DELTA-1: A GLOBAL, MULTICENTER PHASE 2 STUDY OF ITIL-168, AN UNRESTRICTED AUTOLOGOUS TUMOR-INFILTRATING LYMPHOCYTE (TIL) CELL THERAPY, IN ADULT PATIENTS WITH ADVANCED CUTANEOUS MELANOMA

¹Brian Gastman*, ²Omid Hamid, ³Pippa Corrie, ⁴Geoffrey Gibney, ⁵Gregory Daniels, ⁶Bartosz Chmielowski, ⁷Sajeve Thomas, ⁸Evidio Domingo-Musibay, ⁹Donald Lawrence, ¹⁰Yizhou Jiang, ¹¹Audrey Kennedy, ¹⁰Jeff Aycock, ¹⁰Ruben Alvarez-Rodriguez, ¹⁰Paul Robbins, ¹⁰John Le Gall, ¹⁰Zachary Roberts, ¹⁰Robert Hawkins, ¹²Amod Sarnaik. ¹Cleveland Clinic, Cleveland, OH, USA; ²The Angeles Clinic and Research Institute, Los Angeles, CA, USA; ³Cambridge University Hospitals, Cambridge, UK; ⁴Georgetown Lombardi Comprehensive Cancer, Washington, DC, USA; ⁵University of California San Diego, La Jolla, CA, USA; ⁶University of California Los Angeles, Los Angeles, CA, USA; ⁷University of Florida, Orlando, FL, USA; ⁸University of Minnesota Medical Center, Minneapolis, MN, USA; ⁹Massachusetts General Hospital, Boston, MA, USA; ¹⁰Instil Bio, Inc., Dallas, TX, USA; ¹¹Instil Bio, Inc, Dallas, TX, USA; ¹²Moffitt Cancer Center, Tampa, FL, USA

Background Patients with advanced cutaneous melanoma and persistent disease after checkpoint inhibitor therapy have poor outcomes and limited treatment options, highlighting a significant unmet medical need.¹ Autologous TIL cell therapies have shown promise in this population attributable, in part, to their intrinsic and patient-specific antitumor activity²; however, no such therapies are approved. Made from each patient's digested and cryopreserved tumor, ITIL-168 is an autologous TIL cell therapy manufactured to offer an unrestricted T-cell receptor repertoire. A single-center compassionate use clinical series demonstrated the feasibility and clinical utility of an earlier version of ITIL-168.³ DELTA-1 is a global, multicenter phase 2 study to evaluate efficacy and safety of ITIL-168. DELTA-1 will enroll patients with melanoma relapsed after or refractory to PD-1 inhibitors (PD-1i), patients intolerant to PD-1i, and patients whose best response to PD-1i was stable disease.

Methods Patients aged ≥ 18 years with histologically confirmed advanced cutaneous melanoma, ECOG performance status 0–1, and adequate organ function will be enrolled in 1 of 3 cohorts. Cohort 1 (n=80) will include patients who relapsed after or were refractory to ≥ 1 prior line of systemic therapy, including a PD-1i and, if BRAF-mutated, a BRAFi $\pm$ MEKi. Cohorts 2 and 3 (n=25 each) will include patients intolerant to PD-1i and those with stable disease after ≥ 4 doses of PD-1i, respectively. After tumor resection for TIL harvest, patients must have ≥ 1 remaining measurable lesion per Response Evaluation Criteria in Solid Tumors (RECIST) 1.1. Patients with uveal, acral, or mucosal melanoma, prior allogeneic transplant or cell therapy, and with central nervous system (CNS) disorder or symptomatic and/or untreated CNS metastases are ineligible. Patients will receive 5 days of lymphodepleting chemotherapy (cyclophosphamide $\times 2$ days overlapping with fludarabine $\times 5$ days) followed by a single ITIL-168 infusion ($\geq 5 \times 10^9$ cells) and supportive short course high-dose IL-2. The primary endpoint is objective response rate (ORR) per central review. Key secondary endpoints include duration of response, progression-free survival, overall survival, disease control rate, TIL persistence, and safety. Hypothesis testing of ORR will be performed for cohort 1. Two interim analyses will occur after 20 patients in cohort 1 have been followed for ≥ 28 days (safety) and evaluated for response ≥ 3 months after ITIL-168 infusion (futility). The primary analysis will occur when all patients in the cohort 1 modified intent-to-treat population have been followed for ≥ 6 months after the first posttreatment disease assessment.

Acknowledgements Medical writing support was provided by Christopher Waldapfel, PharmD, of Instil Bio, Inc, and Phyllicia Aaron, PhD, of Nexus GG Science, with funding from Instil Bio, Inc.

REFERENCES

- Schadendorf D, van Akkoi ACJ, Berking C, et al. Melanoma. *Lancet* 2018;**392**(10151):971–984.
- Borch TH, Anderson R, Ellebaek E, et al. Future role for adoptive T-cell therapy in checkpoint inhibitor-resistant metastatic melanoma. *J Immunother Cancer* 2020;**8**(2):e000668.
- Hawkins RE, Jiang Y, Lorigan PC, et al. Clinical feasibility and treatment outcomes with unselected autologous tumor infiltrating lymphocyte therapy in patients with advanced cutaneous melanoma. *Cancer Res* 2021;**81**(13):LB150.

Ethics Approval All patients will provide written informed consent. The study will be approved by the Institutional Review Board/Independent Ethics Committee at each site and conducted in accordance with the Good Clinical Practice Guidelines of the International Conference on Harmonisation. **Consent** N/A; the abstract does not contain sensitive or identifiable patient information.

<http://dx.doi.org/10.1136/jitc-2021-SITC2021.544>