TPS1123 **Poster Session**

SOLTI-2201 ACROSS-TROP2 trial: A phase II study to identify predictive biomarkers of sacituzumab govitecan benefit and to understand resistance mechanisms in HR+/HER2- advanced or metastatic breast cancer.

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Background: Sacituzumab Govitecan (SG) is a TROP2-directed antibody-drug conjugate (ADC) linked to a topoisomerase I inhibitor via a hydrolysable CL2A linker. It is approved for the treatment of metastatic triple-negative breast cancer (mTNBC) patients who have undergone at least two prior systemic therapies, including one for advanced disease, and of hormone receptor-positive (HR+)/HER2-negative metastatic breast cancer (mBC) patients after endocrine therapy (ET) and two systemic treatments. Currently, no biomarkers, including TROP2 protein expression, have been identified to predict SG response, highlighting the need to explore biomarkers of efficacy and to identify key resistance mechanisms to the drug. The ACROSS-TROP2 study aims to address this unmet medical need. **Methods:** ACROSS-TROP2 (NCT06236269) is a phase II, open-label, single-arm trial investigating SG in HR+/HER2-negative mBC patients. The study initially planned to enroll 50 pre- or post-menopausal female or male participants who progressed during or after treatment with CDK4/6 inhibitors and received up to one prior chemotherapy or ADC regimen for metastatic disease. Due to high recruitment rates and promising findings demonstrating ADC benefits in earlier treatment lines (Bardia et al., NEJM 2024), a protocol amendment was introduced to expand the sample size to 100 patients. Participants will receive SG at 10 mg/kg via IV infusion on Days 1 and 8 of each 21-day cycle until disease progression (PD). Fresh tumor biopsies will be obtained at baseline, after 2–3 weeks of treatment (C2D1), and at PD. The primary endpoint is to measure changes in the CelTIL score—a composite of tumor cellularity and tumor-infiltrating lymphocytes—between baseline and C2D1 biopsies, as CelTIL is associated with long-term efficacy. Secondary endpoints include overall response rate, progression-free survival, duration of response, time to response, safety, and tolerability. Correlative analyses of molecular markers in tissue and blood will be conducted to correlate biological findings (e.g., CelTIL, Ki67, TROP2, PD-1/PD-L1, PAM50) with clinicopathological data, evaluate the predictive value of early dynamic changes in ctDNA, identify genomic alterations linked to treatment response and resistance, and explore changes from baseline to PD to identify mechanisms of resistance. A paired t-test will assess whether the mean change in CelTIL score is statistically different from zero. The study has been approved in Spain and is actively enrolling participants at 10 sites within the SOLTI network. Previously presented at ESMO Breast 2024, FPN: 265TiP, Eva Ciruelos et al. - Reused with permission. Clinical trial information: NCT06236269. Research Sponsor: None.