TPS9593 **Poster Session**

Phase I/IIa dose finding study of triplet regimen of relatlimab (RELA), ipilimumab (IPI), and nivolumab (NIVO) in first-line therapy of metastatic melanoma (TRINITY).

Elizabeth M. Burton, Tara Marie Davidson, Krysta McVay, Denai R. Milton, Rodabe Navroze Amaria, Isabella Claudia Glitza, Jennifer Leigh McQuade, Theresa H. Nguyen, Alexandra Ikeguchi, Adi Diab, Weiyi Peng, Michael A. Davies, Hussein A. Tawbi; Department of Genomic Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX; The University of Texas MD Anderson Cancer Center, Houston, TX; Department of Biostatistics, The University of Texas MD Anderson Cancer Center, Houston, TX; University of Houston, Houston, TX

Background: NIVO (anti-PD1) alone or in combination with IPI (anti-CTLA-4) or RELA (anti-LAG3) are approved immune checkpoint blockade (ICB) agents for the treatment (tx) of patients (pts) with advanced, unresectable metastatic melanoma. Doublet combinations induce higher rates of durable disease control vs single agent, translating into nominal improvements in survival. While there is no established dose-response relationship for NIVO alone or with RELA, IPI at higher doses induces higher objective response rate (ORR) but increased grade ≥3 immune-related adverse events. Deeper mechanistic understanding points towards potential synergy given IPI's role in expanding the TCR repertoire and modulating suppressive T cell populations while NIVO+RELA regulate the exhaustion signatures of activated T cells and allow for improved effector function. Recently, results from RELATIVITY-048 combining all three ICB agents (NIVO 480 mg Q4W + RELA 160 mg Q4W + IPI 1 mg/kg Q8W) demonstrated impressive efficacy with high response rates (59% ORR) and seemingly improved progression free and overall survival (PFS, OS) over previously reported doublet regimens. This study evaluated a markedly lower IPI dose than the approved regimen and did not include a dose escalation component to optimize the IPI dosing strategy. Our team seeks to optimize the dose and schedule of IPI to combine with NIVO+RELA in order to determine the recommended phase II dose (RP2D) for triplet ICB and maximize clinical benefit while maintaining a toxicity profile comparable to approved regimens. **Methods:** In this single center, investigator initiated, phase I/IIa study evaluating triplet ICB (NCT06683755), all pts will receive FDA approved regimen of NIVO 480mg + RELA 160mg IV Q4W along with escalating doses of IPI . Dose escalation (DE) with IPI will begin at 0.5mg/kg Q4W 4 induction doses and will incrementally escalate up to 2mg/kg Q4W. Maintenance tx will consist of NIVO+RELA Q4W. Bayesian optimal interval (BOIN) design will be used to identify the maximum tolerated dose (MTD) and RP2D (primary objective) in the DE portion, accruing an estimated 12-18 pts. The PhIIa portion will accrue an additional 12-18 pts at the RP2D to better characterize safety, and determine the ORR, (primary objective) by RECIST 1.1. Secondary objectives include PFS, OS, and tumor and immunological correlatives obtained on pre and post tx blood and tumor samples. Pts must be previously untreated, unresectable, or advanced melanoma. Non IPI containing prior adjuvant or neo-adjuvant tx will be permitted if the last dose has been >6 months. Pts with asymptomatic brain metastasis are allowed, provided no immunesuppressive doses of corticosteroids are required. Safely biopsiable lesions are required for pts enrolled in the PhII portion. This study is open for accrual at MD Anderson Cancer Center in Houston, Texas. Clinical trial information: NCT06683755. Research Sponsor: BMS.