Phase 1b Study of PV-10 and anti-PD-1 in Advanced Cutaneous Melanoma

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Background
PV-10 is a liposomal anesthetic microemulsion that is approved for the treatment of pain associated with a variety of indications. Its mechanism of action is thought to involve multiple pathways, including the release of immunosuppressive pro-inflammatory cytokines, the inhibition of leukocyte migration, and the recruitment and activation of NK cells.

PV-10 has been administered as a single agent to over 300 cutaneous melanoma patients (pts) in Phase 1b studies and under required access (UOA). We aim to study immunological monitoring of percutaneous administration to improve understanding of clinical behavior and possible mechanisms of action (MoAs) such as immunological responses.

Methods
Study PV-10-MB-183 (NCT02075477) is a Phase 3b study of PV-10 in combination with anti-PD-1. The study is a randomized multi-center trial with a total of 240 evaluable patients with advanced cutaneous melanoma (M1a-M1c). Patients must have at least 1 symptomatic lesion and be candidates for surgical debulking. In Phase 1b studies, the combination treatment was given 4x 1 cycle then percutaneous administration up to 4 months. The primary endpoint is safety and tolerability with an interim response rate (RR) and progression-free survival (PFS) key secondary endpoints by RECIST 1.1 after 1 cycle then 4 cycles.

The study was single-center and included 2 cohorts:

Cohort 1: Up to 24 checkpoint-naive patients
Cohort 2: Up to 24 chemotherapy-naive patients

All patients included in the Cohort 1 were treated with anti-PD-1 therapy with PV-10. Cohort 2 patients received a single cycle of PV-10 followed by anti-PD-1 therapy.

In the current study, we aimed to investigate the immunological effects of PV-10 in combination with anti-PD-1 in patients with advanced cutaneous melanoma.

Results
The immunological effects of PV-10 in combination with anti-PD-1 were studied in the current study. We observed a significant increase in the production of pro-inflammatory cytokines, such as IL-1β, IL-6, and TNF-α, in the peripheral blood mononuclear cells (PBMCs) of patients treated with PV-10. Moreover, we observed a significant increase in the proportion of CD8+ T cells and a decrease in the proportion of regulatory T cells (Tregs) in the PBMCs of patients treated with PV-10.

Conclusions
These findings suggest that PV-10 may have a therapeutic effect in combination with anti-PD-1 in patients with advanced cutaneous melanoma. Further studies are needed to investigate the mechanisms of action of this combination therapy.