Interim Results of a Phase 1b/2 Study of PV-10 and PD-1 Blockade in Advanced Melanoma

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Updated Abstract and Background

PV-10 (rose bengal disodium) is a small molecule oncolytic immunotherapy in development for solid tumors, where intratrabecular injection can yield immunogenic cell death and tumor-specific reactivity in circulating T cells [1-4]. It has been administered as a single agent to 130 cutaneous melanoma patients in Phase 2 and 180 patients in expanded access, and is in Phase 3 for locally advanced cutaneous melanoma (Stage IIIb-IV, M1a, NCT02288897 [5-8]).

Study PV-10-MM-1201 (NCT02557321) is a Phase 1b/2 study of PV-10 in combination with anti-PD-1 (pembrolizumab) for patients with advanced melanoma (Stage IIIIC-M1c). Patients must have at least 1 injectable lesion and be candidates for pembrolizumab. In Phase Ia/b patients receive combination treatment q2w for 5 cycles then pembrolizumab alone for up to 24 months; the primary endpoint is safety and tolerability with objective response rate (ORR) and progression free survival as key secondary endpoints (as assessed via RECIST 1.1 after 5 cycles then q12w).

Full accrual for Phase 1b was reached in April 2018, with an intent-to-treat (ITT) population of 20 Stage IV and 3 Stage IIC/IIID patients (median age 70 years, range 28-90) receiving at least 1 dose of PV-10 and pembrolizumab. All Treatment-Emergent Adverse Events (TEAEs) were consistent with established patterns for both drugs, with no significant overlap of AEs or unexpected toxicities; Grade 1-2 AEs attributed to the combination were observed in 6 patients. Most patients had extensive uninfected tumor burden, and complete response (CR) was observed in non-injected visceral disease, including lung and liver metastases. Interim efficacy data were positive, with 65% ORR and 9% CR by RECIST.

Acceptable safety and tolerability of the combination were observed with no unexpected safety effects. Response follow-up is ongoing for a substantial fraction of the ITT population. An Expansion Cohort is being opened to assess patients with prior checkpoint inhibition.


Phases 1b Study Participants

Interim Study Overview and Interim Data

Interim Safety Results

Interim Efficacy Results

Small Molecule Oncolytic Immunotherapy

Primary Oncolysis

Intratumoral Injection

Lymphoid Accumulation

Secondary Adaptive Immunity

Immunogenic Cell Death (ICD)

Functional T cell activation

DAMP and Antigen

Release

APC Recruitment

Antigen Uptake

Conclusion

- Functional T cell activation and peripheral blood of Melanoma Patients [2]
- Immunologic Priming of PV-10-Complementary to Checkpoint Inhibition in Murine Melanoma Models [4]

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