Trial in progress: A phase 1/2 open-label study (IOV-GM1-201) of TALEN-mediated PD-1–inactivated autologous tumor-infiltrating lymphocytes (TIL; IOV-4001) in patients with advanced melanoma and NSCLC

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Background
Adoptive cell therapy using autologous tumor-infiltrating lymphocytes (TIL; lifileucel, LN-145) has demonstrated encouraging efficacy in patients with advanced solid tumors, including melanoma and non-small cell lung cancer (NSCLC). 

• One-time TIL cell therapy achieved durable responses in the post-immune checkpoint inhibitor (ICI) setting in patients with advanced (unresectable or metastatic) melanoma.1,2 With an investigational- drug application approved, 29 of 44 patients (66%) achieved a complete response (CR) and 13 of 44 (30%) achieved a partial response (PR) at 33 months of follow-up.3

• In IOV-4001, PD-1 KO efficiency and efficacy and correlative immune biomarkers were assessed in a 21.4% CR and 30.4% PR after a median of 2.1 years of follow-up, showing high CR and PR rates in patients with advanced melanoma.4

• Among patients with advanced melanoma and NSCLC, 80% of the CR and 36% of the PR were observed in patients with advanced melanoma.5

• IOV-GM1-201 is a programmed cell death protein-1 (PD-1)–inactivated autologous TIL cell therapy product generated from patients with metastatic disease or relapsed disease post-ICI who are being considered for enrollment to phase 2 clinical trials.

• To assess the safety and efficacy of IOV-4001 for treatment of patients with advanced melanoma and NSCLC

Objective

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IOV-GM1-201 Study Overview

Objective

• Phase 1: Confirm safety of IOV-4001 during safety run-in and determine recommended phase 2 dose (RP2D) of IOV-4001

• Phase 2: Assessment of efficacy of IOV-4001 (per RECIST v1.1) as assessed by the investigator using RP2D determined in phase 1

• Phase 3: Validation of efficacy and safety based on standard dose

Study Design and Treatment Regimen

Study Endpoints

• Phase 1: Safety as assessed by DLTs and AEs

• Phase 2: Investigator-assessed ORR per RECIST v1.1

Secondary Endpoints

• CR rate, DOR, DCR, PFS, DFS, safety, tolerability, feasibility

• Exploratory endpoints:

• IOV-4001 persistence, relationship between IOV-4001 persistence and efficacy, relationship between IOV-4001 PD-1 KO efficacy and efficacy and cumulative immune biomarkers

Inclusion Criteria

• Cohort 1: Confirmed histologic or pathologic stage IIIA, IIIB, IIC, or IV unresectable or metastatic melanoma that has progressed during or 512 weeks after last anti-PD-1/L1 therapy

• Patients must have also received a BRAF ± MEK inhibitor and IBA/PD-L1-based monotherapy or pembrolizumab ± nivolumab ± ipilimumab

• Age ≥18 years

• ECOG PS 0-1 and an estimated life expectancy >6 months

• 31-resectable lesion(s) per IOV-4001 generation (≤1.5 cm diameter) and 1 remaining RECIST-measurable lesion

• Carcinoma test function required

• Pulmonary function test may be required

Exclusion Criteria

• Uveal/ocular melanoma

• Symptomatic untreated brain metastases

• Organ alloplasty or primary cell transfer within the past 20 years

• Systemic steroid therapy ≥10 mg/day of prednisone or another steroid equivalent

• Any form of primary immunodeficiency

• No other primary malignancy within prior 3 years

• Any form of primary immunodeficiency

• Prior treatment with immunotherapy or interferon alfa

• Prior treatment with tyrosine kinase inhibitors (TKI) or mTOR inhibitors

• Symptomatic untreated brain metastases

Key Inclusion and Exclusion Criteria

References


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Disclosures

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Ethics Approval

Consent

All patients provided written informed consent.

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