

# Percutaneous Oncolytic Rose Bengal Disodium for Metastatic Uveal Melanoma Patients with Hepatic Metastases

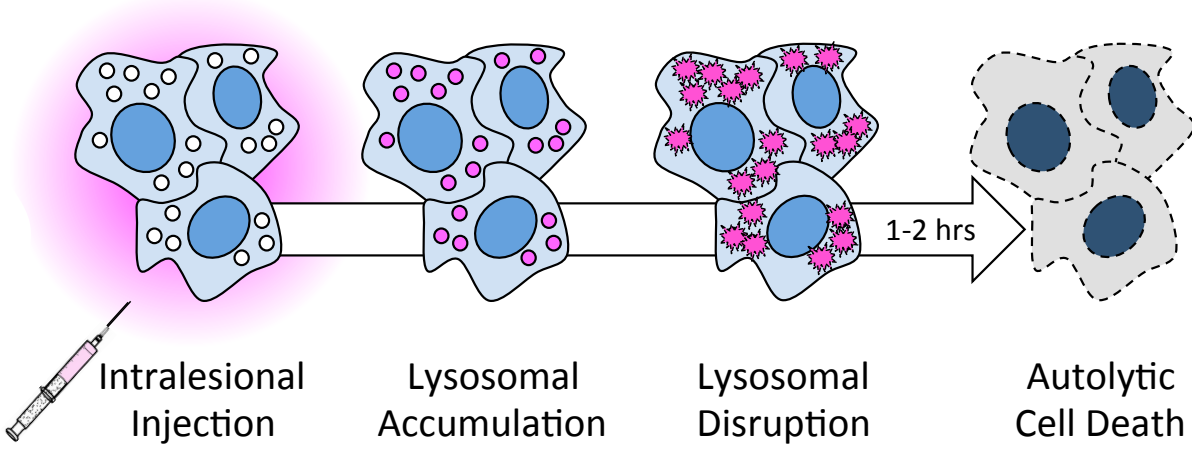
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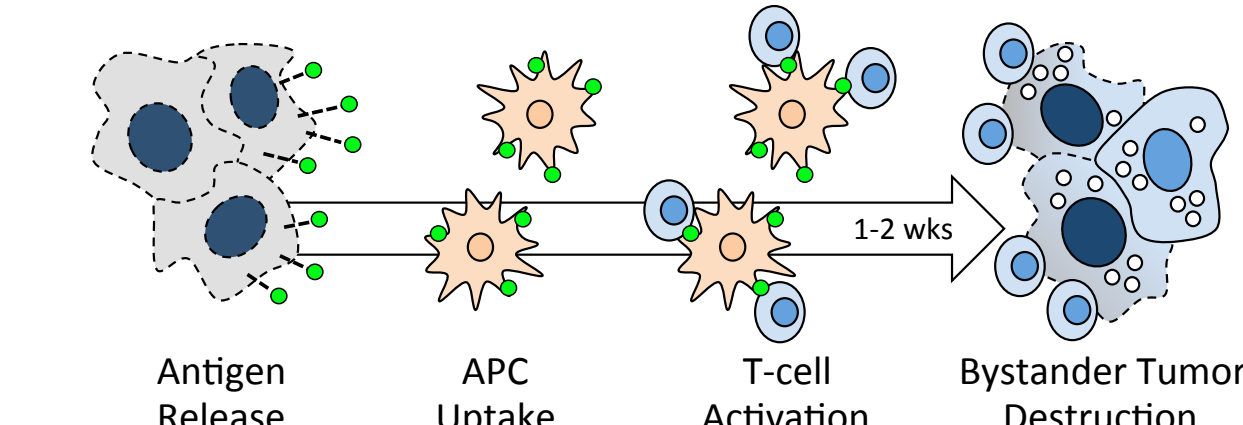
## Abstract

Rose bengal disodium (PV-10) is a small molecule oncolytic immunotherapy in clinical development for treatment of solid tumors. When administered by intralesional 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.

### Primary Ablative Mechanism



### Secondary Immunomodulatory Mechanism



PV-10-LC-01 (NCT00986661) is an open-label Phase 1 study evaluating the safety, tolerability, and preliminary efficacy of intralesional PV-10 in patients with solid tumors metastatic to the liver. A single percutaneous injection of PV-10 is administered to a designated hepatic tumor 1.0-4.9 cm in diameter. Response assessments are performed at Day 28, then every 3 months. Patients with multiple injectable tumors may receive further PV-10 after Day 28. Here we describe the experience of PV-10 in a single-center cohort of uveal melanoma patients. Eligible patients could receive standard of care checkpoint blockade immunotherapy during treatment with PV-10.

## Patient Demographics.

Table 1

| Category               | N (%)         |
|------------------------|---------------|
| Patients treated       | 4 (100)       |
| Age                    | 62.5 (median) |
| Gender                 | Female (100)  |
| Baseline LDH           |               |
| Normal                 | 3 (75)        |
| Elevated               | 1 (25)        |
| Largest tumor diameter |               |
| <3 cm (M1a)            | 3 (75)        |
| 3-8 cm (M1b)           | 1 (25)        |
| >8 cm (M1c)            | 0             |
| Prior lines tx         |               |
| 0                      | 3 (75)        |
| 1                      | 1             |
| Prior tx               |               |
| Immunotx               | 1 (100)       |
| Liver directed         | 0             |

## Subjects

Figure 1A

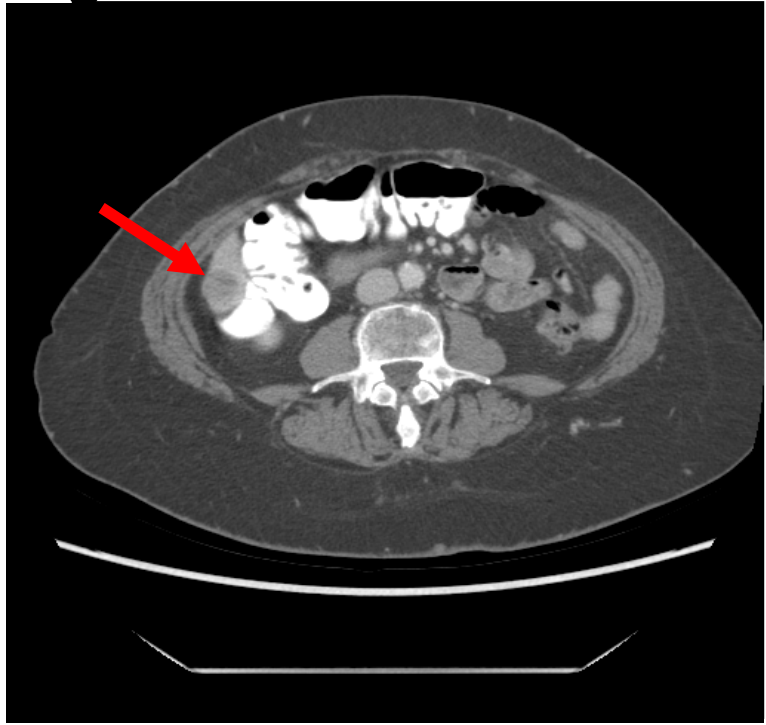


Figure 1B

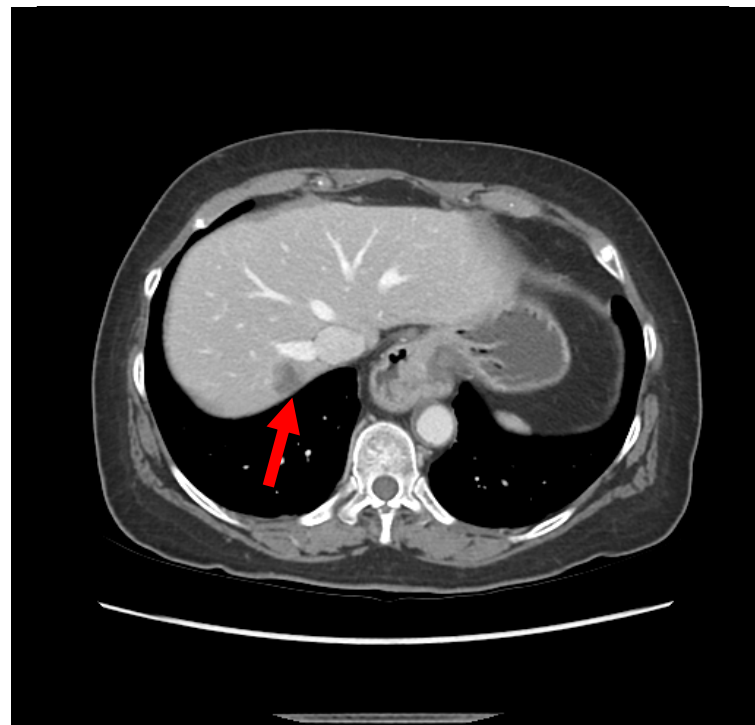
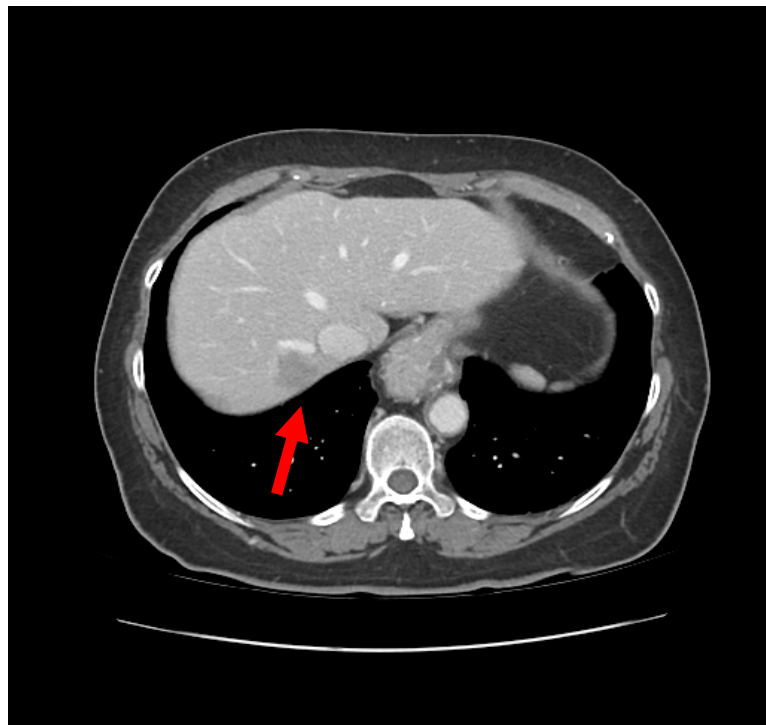
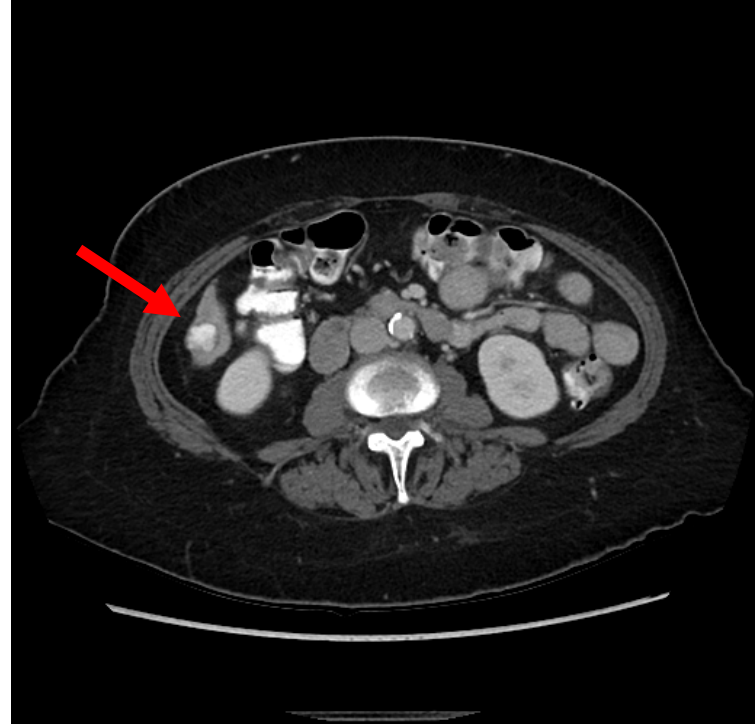


Figure 1C

Figure 1D

**Fig. 1A** Subject 1 pre-treatment and **Fig. 1B** post-treatment in the inferior right hepatic lobe exhibiting PV-10 with radio-opaque persistence at 30 days post-treatment. A second hepatic lesion pre-treatment (**Fig. 1C**) and post-treatment (**Fig. 1D**) with reduction in tumor dimensions, but less retention of PV-10 at 30 days. Red arrows denote location of tumors.

Figure 2A

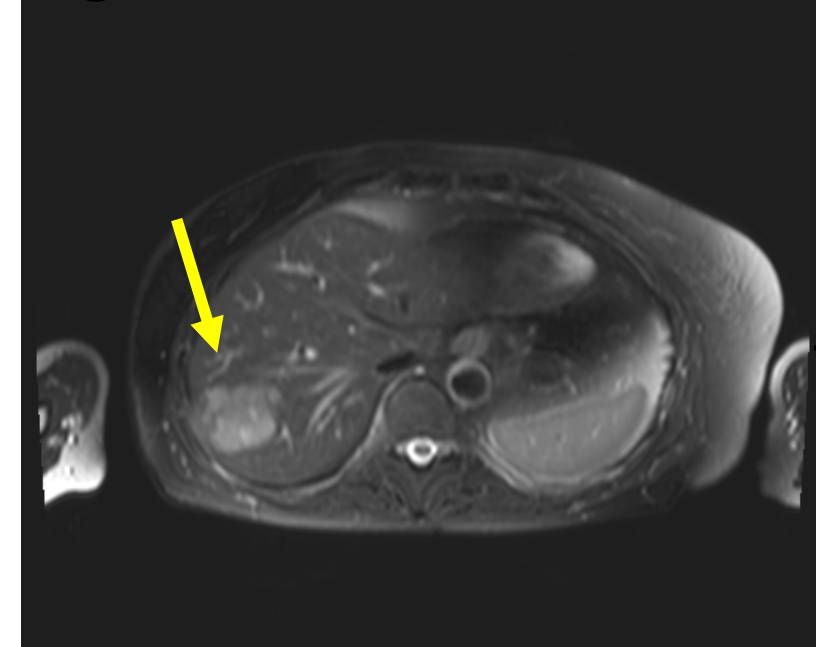
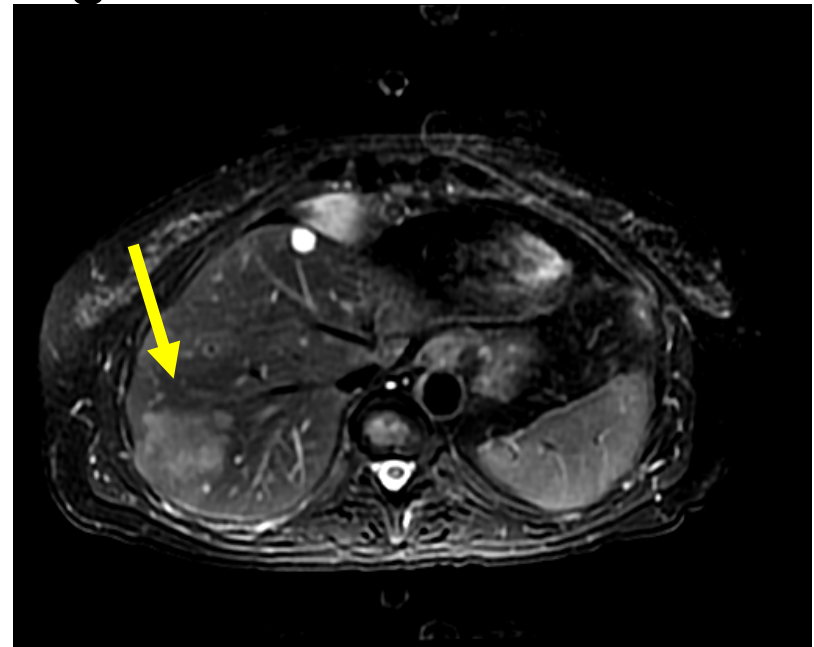


Figure 2B



**Fig. 2A** Subject 2 liver with T2 weighted MRI demonstrating 3.6 cm tumor in right hepatic lobe pre-treatment (yellow arrow). **Fig. 2B** 30-days post-treatment PV-10 imaging via MRI of liver tumor (yellow arrow).

Figure 3A



Figure 3B

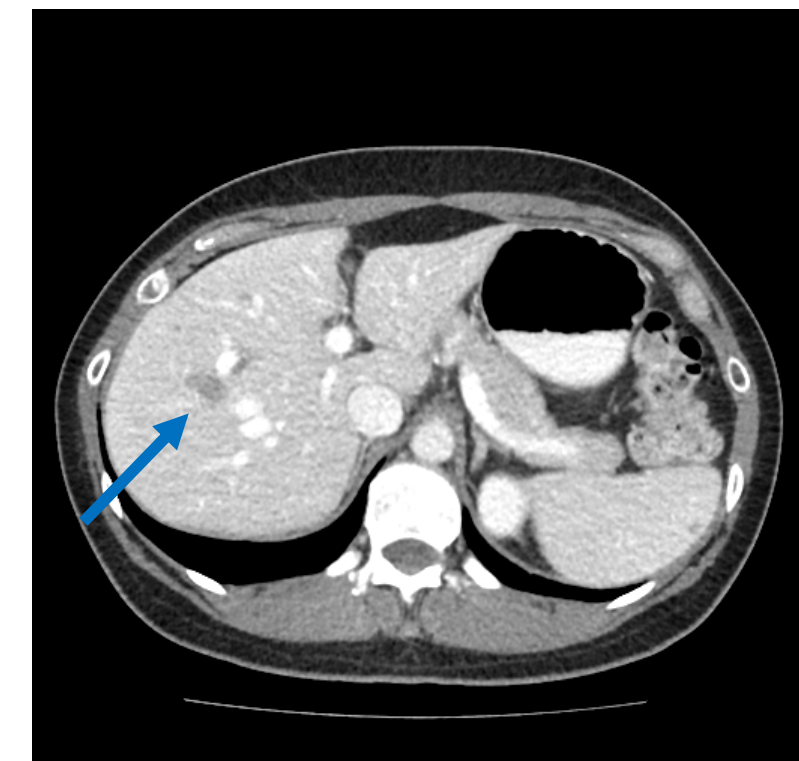
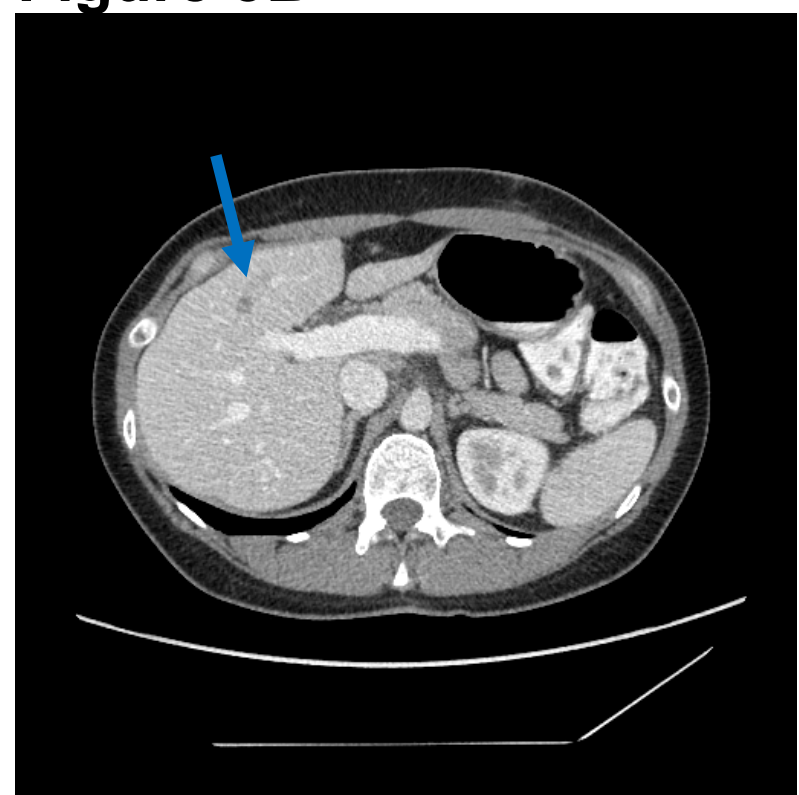


Figure 3C

Figure 3D

**Fig. 3A** Subject 3 pre-treatment and 30-days post-treatment (**Fig. 3B**) with PV-10. After the first intratumoral injection, the subject began nivolumab plus ipilimumab immunotherapy then had a second lesion (**Fig. 3C**, blue arrow) treated with PV-10. **Fig. 3D** denotes 30-day post-treatment imaging (blue arrow).

Figure 4A



Figure 4B



**Fig. 4A** A solitary uveal melanoma liver metastasis pre-treatment (green arrow) and **Fig. 4B** 30-days post-treatment (green arrow) with intratumoral PV-10. An area of central necrosis has developed.

## Adverse Events

Table 2

| Related Adverse Events of interest occurring within 7 days of PV-10 |            |         |         |
|---|------------|---------|---------|
| Category  | All Grades | Grade 3 | Grade 4 |
| AST   | 3 (75)     | 1 (25)  | 0       |
| ALT   | 0          | 1 (25)  | 0       |
| Bilirubin   | 1 (25)     | 0       | 0       |
| Pink urine  | 1 (25)     | 0       | 0       |
| Photosens   | 1 (25)     | 0       | 0       |
| Pain  | 2 (50)     | 0       | 0       |

## Results

- 4 patients have been treated with PV-10 to a single uveal melanoma metastasis in the liver
- 2 patients have undergone a second round of PV-10 to an additional liver tumor
- 1 patient initiated standard of care IO in between rounds of PV-10 (**Fig 3**)
- Tumor reduction has been seen in 5 of 6 injected tumors (all M1a tumors)
- Treatment-related adverse events were predominantly mild and resolved within the first 7 days
- Only 1 patient required hospitalization beyond the observation period for Gr 3 ALT/AST, which resolved to Grade 1 at 7 days post-treatment

## Conclusion

- To date, percutaneous hepatic injection of PV-10 is well-tolerated in uveal melanoma patients
- PV-10 combined with IO is also well-tolerated in this population
- Further evaluation delineating characteristics of responders is underway
- Enrollment is ongoing with up to 10 uveal melanoma patients planned

## Acknowledgements

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