TPS1128 Poster Session

SIMRISE: A randomized phase III trial evaluating SIM0270 in combination with everolimus versus treatment of physician's choice in patients with ER+/HER2- advanced breast cancer, previously treated with CDK4/6 inhibitors.

Jiong Wu, Jian Zhang, Yongmei Yin, Yehui Shi, Xinhong Wu, Tao Sun, Chen Yang, Lili Zhu, Ya Li, Chunyan He; Fudan University Shanghai Cancer Center, Shanghai, China; Jiangsu Province Hospital, Nanjing, China; Tianjin Medical University Cancer Institute and Hospital, Tianjin, China; Hubei Cancer Hospital, Wuhan, China; Liaoning Cancer Hospital & Institute, Shenyang, China; State Key Laboratory of Neurology and Oncology Drug Development & Simcere Zaiming Pharmaceutical Co., Ltd, Nanjing and Shanghai, China

Background: CDK4/6 inhibitors (CDK4/6i) in combination with endocrine therapy (ET) have demonstrated sustained benefits in the first-line treatment of HR+/HER2- advanced breast cancer(aBC). However, effective ET options are limited for patients who progressed after the treatment of ET in combination with CDK4/6i. SIM0270 in combination with everolimus exhibited promising anti-tumor activities in a Phase I study. **Methods:** SIMRISE is an ongoing randomized, open label, Phase III trial designed to evaluate SIM0270 in combination with everolimus versus the treatment of physician's choice (TPC) for patients with ER+/HER2- aBC progressed on previous ET and CDK4/6i. A total of 460 patients will be enrolled across approximately 50 sites in China. Patients are randomized in a 1:1 ratio to receive either SIM0270 + everolimus or TPC (exemestane + everolimus or fulvestrant). Stratification factors include: visceral metastasis (yes or no); prior fulvestrant (yes or no); baseline ESR1 status (mutation detected or not detected). Key eligibility criteria include: ER+/HER2- aBC patients having measurable disease per RECIST 1.1 or bone only disease with at least one predominant lytic bone lesion or mixed lytic-blastic lesion; postmenopausal women and pre-/perimenopausal women or men receiving luteotropic hormone releasing hormone agonist(LHRHa) therapy per local prescribing information; patients must have received at least one line and no more than two lines of ET; recurrence while on or within 12 months of completion of adjuvant ET for ≥24 months is considered as first-line ET, or first line ET in advanced setting for ≥6 months. Patients must have previously received CDK4/6i combined with ET for ≥6 months; one line chemotherapy for aBC is allowed. The Primary endpoint is progression-free survival (PFS) as assessed by blinded independent review committee (BIRC). The secondary endpoints include PFS (assessed by investigators), overall survival (OS), objective response rate (ORR), duration of response (DoR), clinical benefit rate (CBR), time to progression (TTP), safety, pharmacokinetics (PK) and patients-reported outcomes (PRO). The analysis of primary endpoint will use a stratified log-rank test at an overall of 0.05 significance level (two-sided). Futility analyses are planned, and an independent data monitoring committee will be in place. Clinical trial information: NCT06680921. Research Sponsor: Simcere Zaiming Pharmaceutical Co., Ltd.