficacy, rather than to estimate utility by VMS response status; the analysis was not pre-specified and no sample size or power calculation was performed for these comparisons. No adjustment for multiplicity has been applied, and therefore nominal p-values should be interpreted as exploratory rather than confirmatory.
- The subgroup within one year of menopause is relatively small (14.7% of the overall study population), and although the difference associated with VMS was statistically significant (0.052; 95% CI 0.033 to 0.071), confidence intervals were wider than those observed for the overall population (0.024; 95% CI 0.016 to 0.031).
- EQ-5D index values were obtained by mapping from EQ-5D-5L responses; the additional uncertainty introduced by the mapping algorithm is not reflected in the confidence intervals reported here.

CONCLUSIONS

- Participants with a ≥50% reduction in moderate-to-severe VMS frequency had significantly higher EQ-5D index values than those with a <50% reduction (difference 0.024;p<0.0001).
- These results suggest that VMS improvement due to elinzanetant treatment results in overall greater HRQoL (utility difference: 0.052 vs 0.024 overall; interaction p=0.0017); HRQoL benefit is greater in women treated with elinzanetant earlier or closer to menopause onset.

REFERENCES

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DISCLOSURES

Catia C Proenca (Bayer Consumer Care AG), Landan Zhang (Bayer plc, Medical Affairs Statistics) and Bernard Wilson (Bayer plc, Health Economics and Outcomes Research) are employees of Bayer. Zoe Schaedel (Brighton and Hove Primary Care Ltd, Brighton, UK) and Susanna Weidlinger (Division of Gynaecological Endocrinology and Reproductive Medicine, University Women's Hospital, Inselspital, Bern, Switzerland) serve as consultants for Bayer Pharmaceuticals.

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