A phase 1/2 study to evaluate the safety and efficacy of intratumoral injection of the TLR9 agonist tilsotolimod (IMO-2125) in combination with PD-1 inhibitor refractory metastatic melanoma

METHODS

A single-phase 1/2 study to evaluate the safety and efficacy of intratumoral injection of tilsotolimod (IMO-2125) in combination with anti-PD-1 therapy in patients with advanced melanoma with a confirmed PD-L1 of at least 5%.

Patients who have received at least one prior systemic therapy for metastatic melanoma and are refractory to at least one PD-1 inhibitor and/or ipilimumab are eligible.

Primary Objective

To evaluate the overall survival of patients in combination with tilsotolimod plus ipilimumab compared to historical data for PD-1 refractory melanoma.

Secondary Objectives

- Assess the safety and tolerability of tilsotolimod plus ipilimumab.
- Evaluate the efficacy of tilsotolimod plus ipilimumab in terms of objective response rate and disease control rate.
- Assess the pharmacokinetics and pharmacodynamics of tilsotolimod and ipilimumab.

RESULTS

- 21 patients were enrolled and received at least one dose of tilsotolimod plus ipilimumab.
- 3 patients did not complete the study due to adverse events (AEs).
- 5 patients had grade 4 AEs (related to study drug).
- 1 subject has an ongoing complete response of 23 months duration.
- 1 subject has an ongoing partial response of 12 months duration.
- 1 subject had grade 3 AEs (related to study drug).
- 1 subject had grade 4 AEs (related to study drug).

CONCLUSIONS

- Tilsotolimod plus ipilimumab appears to be safe and well tolerated in patients with PD-1 refractory melanoma.
- Significant anti-tumor activity was observed, with 71.4% of patients experiencing disease control (CR, PR, or SD).
- The combination of tilsotolimod plus ipilimumab demonstrated a promising clinical benefit in terms of overall survival and disease control.

Abbreviations: 5FU, 5-fluorouracil; ALT, alanine transaminase; AST, aspartate transaminase; BM, brain metastases; PD-L1, programmed death-ligand 1; PD-1, programmed death-1; RECIST, Response Evaluation Criteria In Solid Tumors; SD, stable disease; TILs, tumor-infiltrating lymphocytes; TNM, tumor-node-metastasis; VEGF, vascular endothelial growth factor.

Data cut-off date: 9 May 2018.

ILUMINATE-204 Responders: 19 (88.5%) had confirmed partial response (PR), 2 (9.5%) had unconfirmed partial response (uPR), and 0 (0%) had unconfirmed complete response (uCR).