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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