

DELTA-2: A PHASE 1, OPEN-LABEL, MULTICENTER STUDY OF ITIL-168, AN AUTOLOGOUS TUMOR-INFILTRATING LYMPHOCYTE (TIL) CELL THERAPY, WITH PEMBROLIZUMAB IN PATIENTS WITH ADVANCED SOLID TUMORS

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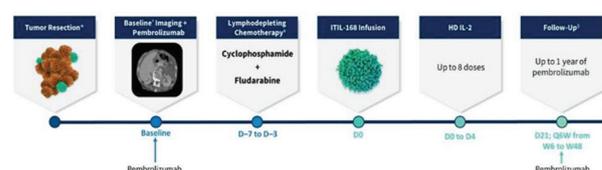
Background Despite the benefits of immune checkpoint inhibitors (ICIs) in solid tumors, additional treatment options are needed for patients with primary or acquired resistance.¹ TILs are present in various solid tumors, and TIL therapy has demonstrated efficacy and durable responses in some advanced solid tumors due to its antitumor reactivity and broad T-cell repertoire.²⁻⁴ Additionally, preclinical data suggest ICIs may further support the persistence of TILs in immunogenic tumors.⁵ Here, we describe a study that will explore the safety, feasibility, and preliminary efficacy of an autologous TIL therapy, ITIL-168, in combination with pembrolizumab in patients with cervical cancer (CC), head and neck squamous-cell carcinoma (HNSCC), or non-small cell lung cancer (NSCLC).

Methods DELTA-2 (NCT05393635) is an ongoing phase 1, multicenter, multicohort, open-label trial evaluating ITIL-168 with pembrolizumab in previously treated patients with advanced solid tumors. Patients will be enrolled in 1 of 3 cohorts (n≈9-15 patients per cohort): advanced CC (Cohort 1), HNSCC (Cohort 2), or NSCLC (Cohort 3). Eligible patients must have progressed during or following ≥1 prior line of chemotherapy along with an ICI. EGFR mutations or ALK translocations in NSCLC are included in Cohort 3, and patients are required to have progressed on targeted therapy but not ICI. Eligibility criteria across all cohorts include ECOG PS ≤1, adequate organ function, resectable tumor lesion(s), and ≥1 remaining measurable lesion per RECIST v1.1 post-tumor resection. Bridging therapy is allowed but must be discontinued at least 2 weeks or 5 half-lives before baseline imaging. Patients with prior cell therapy treatment, symptomatic and/or untreated central nervous system metastases, or requiring chronic steroids are ineligible. Treatment will include lymphodepleting chemotherapy (the dosage of cyclophosphamide and fludarabine will be adjusted based on cohort and patient comorbidities) followed by a single infusion of ITIL-168 and up to 8 doses of high-dose IL-2 (figure 1). Patients will receive pembrolizumab at baseline before ITIL-168 infusion, day 21 postinfusion, and then every 6 weeks for ≤48 weeks or until disease progression or intolerable toxicity. An interim and a primary analysis for each cohort will be conducted. The primary endpoint is the frequency and severity of ITIL-168 treatment-emergent adverse events (AEs) per Common Terminology Criteria for AEs version 5.0. Secondary endpoints include manufacturing success rate, objective response rate per modified RECIST v1.1, duration of response, progression-free survival, and overall survival. The study opened in July 2022 and is currently recruiting patients. **Acknowledgements** Medical writing support was provided by Christopher Waldapfel, PharmD, of Instil Bio, Inc. and Lauryn Samelko, PhD, and Phylcia Aaron, PhD, of Nexus Global Group Science, with funding from Instil Bio, Inc.

REFERENCES

1. Nordstrom BL, Hamilton M, Collins JM, *et al.* Treatment patterns and outcomes following disease progression on anti-PD-1 therapies for advanced melanoma. *Future Oncol.* 2022;**18**:1343–1355.
2. Gooden MJ, de Bock GH, Leffers N, Daemen T, Nijman HW. The prognostic influence of tumour-infiltrating lymphocytes in cancer: a systematic review with meta-analysis. *Br J Cancer.* 2011;**105**(1):93–103.
3. van den Berg JH, Heemskerk B, van Rooij N, *et al.* Tumor infiltrating lymphocytes (TIL) therapy in metastatic melanoma: boosting of neoantigen-specific T cell reactivity and long-term follow-up. *J Immunother Cancer.* 2020;**8**:e000848.
4. Borch TH, Andersen R, Ellebaek E, *et al.* Future role for adoptive T-cell therapy in checkpoint inhibitor-resistant metastatic melanoma. *JITC.* 2020;**8**:e000668.
5. Donia M, Kjeldsen JW, Andersen R, *et al.* PD-1+ polyfunctional T cells dominate the periphery after tumor-infiltrating lymphocyte therapy for cancer. *Clin Cancer Res.* 2017;**23**:5779–5788.

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 Council for Harmonisation.



Abstract 781 Figure 1 DELTA-2 Treatment Schema

DELTA-2 is a phase 1 trial evaluating the safety, feasibility, and preliminary efficacy of ITIL-168 in combination with pembrolizumab in patients with select advanced solid tumors with progressive disease during or after 1 prior line of treatment.

*Tumor resection occurs within 30 days after patient consent, followed by optional bridging therapy.

†Baseline visit occurs within 14 days prior to lymphodepleting chemotherapy, followed by pembrolizumab (200 mg).

‡Cohorts 1/3 will receive lymphodepleting chemotherapy on days –7 to –3; Cohort 2 will receive lymphodepleting chemotherapy on days –5 to –3.

§Pembrolizumab is administered once on day 21 (200 mg), followed by every 6 weeks from weeks 6 to 48 (400 mg).

D, day; HD, high-dose; IL-2, interleukin-2; Q6W, every six weeks; W, week.

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