TPS1122 Poster Session

Phase II study evaluating 68Ga-FAPI PET uptake heterogeneity as a predictor of T-DXd treatment response in HER2-positive breast cancer brain metastases.

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Background: Breast cancer is a leading cause of metastasis to the central nervous system (CNS). Approximately 30% of patients with HER2-positive breast cancer develop brain metastases, which are associated with a poor prognosis and limited treatment options. T-DXd has shown promise in treating brain metastases from HER2-positive breast cancer. However, up to 10% patients showed brain metastasis progression at the initial evaluation of treatment and may require radiotherapy or neurosurgery immediately. Identifying predictors of treatment response and determining the timing for local therapy intervention is crucial for personalized medicine. Heterogeneity in tumor metabolism, as assessed by (68Ga)–labeled fibroblast-activation protein inhibitor (68Ga-FAPI) PET-CT which displays the activity of cancer-associated fibroblasts (CAFs) in the tumor microenvironment, with good sensitivity and specificity in brain metastasis imaging, may serve as a biomarker for treatment response. This study aims to investigate the predictive value of 68Ga-FAPI PET uptake heterogeneity for T-DXd treatment response in HER2-positive breast cancer brain metastases. **Methods:** This open-label, single-center, phase II clinical trial will investigate the heterogeneity of brain metastasis and analyze the difference between stable and active brain metastasis evaluated by 68Ga-FAPI uptake in HER2-positive MBC. Patients with HER2-positive metastatic breast cancer and confirmed brain metastases by MRI were enrolled; at least one measurable intracranial lesion ($\geq$ 1.0 cm) that has not previously been treated with radiation. Radiotherapy or neurosurgery is allowed with an interval $\geq$ 4 weeks. Patients will receive T-DXd treatment and undergo 68Ga-FAPI PET-CT scans before and after two cycles of treatment. The primary endpoint is the difference in baseline heterogeneity index by 68Ga-FAPI PET-CT between cerebral lesions achieving ORR and those that do not. Secondary endpoints include 68Ga-FAPI PET-CT value changes (SUVmax, SUVmean) at baseline and after treatment; difference in baseline heterogeneity index for PFS, CBR and OS; difference of baseline heterogeneity index, SUVmax and SUVmean between active or stable brain metastasis; 68Ga-FAPI PET-CT value changes (heterogeneity index, SUVmax, SUVmean) at baseline and 2 cycles after T-DXd treatment of whole body metastasis lesions. The study plans to enroll 50 patients and is actively enrolling. Clinical trial information: NCT06797622. Research Sponsor: CSCO-LingHang Oncology Research Foundation (Y-2022HER2AZQN-0378).