Lasofoxifene (LAS) Plus Abemaciclib (Abema) for Treating ESR1-mutated ER+/HER2- Metastatic Breast Cancer (mBC) after Progression on Prior Therapies: ELAINE 2 Study Update

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Introduction

- Endocrine therapy (ET), particularly aromatase inhibitors (AIs), for estrogen receptor (ER)-positive breast cancer can lead to acquired ESR1 mutations (mESR1), which drives resistance and tumor progression.1,4
- Current therapies have limited activity for mBC with mESR1, especially in the post CDK4/6 inhibitor (CDK4/6i) setting.5-6
- LAS is a next-generation ET and breast ER antagonist that prolonged progression-free survival (PFS; median 5.6 vs 3.7 mos; P=0.138) compared with fulvestrant (Fulv) and provided a greater clinical benefit rate (CBR, 37% vs 22%; P=0.117) and objective response rate (ORR, 13% vs 3%; P=0.124), in patients with mESR1 mBC that progressed on an AI plus CDK4/6i,
- In the phase 2, ELAINE 2 study, LAS/Abema was associated with a clinically meaningful PFS (median ~13 mos), ORR (55%), and CBR (68%) in women with ER+/HER2- mBC and acquired mESR1.
- ESR1 MAF decreased with LAS/Abema, consistent with target engagement.

Results

- At April 2023, 6 of 29 enrolled patients were continuing treatment as of April 2023. Abema, abemaciclib; CBR, clinical benefit rate; CI, confidence interval; LAS, lasofoxifene. Table 1.
- Table 1. Most frequently reported TEAEs (incidence ≥10%, N=29)*
- Table 2. Treatment response by baseline genomic alterations concurrent with mESR1 (n=25)

Key Takeaways

- In ELAINE 2, LAS/Abema was well tolerated with an acceptable safety profile.
- LAS/Abema was associated with a clinically meaningful PFS (median ~13 mos), ORR (55%), and CBR (68%) in women with ER+/HER2- mBC and acquired mESR1.
- ESR1 MAF decreased with LAS/Abema, consistent with target engagement.

Conclusions

- With longer ELAINE 2 follow up, LAS/Abema continued to be well tolerated; no new safety signals were noted.
- Incidence of venous thromboembolism in ELAINE 2 was within the range previously reported for Abema-based therapies.1-6
- LAS/Abema exhibited meaningful antitumor activity in patients with mESR1, ER+/HER2- mBC that had progressed on ET and CDK4/6i.
- Observed decreases in mESR1 ctDNA suggest target engagement with LAS.
- Other genomic alterations associated with resistance that were detected concurrently with mESR1 at baseline did not appear to compromise the efficacy of LAS/Abema.
- A confirmatory, phase 3 study (ELAINE 3; NCT05696626) will compare LAS/Abema with Fulv/Abuma. If ELAINE 2 results are corroborated, the combination of LAS and Abema may provide a practice-changing option for treating mESR1 mBC.

Disclosures

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- SANOIT was the sponsor of the study, Semmonix Pharmaceuticals sponsored the study and provided support for the principal investigator (SD), and Kathleen Chook, PhD (Pricer Publications, LLC).


Objective

- The objective of the ELAINE 2 study was to evaluate the safety and efficacy of LAS combined with Abema in patients with ESR1-mutated, ER+/HER2- mBC in the post-CDK4/6i setting.

Methods

- The open-label, phase 2, single-arm ELAINE 2 study (NCT04432454) enrolled women (n=18 years) with ER+/HER2- mBC and acquired mESR1 identified in circulating tumor DNA (ctDNA) who had disease progression on prior ET for mBC (52 lines).
- Prior CDK4/6i and/or one line of chemotherapy for mBC was allowed.
- Patients took oral LAS 5 mg/day and Abema (supplied by Eli Lilly and Co) 150 mg BID until disease progression, death, toxicity, or withdrawal.
- Primary endpoint: safety and tolerability (AEs).
- Secondary endpoints: PFS, CBR, ORR, duration of response, and time to response.
- Staging scans were performed every 8 weeks.
- ESR1 mutant allele fractions (MAF) were analyzed in ctDNA at baseline and wk 4 using the Sysmex-inostics SafeSeq assay.
- Guardian 360 ctDNA analysis was utilized to identify other genomic alterations.
- Data were summarized descriptively with no formal hypothesis testing.