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Final OS analysis of sacituzumab tirumotecan versus chemotherapy in previously treated locally recurrent or metastatic triple-negative breast cancer: Phase III OptiTROP-Breast01

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Background

Sacituzumab tirumotecan (sac-TMT) is a TROP2-directed ADC with a unique bifunctional linker and a belotecan-derivative topoisomerase I inhibitor payload. In phase III OptiTROP-Breast01, sac-TMT significantly improved PFS and demonstrated a statistically significant OS benefit vs physician's choice chemotherapy at the prespecified interim OS analysis (HR, 0.53; 95% CI, 0.36–0.78; one-sided p=0.0005) in previously treated locally recurrent/metastatic TNBC. Here, we report final OS with extended follow-up.

Methods

Pts with mTNBC who had received ≥ 2 prior systemic therapies, including ≥ 1 in the metastatic setting, were randomized 1:1 to sac-TMT or physician's choice chemotherapy. OS was a key secondary endpoint. OS was adjusted for subsequent ADC therapy using RPSFT model; censoring at subsequent ADC initiation was performed as a sensitivity analysis.

Results

A total of 263 pts were randomized to sac-TMT (n=130) or chemotherapy (n=133). As of Sep 17, 2025, the median follow-up was 29.4 mo. The statistically significant OS benefit observed at interim analysis was sustained in the final analysis. Median OS was 14.7 mo (95% CI, 12.1–20.1) with sac-TMT vs 9.9 mo (95% CI, 8.6–11.8) with chemotherapy (HR, 0.60; 95% CI, 0.45–0.80). The survival benefit was durable, with 24-mo OS rates of 33.8% vs 21.4% and 30-mo OS rates of 26.8% vs 13.2%. OS benefit was generally consistent across prespecified subgroups, including prior PD-1/PD-L1 inhibitor exposure and HER2-low disease. Subsequent ADC therapy was received by 27.8% of pts in the chemotherapy arm. After adjustment for subsequent ADC therapy, median OS was 14.7 vs 9.4 mo, with an adjusted HR of 0.55 (95% CI, 0.39–0.73); sensitivity analysis censoring pts at subsequent ADC initiation was consistent. No new safety signals were observed.

Conclusions

With nearly 30 mo of follow-up, sac-TMT sustained the statistically significant OS benefit previously observed at interim analysis. Sac-TMT provided durable survival benefit vs chemotherapy, including across clinically relevant subgroups and after adjustment for subsequent ADC therapy, supporting the use of sac-TMT in previously treated mTNBC.

Clinical trial identification

NCT05347134; first posted on April 26, 2022.

Legal entity responsible for the study

Sichuan Kelun-Biotech Biopharmaceutical Co., Ltd., Chengdu, China.

Funding

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Disclosure

B. Xu: Financial Interests, Personal, Advisory Role: Novartis, AstraZeneca. G. Liu: Financial Interests, Personal, Full or part-time Employment: Sichuan Kelun-Biotech Biopharmaceutical Co., Ltd.. Y. Diao: Financial Interests, Personal, Full or part-time Employment: Sichuan Kelun-Biotech Biopharmaceutical Co., Ltd.. X. Jin: Financial Interests, Personal, Full or part-time Employment: Sichuan Kelun-Biotech Biopharmaceutical Co., Ltd.. J. Ge: Financial Interests, Personal, Full or part-time Employment: Sichuan Kelun-Biotech Biopharmaceutical Co., Ltd.. All other authors have declared no conflicts of interest.

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