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Vaginal and Vulvar Symptoms in Patients with *ESR1*-Mutated, ER+/HER2- Metastatic Breast Cancer by Baseline Characteristics

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Introduction

- Endocrine therapy (ET) for treating breast cancer, particularly aromatase inhibitors (AIs) that lower estrogens subphysiologically, can induce vaginal and vulvar symptoms of genitourinary syndrome of menopause (GSM)[1-4]
- In the phase 2, ELAINE 1 study, lasofoxifene improved median progression-free survival (PFS) compared with fulvestrant (5.6 vs 3.7 months; *P*=0.138) in patients with *ESR1*-mutated, metastatic breast cancer (mBC) that had progressed on a combination of AI and cyclin-dependent kinase 4 and 6 inhibitor (CDK4/6i), and exhibited a favorable safety profile[5]
- An exploratory analysis from ELAINE 1 showed numeric improvements in vaginal/vulvar symptoms with lasofoxifene versus fulvestrant[6]
- Whether patient and disease characteristics impact the severity of vaginal/vulvar symptoms in patients with mBC is unknown

Objective

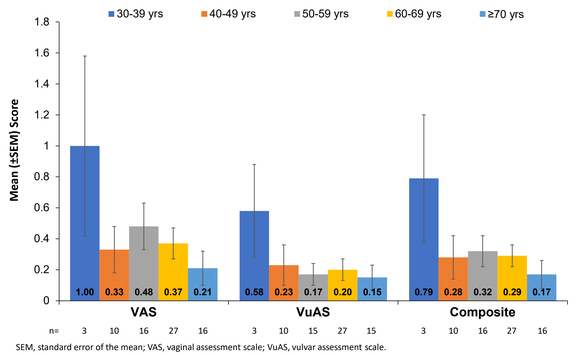
To evaluate the effects of patient and disease characteristics on baseline vaginal/vulvar symptoms in patients from ELAINE 1

Design

- Pre- or postmenopausal women with ER+/HER2- mBC and *ESR1*-mutated circulating tumor DNA who had disease progression on prior AI-CDK4/6i treatment (duration ≥12 months) were enrolled in the phase 2, ELAINE 1 study (NCT03781063)
- Eligible patients were randomized to receive oral lasofoxifene 5 mg (daily) or IM fulvestrant 500 mg (days 1, 15, and 29, then every 28 days) until disease progression/severe toxicity
- The primary endpoint was PFS; vaginal/vulvar symptoms were evaluated as a secondary endpoint using the vaginal (VAS) and vulvar (VuAS) assessment scales, validated instruments that assess vaginal/vulvar dryness, soreness, irritation, and pain using a 4-point scale (0=none, 1=mild, 2=moderate, 3=severe)
  - English-speaking patients completed the VAS/VuAS at baseline and every 8 weeks until disease progression
  - An exploratory analysis stratified baseline mean scores for VAS, VuAS, and the composite VAS/VuAS (average of all reported scores for a patient) by age, visceral disease, prior adjuvant tamoxifen use, duration of prior AI use in the adjuvant or adjuvant/metastatic settings for those who completed the VAS/VuAS at baseline, irrespective of treatment assignment
  - Data were descriptively summarized

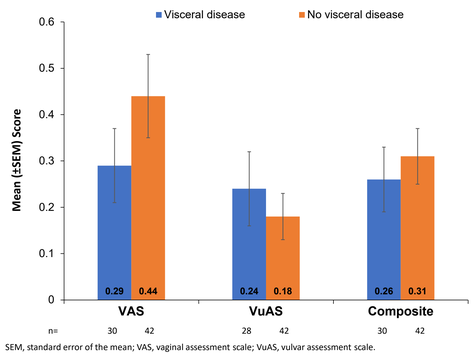
Results

Figure 1. Baseline VAS/VuAS scores by patient age



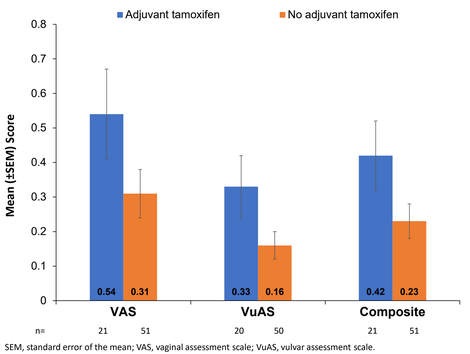
SEM, standard error of the mean; VAS, vaginal assessment scale; VuAS, vulvar assessment scale.

Figure 2. Baseline VAS/VuAS scores by the presence of visceral disease



SEM, standard error of the mean; VAS, vaginal assessment scale; VuAS, vulvar assessment scale.

Figure 3. Baseline VAS/VuAS scores by prior use of adjuvant tamoxifen



SEM, standard error of the mean; VAS, vaginal assessment scale; VuAS, vulvar assessment scale.

Participant disposition and baseline characteristics

- Of 103 enrolled patients, 72 (69.9%) patients with a mean age of 61.5 years completed the VAS/VuAS at baseline (**Table**). Among these patients:
  - Vaginal dryness (40.3%), vulvar dryness (25%), and vaginal pain (22.2%) were the most frequently reported symptoms at baseline
  - Mean baseline composite VAS/VuAS score was 0.29
    - 53 (74%) patients reported no to mild baseline symptoms (score 0 or 1)

Table. Patient disposition and baseline VAS/VuAS scores

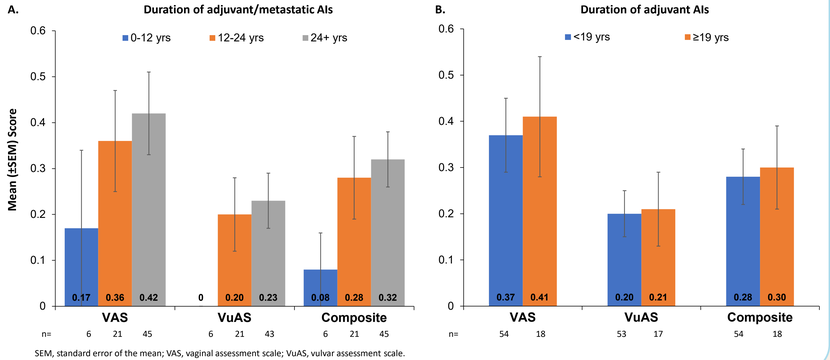
		Total
Total randomized, n		103
Completed the VAS/VuAS, n (%)		72 (69.9)
≥1 moderate/severe symptom*, n (%)		19 (26.4)
Age*, median (range), yrs		61.5 (37–84)
Composite VAS/VuAS score*, mean±SD		0.29±0.41
Symptoms present*, n (%)		
VAS	Dryness	29 (40.3)
	Soreness	13 (18.1)
	Irritation	11 (15.3)
	Pain	16 (22.2)
VuAS	Dryness	18 (25)
	Soreness	10 (13.9)
	Irritation	13 (18.1)
	Pain	6 (8.3)

*Characteristics in patients who completed the VAS/VuAS at baseline.
SD, standard deviation; VAS, vaginal assessment scale; VuAS, vulvar assessment scale.

Effects of patient and disease characteristics on baseline vaginal/vulvar symptoms

- Compared with patients of other subgroups by age, vaginal/vulvar symptoms were more severe in those under age 40, although the number of patients were small (n=3) in this subgroup (**Figure 1**)
- Patients without visceral disease appeared to have more severe vaginal symptoms compared with those who had visceral disease (**Figure 2**)
- Prior use of adjuvant tamoxifen was associated with more severe vaginal/vulvar symptoms (**Figure 3**)
- Patients with a longer total duration (>12 yrs) of AI treatment in both adjuvant and metastatic settings reported more severe vaginal/vulvar symptoms at baseline (**Figure 4A**), although duration of prior AI in the adjuvant setting alone did not impact either vaginal or vulvar symptoms (**Figure 4B**)

Figure 4. Baseline VAS/VuAS scores by the duration of AI use (A) in the adjuvant/metastatic settings and (B) in the adjuvant only setting



SEM, standard error of the mean; VAS, vaginal assessment scale; VuAS, vulvar assessment scale.

References: **1.** Morales L, et al. *Anticancer Drugs*. 2004;15:753-760. **2.** Baumgart J, et al. *Am J Obstet Gynecol*. 2011;204:26 e21-27. **3.** Kyvernitakis I, et al. *Climacteric*. 2014;17:252-259. **4.** Portman DJ, et al. *Menopause*. 2014;21:1063-1068. **5.** Goetz MP, et al. *Ann Oncol*. 2022;33:S1387-S1388. **6.** Goldfarb SB, et al. *J Sex Med*. 2023;20. **7.** Cella D, et al. *Breast Cancer Res Treat*. 2006;100:273-284. **8.** Antoine C, et al. *Climacteric*. 2008;11:322-328. **9.** Gallicchio L, et al. *Climacteric*. 2012;15:339-349.

Key Takeaways

- Vaginal/vulvar symptoms of GSM were prevalent in ELAINE 1 patients with *ESR1*-mutated mBC that had progressed on an AI-CDK4/6i combination
- The severity of baseline vaginal/vulvar symptoms was associated with younger age, absence of visceral disease, prior use of adjuvant tamoxifen, and longer total duration of AIs in both adjuvant and metastatic settings

Conclusions

- Results from this exploratory analysis, although limited by the small number of patients with ER+/HER2- mBC and vaginal and/or vulvar symptoms in ELAINE 1, showed that these symptoms at baseline were more severe in those who were younger, or had no visceral disease, prior use of adjuvant tamoxifen, or a longer total duration of AI treatment in both adjuvant and metastatic settings (but not in the adjuvant setting alone)
- The baseline prevalence of moderate or severe vaginal/vulvar symptoms (26%) was lower than that previously reported for AI-treated breast cancer patients (58%),[2] potentially due to patients minimizing symptoms that are less important than metastatic disease control or being embarrassed to communicate sexual concerns to their oncologists
- The most frequently reported symptom was vaginal dryness (40%), which was previously reported by 19%–88% of postmenopausal breast cancer patients/survivors taking AIs[1-3,7-9]
- We will further evaluate the impact of patient and disease characteristics on baseline vulvar/vaginal symptoms in patients with *ESR1*-mutated ER+/HER2- mBC, as well as the effect of either lasofoxifene or fulvestrant plus the CDK4/6i abemaciclib on vaginal and sexual health, using patient-reported outcomes in the phase 3, registrational, ELAINE 3 trial (NCT05696626)

Disclosures

- **SBG** has CME activities from Research to Practice, Clinical Education Alliance, and Medscape; was a panelist for Total Health Conferencing; a moderator for Curio Science; has done consulting for AstraZeneca, Biovica, Biotheranostics, Blueprint Medicines, Eagle, Eli Lilly, Novartis, Pfizer, Sanofi Genzyme, and Sermonix; and has received research support from Eli Lilly, Pfizer, and Sermonix. **SLS** has received research funding (paid to institution) from Astra Zeneca, Abbvie, Bristol Myers Squibb, Eli Lilly, Seagen, and Sermonix; and consults for Foundation Medicine, AstraZeneca, DaichiiSankyo, Eli Lilly, Pfizer, Sermonix, and Novartis. **JLM** received research funding from Seagen, Pfizer, AstraZeneca; and has consulted for AstraZeneca, Clovis, Genentech, Glaxo SmithKline, Novartis, Pfizer, Puma, Sanofi Genzyme, and Seagen. **TJP** is a consultant for AstraZeneca, Gilead, Hibercell, Novartis, Pfizer, Sanofi and Seagen; has received research support from AstraZeneca, Gilead, Hibercell, Novartis, Pfizer, Sanofi, Nuvation, and Olema; and has been a speaker for AstraZeneca, Gilead, and Seagen. **BK**, **SNJ**, and **DC** are consultants for Sermonix. **DJP** is an employee and stockholder of Sermonix.
- Sermonix Pharmaceuticals sponsored the study and provided support for the medical writing assistance of Hui Zhang, PhD and Kathleen Ohleth, PhD (Precise Publications, LLC).