TPS2088 **Poster Session**

Phase IIa study of αDC1 vaccines targeting HER2/HER3 combined with pembrolizumab in patients with asymptomatic brain metastasis from breast cancer.

Shipra Gandhi, Peter A. J. Forsyth, Mateusz Opyrchal, Audrey Rawleigh, Matthew Sydor, Kamran A. Ahmed, Kristopher Attwood, Patrick Michael Dillon, Camilo E. Fadul, Dheerendra Prasad, Sheheryar Kairas Kabraji, Ellis Glenn Levine, Kevin Kalinsky, Brian J. Czerniecki, Pawel Kalinski; Roswell Park Comprehensive Cancer Center, Buffalo, NY; H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL; Indiana University, Indianapolis, IN; Roswell Park Comprehemsive Cancer Center, Buffalo, NY; University of Virginia, Charlottesville, VA; University of Virginia School of Medicine, Charlottesville, VA; Winship Cancer Institute at Emory University, Atlanta, GA

Background: Brain metastases develop in up to 50% of patients (pts) with metastatic breast cancer. Overexpression of HER3 in brain metastatic breast cancer (BMBC) is a resistance factor to HER2-targeted therapies and a driver of brain metastasis. Disease progression is associated with loss of anti-HER2 and anti-HER3 immunity. Previously, we have demonstrated that glioma-specific peptide-loaded αDC1 which produces CXCL9, CXCL10, CXCL11, and CCL5, the chemokines that attract CXCR3- and CCR5- expressing cytotoxic T-lymphocytes (CTLs) and T-helper 1 (Th1) cells, induce clinical responses and long-term disease stabilization in pts with aggressive recurrent primary brain tumors (Okada et al. JCO 2011. PMID: 21149657). We hypothesized that anti-HER2/3-loaded αDC1 combination with PD1 blockade will result in a strong Th1/CTL response against HER2/3 epitopes (Basu A et al. Cancer Immunol Res. 2022 PMID: 34785506) that will translate into anti-cancer benefit in the central nervous system (CNS) and systemically. **Methods:** This is a phase II single-arm, non-randomized multicenter study (NCT04348747). Eligibility includes pts with BMBC ≥18 years, ECOG PS ≤1, normal marrow and organ function with asymptomatic untreated brain metastases ≥ 5 mm. The study subjects receive αDC1 q3 weeks x 3 along with pembrolizumab every 3 weeks. Thereafter, αDC1 booster doses can be administered every 3 months until disease progression, intolerable side effects, or withdrawal from study, up to 24 months. Baseline and 9-week post-αDC1 peripheral biopsies (non-CNS) are required for six pts. The primary endpoint is CNS response rate (RR) by RANO-BM criteria. If no CNS response is observed after 12 pts, the study will be terminated. If ≥ 1 response is observed, then 9 more pts will be enrolled, for a total of 21 pts. If ≥ 3 CR are observed, the proposed therapy will be considered promising for further evaluation. Secondary endpoints include non-CNS RR per RECIST v1.1, median CNS, non-CNS and overall progression-free survival, overall survival, and safety. Exploratory endpoints include changes in intratumoral biomarkers (CTLs, PDL1, chemokines) in pre- and post-treatment peripheral tumor biopsies and immune changes in the blood. So far, 7 of the planned 21 pts have been enrolled. Clinical trial information: NCT04348747. Research Sponsor: U.S. Department of Defense.