TPS1134 Poster Session

DATO-Base: A phase II study of DATOpotamab deruxtecan for patients with breast cancer brain metastases or leptomeningeal disease.

Paolo Tarantino, Tianyu Li, Clare Strickland, Michelle DeMeo, Leilani Anderson, Esther Pasternak, Carey K. Anders, Manmeet Singh Ahluwalia, Reshma L. Mahtani, Liangge Hsu, Sarah Ossing, Nabihah Tayob, Sara M. Tolaney, Nancy U. Lin, Sarah L. Sammons; Dana-Farber Cancer Institute, Boston, MA; Duke Cancer Institute, Durham, NC; Miami Cancer Institute, Baptist Health South Florida, Miami, FL; Brigham and Women's Hospital, Boston, MA; Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA

Background: Approximately half of patients with metastatic TNBC and one fifth of those with estrogen receptor (ER)+/HER2-negative metastatic breast cancer (MBC) eventually develop breast cancer brain metastases (BCBM), with an adverse prognostic effect. Intracranially penetrant systemic therapies in HER2-negative MBC are very limited. In this setting, antibody-drug conjugates (ADCs) have shown promise, with impressive intracranial activity observed with trastuzumab deruxtecan. Datopotamab deruxtecan (Dato-DXd) is a novel anti-Trop2 ADC with robust antitumor activity in HER2-negative MBC. In the TROPION-Breast01 phase 3 trial, Dato-DXd outperformed chemotherapy for ER+/HER2-negative MBC, and promising early-phase data was also reported in triple-negative MBC. Preclinical data in tumor models found favorable intracranial penetration for Dato-DXd, and encouraging clinical data were reported in patients with lung cancer brain metastases. Based on the relevant unmet need and the promising preclinical and clinical data seen with Dato-DXd, there is a strong rationale in testing Dato-DXd for patients with HER2-negative MBC and BCBM or leptomeningeal disease (LMD). **Methods:** DATO-Base is an ongoing, open label, multicenter, investigator-initiated phase II trial for patients with HER2-negative MBC with active BCBM and/or LMD. Eligible participants are women and men with HER2-negative active (newly diagnosed/untreated or treated/progressive) brain metastases or LMD. Patients are enrolled in one of three cohorts: Cohort A (n = 24) for HR+/HER2-negative BCBM; Cohort B (n = 24) for triple-negative BCBM; Cohort C (n = 10) for HER2-negative LMD (any ER status). Patients in Cohort A require prior treatment with at least one line of endocrine treatment in the metastatic setting; no prior treatment is required for Cohorts B and C. Prior treatment with approved or investigational ADCs is allowed. Participants receive Dato-DXd 6 mg/kg IV on day 1 of each 21-day cycle until progression, unacceptable toxicity, withdrawn consent, noncompliance, or death. The primary endpoint for Cohorts A and B is intracranial objective response rate per RANO-BM criteria. Patients in each cohort will be enrolled based upon Simon two-stage designs: if ≥1/9 patients respond, a total of 24 patients will be enrolled. Cohort C is exploratory, with description of overall survival and exploratory endpoints. Blood and cerebrospinal fluid is being collected at baseline, C2D2, and at progression for translational studies. The trial was activated in December 2023, with enrollment ongoing. Clinical trial information: NCT06176261. Research Sponsor: None.