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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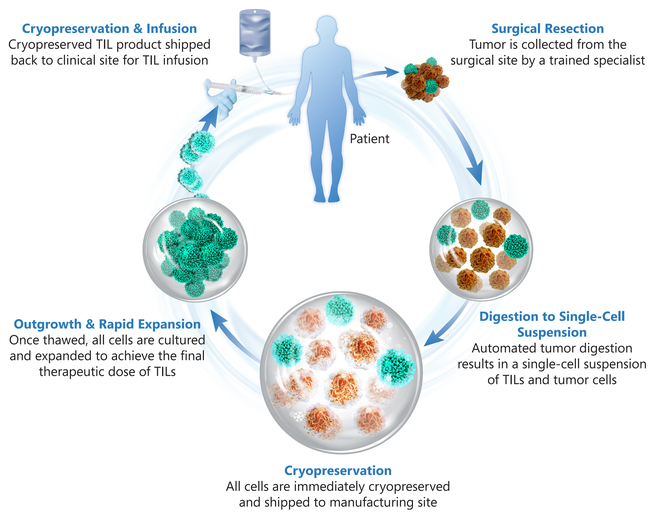
BACKGROUND

- 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**)

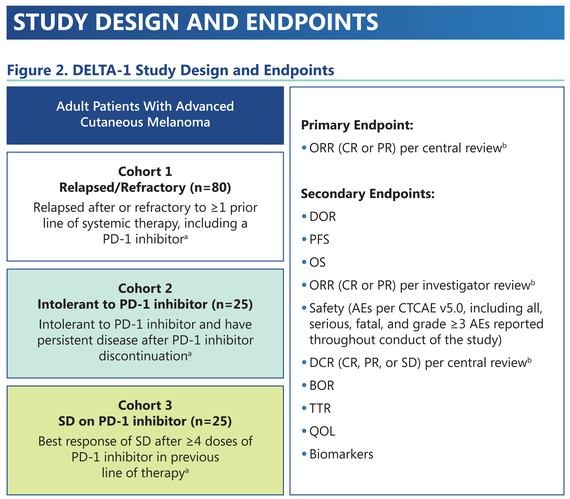
Figure 1. TIL Journey



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

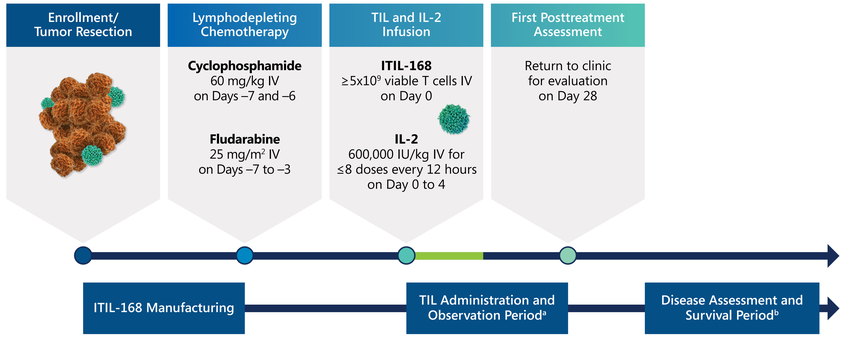
Key Exclusion Criteria

- 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

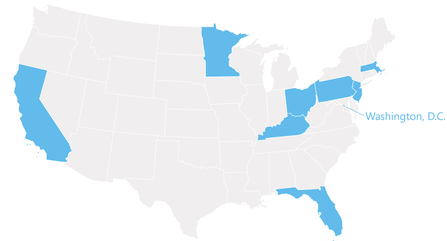
Figure 3. DELTA-1 Treatment Schema



[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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FUNDING

This study is funded by Instil Bio, Inc.

ACKNOWLEDGMENTS

We would like to thank the patients and their families, caregivers, and the study investigators, staff, and clinical sites for participating in this study

Medical writing support was provided by Christopher Waldapfel, PharmD, of Instil Bio, Inc., and Phylicia Aaron, PhD, of Nexus Global Group Science, with funding from Instil Bio, Inc.

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

DISCLOSURES

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Presented at the Society for Immunotherapy of Cancer (SITC) Annual Meeting, November 10-14, 2021.