TPS9611 **Poster Session**

A phase Ib study to assess the safety and efficacy of autologous tumor infiltrating lymphocytes (lifileucel) with adjuvant pembrolizumab (PEMBRO) for treatment of immunotherapy naïve patients with high-risk clinical stage IIIb-d resectable melanoma (MEL).

James Isaacs, Lucy Boyce Kennedy, Anthony P. Tufaro, Mark D. DeLacure, Anthony Visioni, Eren Berber, Daniel Raymond, Paolo Fabrizio Caimi, John C. Molina, Yee Peng Phoon, Joshua Arbesman, Jennifer S. Ko, Jan Joseph Melenhorst, Joseph J. Skitzki, Craig Steven Sauter, Brian Gastman, Thach-Giao Truong; Cleveland Clinic, Cleveland, OH; Cleveland Clinic Foundation - Taussig Cancer Institute, Cleveland, OH; Iovance Biotherapeutics, Inc., San Carlos, CA

Background: Despite significant advances in the treatment (Tx) of stage III MEL, there remains a high risk of recurrence after surgical resection. Adjuvant immune checkpoint inhibitors (ICI) are a standard of care, but recurrence rates remain greater than 40% at 5 years. Neoadjuvant ICI have shown improved event-free survival compared to adjuvant ICI. However, at time of surgery a significant proportion of patients' (PTS) MEL still do not show a response. Lifileucel is an autologous tumor infiltrating lymphocyte therapy (TIL) that was recently FDA-approved after showing sustained high tumor response rates for pts with ICI-refractory metastatic MEL. For patients with IO naïve stage IV MEL, ORR was 65% for lifileucel + PEMBRO. Offering TIL at earlier stages of MEL may offer several potential benefits to anti-PD-1 alone. In the Tx-naïve setting, T cells are not previously exposed to ICI that can impact the quality of the TIL product. After curative-intent resection, pts will be rendered clinically tumor-free. When TIL are then utilized to address residual microscopic MEL, they will be less impacted by an immunosuppressive tumor microenvironment often accompanying larger disease burden. Earlier stage also limits tumor heterogeneity that can emerge in more advanced Tx-refractory metastatic MEL. Here we share details of a first clinical trial to evaluate lifileucel with adjuvant PEMBRO for resectable clinically detected high-risk MEL. **Methods:** This phase 1B trial is enrolling pts with clinically detectable stage IIIB-D MEL who are planned to undergo surgical resection and eligible for standard adjuvant anti-PD1. Pts' MEL must be considered fully resectable and pts cannot have previously received ICI. Pts proceed to standard of care resection after enrollment at which time tumor is procured for lifileucel/TIL manufacturing. Once the TIL product has completed manufacturing, pts will receive lymphodepleting chemotherapy followed by TIL infusion and IL2, for up to 6 doses. At week 12 after receiving lifileucel, pts start adjuvant PEMBRO to complete 1 year of Tx. The primary endpoints of this trial are disease free survival at 1 year and safety. The trial is planned to enroll 12 pts. Sample size justification is aimed on detecting 20% improvement on 12-month RFS for lifileucel+ PEMBRO compared to standard Tx. Based on Simon's two-stage design with a one-sided type I error of 0.05 and power of 80%, if 7 or fewer of 11 pts remain relapse-free at 12 months, futility is determined. If 8 or more of 11 are still relapse-free at 12 months, then futility is rejected. Correlative studies include analysis of the phenotype, function and TCR repertoire of baseline TIL samples. Serial PBMC will be collected to monitor TIL persistence (based on TCR analysis) and functional activity. Clinical trial information: NCT06190249. Research Sponsor: Iovance.