## 177 TREATMENT OUTCOMES WITH UNSELECTED AUTOLOGOUS TUMOR INFILTRATING LYMPHOCYTES IN PATIENTS WITH CHECKPOINT INHIBITION–REFRACTORY ADVANCED CUTANEOUS MELANOMA

[1]Robert Hawkins*, [2]Yizhou Jiang, [3]Paul C Lorigan, [4]Fiona C Thistlethwaite, [3]Manon Pillai, [2]Martine Thomas, [2]Natalia Kirillova, [2]John S Bridgeman, [2]Gray Kueberuwa, [2]Ryan D Guest, [2]Zachary J Roberts. *[1]Instil Bio, Inc., Dallas, TX, USA and The Christie, NHS Foundation Trust and University of Manchester, Manchester, TX, UK; [2]Instil Bio, Inc., Dallas, TX, USA; [3]The Christie, NHS Foundation Trust, Manchester, UK; [4]The Christie, NHS Foundation Trust, Manchester, UK and University of Manchester, Manchester, UK*

**Background** Tumor infiltrating lymphocyte (TIL) products made from tumor digests showed a high overall response rate (ORR; 67%) and complete response (CR) rate (19%) and a safety profile consistent with lymphodepletion and high-dose interleukin (IL)-2 in a retrospective analysis of a single center experience of TILs for compassionate use treatment of advanced cutaneous melanoma (n=21; Hawkins, et al. AACR 2021. ePoster LB150). This subanalysis assesses outcomes for patients who received TILs after prior checkpoint inhibition, a subset with limited treatment options.

**Methods** Patients with advanced cutaneous melanoma and no standard of care treatment options received lymphodepleting chemotherapy (cyclophosphamide ×2 days; fludarabine ×5 days) followed by TIL infusion and post TIL high-dose IL-2. Safety was assessed by clinically significant adverse events (AEs). Efficacy assessments included ORR, CR rate, and overall survival (OS).

**Results** Of 21 patients who underwent treatment between October 2011 and August 2019, median age was 45 years, median number of disease sites was 4, 100% of patients had M1c or M1d disease (33% with M1d), average number of prior therapies was 3 (any checkpoint inhibitor, 91%; BRAF inhibitor [BRAFi], 52%; and MEKi, 24%), and 52% were BRAF-mutated. Twelve patients received prior PD-1i therapy and are reported herein. Baseline characteristics were similar between the overall and prior PD-1i subgroup populations. All patients in the prior PD-1i subgroup received prior CTLA-4i, and all BRAF-mutated patients received prior BRAFi alone ± MEKi. The most commonly reported AEs post-TIL infusion were consistent between the overall and prior PD-1i subgroup populations and included thrombocytopenia (62% and 75%, respectively), pyrexia (57% and 50%), and rigors (43% and 50%). No treatment-related deaths occurred. With a median follow-up of 45.5 months, the ORR and CR rate for the prior PD-1i subgroup were 58% and 8%, respectively. At data cutoff, 2 of 12 patients (17%) had durable ongoing responses (>30 months post-TIL infusion). Median OS in the prior PD-1i subgroup and overall population was 21.3 months.

**Conclusions** In this subanalysis of patients with relapsed advanced melanoma after both PD-1i and CTLA-4i, and for some, BRAFi, outcomes of unselected autologous TILs were similar to those observed in all treated patients, with high response rates and a safety profile consistent with that of TIL therapy. Unselected TILs may address the unmet medical need for the poor-risk subset of patients with advanced melanoma who experience disease progression following checkpoint inhibition and, if applicable, targeted therapy.

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**Ethics Approval** As a compassionate use study, the treatment was approved by institutional review board and National Health Service commissioning.

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