The safety and efficacy of intratumoral injection of the TLR9 agonist tilsotolimod (IMO-2125) in combination with ipilimumab in patients with PD-1 inhibitor refractory metastatic melanoma: An analysis of efficacy in injected and uninjected lesions

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BACKGROUND

Thrombosis (IPD-2125) is a class IIb/III indicated by the National Comprehensive Cancer Network (NCCN) guidelines, although the specific mechanism of action remains unclear. The results of the study will help elucidate potential differences in the efficacy and safety of different therapeutic doses and modalities with a subsequent proliferation of targeted immune responses. In a Phase 1/2 study in both injected and uninjected tumors, multimodal tumor cell death was observed.

There is a high proportion of treated melanoma patients who progress after PD-1 inhibition, as treatment options are limited.

- Immunohistology shows that only a modest benefit (15%–20% objective response rate (ORR) of PD-L1).
- Current data suggest that the ipilimumab plus nivolumab combination is promising. These results support the design of a randomized phase III trial study Illuminate-204, which was an unblinded, multicenter, global study of patients with metastatic melanoma who received one or more doses of tilsotolimod 8 mg plus ipilimumab in combination with nivolumab. The primary outcomes were the disease control rate (CR, uCR, or PR) and the overall response rate (CR, uCR, or PR) in injected and uninjected tumors, resulting in tumor cell death.

METHODS

The study was a single-arm, multicenter, open-label, global study of patients with metastatic melanoma who received one or more doses of tilsotolimod 8 mg plus ipilimumab in combination with nivolumab. The primary outcomes were the disease control rate (CR, uCR, or PR) and the overall response rate (CR, uCR, or PR) in injected and uninjected tumors, resulting in tumor cell death.

RESULTS

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HAYMAKER C. TLR9 agonist harnesses innate immunity to drive tumor-regression in injected and uninjected tumors

1. Efficacy in Uninjected Lesions
   - Complete response (CR): 4 (38%)
   - Partial response (PR): 3 (29%)
   - Stable disease (SD): 1 (5%)
   - Progression of disease (PD): 0 (0.0%)

2. Response Evaluation Criteria in Solid Tumors (RECIST v1.1)
   - Tumor regression in injected tumors
   - Tumor shrinkage in uninjected tumors

The results of this study suggest that tilsotolimod plus ipilimumab is a promising treatment option for patients with PD-1 inhibitor refractory metastatic melanoma. These data support the design of a randomized phase III trial to further explore the potential benefits of this combination.

CONCLUSIONS

Thrombosis (IPD-2125) is an associated clinical risk factor in thrombosis and a Class IIb/III indicated by the National Comprehensive Cancer Network (NCCN) guidelines, although the specific mechanism of action remains unclear. The results of this study will help elucidate potential differences in the efficacy and safety of different therapeutic doses and modalities with a subsequent proliferation of targeted immune responses.

Efficacy was observed in injected and uninjected distant lesions, demonstrating an overall effect.

This combination treatment has produced durable responses and demonstrates clinical efficacy in both injected (favoring) and uninjected distant lesions in a Phase 1/2 study, suggesting that tilsotolimod plus ipilimumab in combination with anti-PD-1 inhibition represents a promising treatment option.