Patients With Advanced and/or Metastatic Estrogen Receptor (ER)-Positive, HER2-Negative Breast Cancer

Methods

• OP-DP-1250 (Olema032) is a fixed-dose, phase 1b study of daily oral and DP in adults with ER+/HER2- MBC (Figure 1)

Figure 1. OP-DP-1250 Trial Design

Pharmacokinetics

• OP-DP-1250 is a multi-dose schedule with a median LSW ranging between 2 and 3 hours
• Early cyclic OP-DP plasma concentration needed to target efficacious average concentration for dose levels 60 mg QD (Figure 2).

Table 3. OP-DP-1250 Phase Dose Concentrations Following Multiple Dose Administration (On-Cycle Day 2)

Table 7. Safety

Efficacy

• Time failed to reach 0% reduction in PD for all drug cut-off dates, each featuring a histogram of PD
• 60 mg and above, treatment-emergent new lesions occurred at all dose levels

Table 7. Efficacy Parameters Computed to the Anticipated PD Range

Conclusions

• At dose levels of 60 mg and above, OP-DP-1250 demonstrated high and steadily increasing levels that were above the predicted efficacy concentration based on preclinical models, supporting once-daily dosing.
• No Grade 3/4 observed and P1D was not reached.
• Median TTD at all dose levels.
• Efficacy at all dose levels observed as either partial or complete (PD is defined as achieving >50% tumor shrinkage).
• Anticipated PD range of 60 mg to 1250 mg (Table 7).
• ≤ 30 mg and above, treatment-emergent new lesions occurred at all dose levels.
• 60 mg and above, treatment-emergent new lesions occurred at all dose levels

Background

• Advanced and/or metastatic breast carcinoma is a major unmet clinical need in breast cancer.
• There are currently a number of available options for advanced breast cancer.
• Fulvestrant is widely used and approved in many countries.

Acknowledgments

The study was sponsored by Olema. An independent medical professional monitored and oversaw the trial to ensure patient safety and data integrity.

References


Results

Patient Population

• At date of last efficacy analysis was October 1, 2021
• A total of 34 patients were enrolled at 2 different dose escalation cohorts
• The most common ETS were lengthening, and osseous metastases.
• 80% of patients were adults, 60% of patients were at least 60 years of age (Table 5).
• 2 patients were in the 60 mg dose cohort; 1 patient was ≥70 years old and 1 patient was 65 years old

Table 3. Descriptive and Baseline Disease Characteristics

Safety

• Most treatment-emergent adverse events (TEAEs) were grade 1 or 2 at all dose levels (Table 4).
• No drug-related deaths were observed and the maximum tolerated dose (MTD) was not reached.
• The most common TEAEs were lengthening, nausea, and constipation (Table 4).
• 60 mg and above, there was a higher frequency of papular rash, hypophosphatemia and papular rash.

Table 4. Treatment Emergent Adverse Events (TEAEs) Occurring in ≥20% of Patients

Table 5. Treatment-Related Adverse Events (TRAEs) Occurring in ≥20% of Patients

Table 6. Summary of Observations

Table 7. Safety

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Preliminary Data From a Phase 1/2, Multicenter, Dose Escalation Study of OP-1250, an Oral CERAN/SERD, in Patients With Advanced and/or Metastatic Estrogen Receptor (ER)-Positive, HER2-Negative Breast Cancer

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