Background

Rose bengal disodium (PV) is a small molecule oncolytic immunotherapy in clinical development for treatment of solid tumors. When administered by intratumoral injection, PV-10 can produce an immunogenic cell death that may induce a T-cell mediated immune response against treatment-refractory and immunologically cold tumors.1-8 It has been administered as a single agent to over 300 patients with cutaneous melanomas9 and is currently under investigation in combination with anti-PD-1.10 Given this mechanism of action, we investigated treatment of metastatic uveal melanomas with percutaneous, PV-10 directed antitumor therapy.

Methods

We conducted an open-label Phase 1b study evaluating the safety, tolerability, and efficacy of intratumoral PV-10 as a cohort of patients with uveal melanomas metastatic to the liver (NCT01686681). Percutaneous injections of PV-10 are administered to one or more designated hepatic tumors with a maximum diameters ≤4 cm and a maximum volume of 15 mL. Response assessments using 2D EASL criteria are performed at Day 28, then every 3 months. Patients with additional injectable tumors may receive further PV-10 after Day 28. Eligible patients may receive standard of care check point blockade immunotherapy during treatment with PV-10. European Association of the Study of the Liver (EASL) guidelines were developed in 2015 and recommend measuring only enhancing tissue in the tumor.11 EASL response is an early predictor of necrosis at 1-2 months. There were few reports using EASL tumor response assessment on patients with metastatic melanoma to the liver.12

Results

To date, 13 uveal melanoma patients received treatment with intratumoral PV-10 for the liver: 6 patients received a second cycle of PV-10; in total, 26 tumors were injected.

- 9 patients received concomitant standard of care checkpoint blockade
  - 1 patient entered study on maintenance anti-PD-1.
  - 5 patients entered study within 4 weeks of first dose of PV-10.
  - 7 patients received combination checkpoint blockade after first dose of PV-10.

- Tumor assessments available on 22 injected target lesions:
  - 7 tumors with partial response (32%)
  - 11 tumors with stable disease (50%)
  - 4 tumors with progression of disease (18%)

- Adverse events (AEs) of note were 3 cases of Grade 3-4 transaminase that resolved to Grade 1 or better within 72 hours (10%)
  - Grade 1-2 related events seen in 1 patient each include: pink stool, pink urines, photosensitivity, injection site pain, and hypothyroidism.

- Additional AEs such as nausea, headaches, myalgia, blurry vision, decreased WBC, and fatigue were attributed to concomitant checkpoint blockade.

Conclusions

- PV-10 is an image-guided percutaneous injection of hepatic metastases in uveal melanoma is well-tolerated.
- Alternate needle selection may overcome high intra-tumoral pressure and extravasation to obtain optimal drug delivery.
- PV-10 in combination with checkpoint inhibitors demonstrates no additional safety signals.
- Partial responses (32%) and stable disease (50%) have been seen in injected tumors.
- Further follow-up is needed to calculate survival benefit with this approach.

References

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A phase 1 study of percutaneous oncolytic rose bengal disodium for metastatic uveal melanoma patients with hepatic metastases – a single-center cohort summary (#124P)

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