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 ± 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 ×2 days overlapping with fludarabine ×5 days) followed by a single ITIL-168 infusion (≥5×10^9 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 cohort 1 modified intent-to-treat population have been followed for ≥6 months after the first posttreatment disease assessment.

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References

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.

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