A Phase 1/2 Open-Label Study of IOV-GM1-201 of TALEN®-Mediated PD-1 Inactivated Autologous Tumor-Infiltrating Lymphocytes (TIL; IOV-GM1-401) in Patients with Advanced Melanoma and NSCLC

Objective

Here, we describe the IOV-GM1-201 study investigating IOV-401 for treatment of patients with advanced melanoma and NSCLC.

Study Design and Treatment Regimen

Figure 1. IOV-GM1-201 Manufacturing and Patient Journey

Figure 2. IOV-GM1-201 Study Design

Figure 3. Treatment Schema for Phase 2

Study Endpoints

Primary Endpoints

• Phase 1: Safety as assessed by DLTs and AEs
• Phase 2: Investigator-assessed ORR per RECIST v1.1

Secondary Endpoints

• OR rate, OS, safety, tolerability, feasibility

Exploratory Endpoints

• IOV-401 persistence, relationship between IOV-401 persistence and efficacy, and relationship between IOV-401 persistence and efficacy and correlative immune biomarkers

Inclusion Criteria

• Cohort 1: Confirmed histologic or pathologic stage IIIC, IIID, or IV unresectable or metastatic melanoma that has progressed during or ≤12 weeks after last anti–PD-1/PD-L1 line
– Patients must have also received a BRAF ± MEK inhibitor if V600 mutation-positive
• Cohort 2: Stage III or IV NSCLC with 13 prior lines of therapy and disease progression either:
– DURING or after ≥1 targeted therapy and either platinum-doublet chemotherapy or during or ≤12 weeks after last anti–PD-1/PD-L1 dose
– Patients must have also received a BRAF ± MEK inhibitor if V600 mutation-positive

• Age ≥18 years
• ECOG PS 0-1 and an estimated life expectancy >6 months
• 21–360 kg

• Patients with uveal/ocular melanoma

Exclusion Criteria

• Uveal or choroidal melanoma
• Systemic uncontrolled or unmanaged metastatic disease
• Organ allograft or organ transplant within 2 years
• Systemic antitumor therapy 
• Any form of antipsychotic therapy
• Any other primary malignancy within prior 3 years
• Live or attenuated vaccination within 28 days prior to the start of NMA-LD
• Systemic steroid therapy ≥10 mg/day of prednisone or another steroid equivalent
• Cardiac function test required
• No other primary malignancy within prior 3 years
• Any other primary malignancy within prior 3 years

A process has been established for the generation of TALEN®-mediated PD-1 KO TILs and their expansion by recombinant human interleukin-2 (rhuIL-2) and rhuIL-15. Immune cells are collected and processed as part of the manufacturing process resulting in genetically modified TIL cell therapies, such as IOV-401, where this technology may allow for PD-1 KO efficiency and efficacy and correlative immune biomarkers.

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AUTHOR CONTRIBUTIONS


ABSTRACTS

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