DELTA-1: A Global, Multicenter, Phase 2 Study of ITIL-168, an Unrestricted Autologous Tumor-Infiltrating Lymphocyte Cell Therapy, in Adult Patients With Advanced Cutaneous Melanoma

Poster 544

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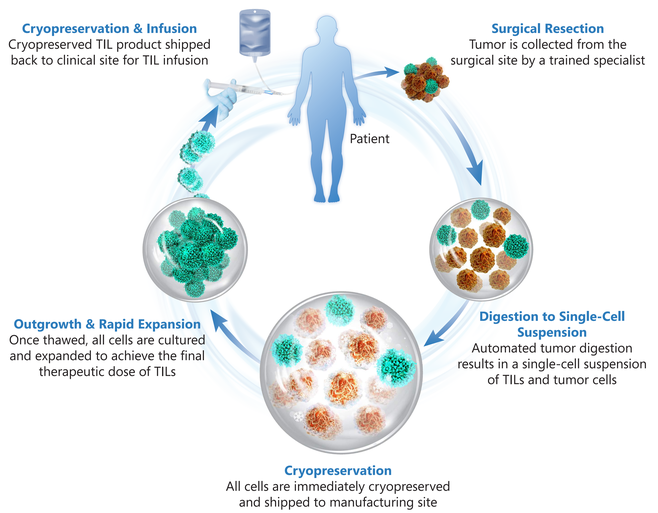
BACKGROUND

- Patients with advanced melanoma and persistent disease after checkpoint inhibitor and B-raf proto-oncogene, (*BRAF*)–targeted therapy have poor outcomes and limited treatment options[1-3]
- Autologous tumor-infiltrating lymphocytes (TILs) may provide advantages due in part to their intrinsic antitumor activity and unrestricted T-cell receptor repertoire[3]
- TIL therapy has shown durable responses in patients with advanced cutaneous melanoma, including those refractory to programmed cell death protein 1 inhibitor (PD-1i) therapy[4-7]; however, to date no TIL therapy is approved for the treatment of patients
- In a retrospective analysis of a single-center compassionate use clinical series of 21 patients with advanced melanoma, TIL products made from tumor digests showed a high overall response rate (58%) among patients (n=12) who received previous PD-1i therapy[8,9]
- Taken together, these findings suggest TILs may address the unmet medical need for the poor-risk subset of patients with advanced melanoma who experience disease progression after checkpoint inhibition and, if applicable, targeted therapy[4,7-9]
- ITIL-168 is an autologous TIL cell therapy made from each patient's digested and cryopreserved tumor, offering an unrestricted T-cell receptor repertoire
- ITIL-168 manufacturing has been optimized and automated to improve the robustness, consistency, and scalability of the closed-system TIL manufacturing process (**Figure 1**)
  - Tumor is resected by a surgeon, collected by a trained tumor recovery specialist, and immediately digested into a single-cell suspension and cryopreserved, reducing variability in handling and transport of starting material prior to closed-system TIL manufacturing
  - Tumor cryopreservation unlinks the tumor resection from manufacturing start time and allows for flexibility in scheduling of surgery
- DELTA-1 is a global, multicenter, phase 2 study evaluating the efficacy and safety of ITIL-168 in patients with melanoma who have relapsed after or are refractory to a PD-1i, intolerant to a PD-1i, or whose best response to PD-1i was stable disease (**Figure 2**)

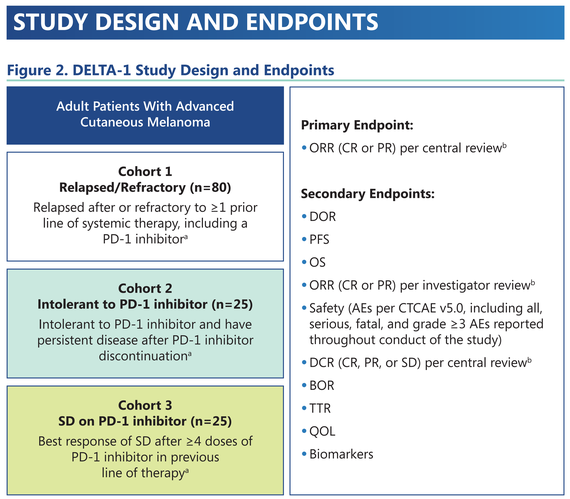
Figure 1. TIL Journey



TIL, tumor-infiltrating lymphocyte.

STUDY DESIGN AND ENDPOINTS

Figure 2. DELTA-1 Study Design and Endpoints



[a] Patients with a *BRAF* mutation must have progressed after receiving a BRAF inhibitor ± a MEK inhibitor.
[b] Modified RECIST v1.1.
AE, adverse event; BOR, best overall response; *BRAF*, B-raf proto-oncogene, serine/threonine kinase; CR, complete response; CTCAE, National Cancer Institute Common Terminology Criteria for Adverse Events version 5.0; DCR, disease control rate; DOR, duration of response; MEK, mitogen-activated protein kinase kinase; ORR, objective response rate; OS, overall survival; PD-1, programmed cell death protein 1; PFS, progression-free survival; PR, partial response; QOL, quality of life; RECIST v1.1, Response Evaluation Criteria for Solid Tumors version 1.1; SD, stable disease; TTR, time to response.

STATISTICAL METHODS

STUDY POPULATIONS

- Full analysis set: all enrolled patients; used for the summary of patient disposition and listings of deaths
- Modified intent-to-treat (mITT) analysis set: includes patients enrolled and treated with ITIL-168; used for analysis of efficacy endpoints
- Safety analysis set: all patients treated with ITIL-168

STUDY ANALYSIS

- Hypothesis testing of objective response rate (ORR) will be performed for cohort 1
- Primary analysis: will be conducted when all patients in the cohort 1 mITT analysis set have had the opportunity to be followed for ≥6 months after their first posttreatment disease assessment or are considered lost to follow-up
  - At the time of the primary analysis, data for cohorts 2 and 3 will be summarized descriptively

STATISTICAL OUTPUTS

- ORR, best overall response, disease control rate: incidence and exact 2-sided 95% CIs
- Duration of response, progression-free survival, and overall survival: Kaplan-Meier estimates and 2-sided 95% CIs
- Safety: incidence of adverse events (AEs) per National Cancer Institute Common Terminology Criteria for Adverse Events version 5.0, including all, serious, fatal, and grade ≥3 AEs reported throughout conduct of the study

PATIENT ELIGIBILITY

Table 1. DELTA-1 Key Inclusion and Exclusion Criteria

Key Inclusion Criteria

- Histologically confirmed advanced cutaneous melanoma
- **Cohort 1**: Disease that is relapsed after or refractory to at least 1 prior line of systemic therapy that must include a PD-1 inhibitor[a]
- **Cohort 2**: Disease that is persistent after discontinuing a PD-1 inhibitor due to toxicity[a]
- **Cohort 3**: Disease that is stable after at least 4 doses of a PD-1 inhibitor[a]
- Age ≥18 years
- ECOG performance status 0 or 1
- Medically suitable for surgical resection of tumor tissue
- After tumor resection for TIL harvest, patients must have ≥1 remaining measurable lesion as identified by CT or MRI per RECIST v1.1
- Adequate bone marrow and organ function

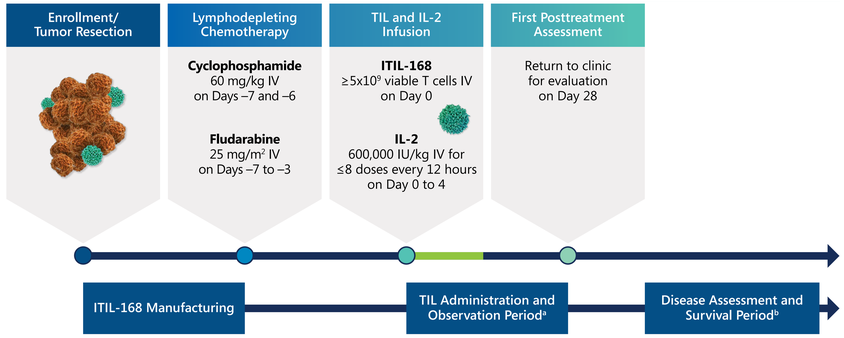
Key Exclusion Criteria

- History of another primary malignancy within the previous 3 years
- Melanoma of uveal, acral, or mucosal origin
- Previous allogeneic stem cell transplant or organ allograft
- Prior TIL or engineered cell therapy (eg, CAR T-cell therapy)
- Stroke or transient ischemic attack ≤12 months before enrollment
- Significant CNS disorder
- Symptomatic and/or untreated CNS metastases
- Significant autoimmune disease ≤2 years prior to enrollment
- History of severe, immediate hypersensitivity reaction to cyclophosphamide, fludarabine, or IL-2

[a] Patients with a *BRAF* mutation must have progressed after receiving a BRAF inhibitor ± a MEK inhibitor.
BRAF, B-raf proto-oncogene, serine/threonine kinase; CAR, chimeric antigen receptor; CNS, central nervous system; CT, computed tomography; ECOG, Eastern Cooperative Oncology Group; IL-2, interleukin-2; MEK, mitogen-activated protein kinase kinase; MRI, magnetic resonance imaging; PD-1, programmed cell death protein 1; RECIST v1.1, Response Evaluation Criteria for Solid Tumors version 1.1; TIL, tumor-infiltrating lymphocyte.

TREATMENT SCHEMA

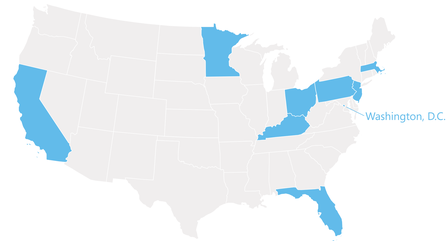
Figure 3. DELTA-1 Treatment Schema



[a] Patients will be hospitalized until resolution of non-hematologic adverse events to ≤grade 1 or until deemed safe for discharge by the investigator.
[b] Disease assessment and survival period begins at week 6.
IL-2, interleukin-2; IV, intravenous; TIL, tumor-infiltrating lymphocyte.

- Patients will receive 5 days of lymphodepleting chemotherapy (cyclophosphamide ×2 days overlapping with fludarabine ×5 days) followed by a single ITIL-168 infusion (≥5×10⁹ cells) and supportive short-course high-dose interleukin-2 (**Figure 3**)

STATUS



Locations With Active Sites:

California	New Jersey
Florida	Ohio
Kentucky	Pennsylvania
Massachusetts	Washington, D.C.
Minnesota	

- The study opened to accrual in September 2021 and is currently enrolling participants from sites in the United States
- Additional sites are being added; refer to ClinicalTrials.gov for the most up-to-date list of activated sites

REGISTRATION

- This study is sponsored by Instil Bio, Inc. and is registered at ClinicalTrials.gov (NCT05050006)

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For questions or comments, please email: medical@instilbio.com

DISCLOSURES

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