Metabolic complete responses (mCR) in metastatic uveal melanoma (MUM) patients treated with image-guided injection of PV-10

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Disclosures

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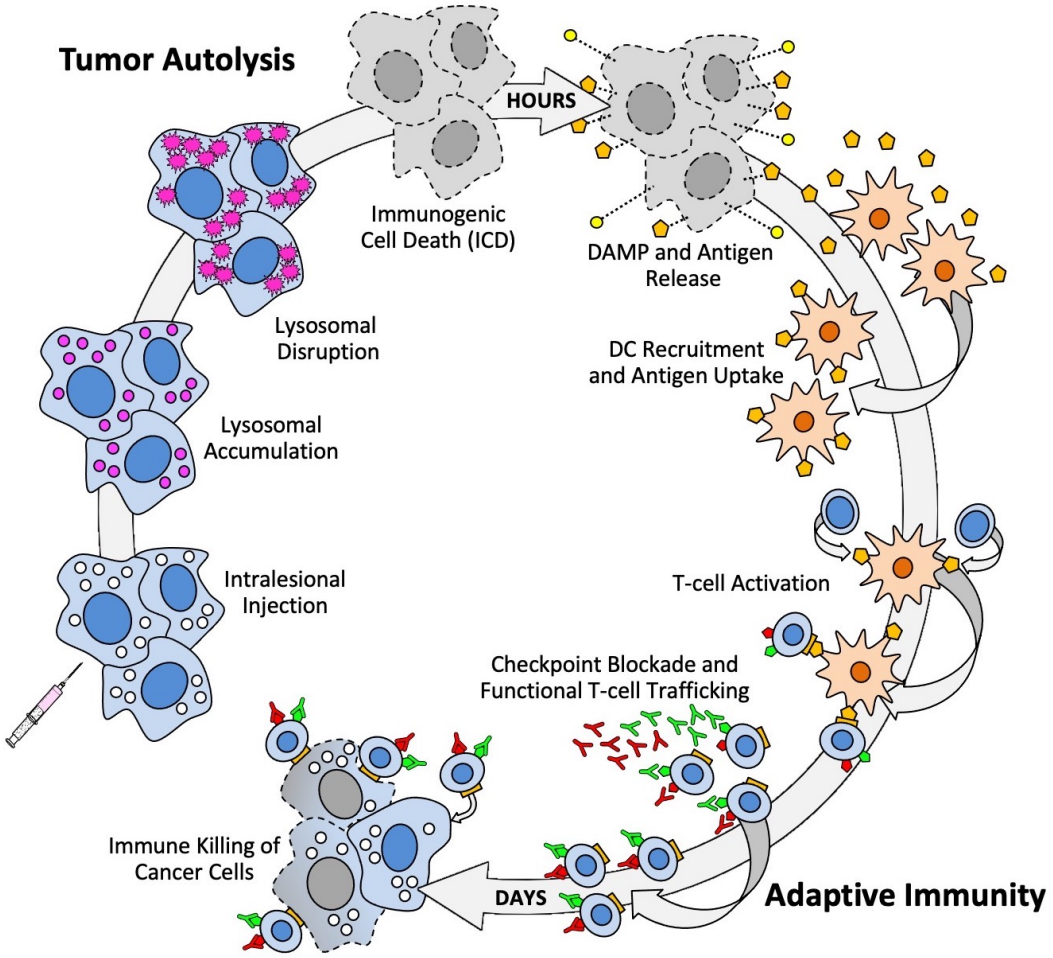
Background



- Injection of PV-10 into tumor tissue initiates tumor autolysis
  - Rapid accumulation of PV-10 in tumor lysosomes triggers lysosomal disruption and immunogenic cell death (ICD)
- ICD causes the release of damage-associated molecular pattern (DAMP) molecules (DAMPs), cytokines, and tumor antigens, leading to dendritic cell (DC) recruitment and antigen uptake
- Presentation of these antigens serves to educate and activate T cells, leading to maturation into functional T cells: primarily CD8 cytotoxic T cells, and also CD4 and NKT cells
- T cell function against tumor can be further augmented by addition of immune checkpoint blockade

Seminal references to date

(1) Wachter et al. Functional Imaging of Photosensitizers using Multiphoton Microscopy. Proceedings of SPIE 4620, 143, 2002.

(2) Liu et al. Intralesional rose bengal in melanoma elicits tumor immunity via activation of dendritic cells by the release of high mobility group box 1. Oncotarget 7, 37893, 2016.

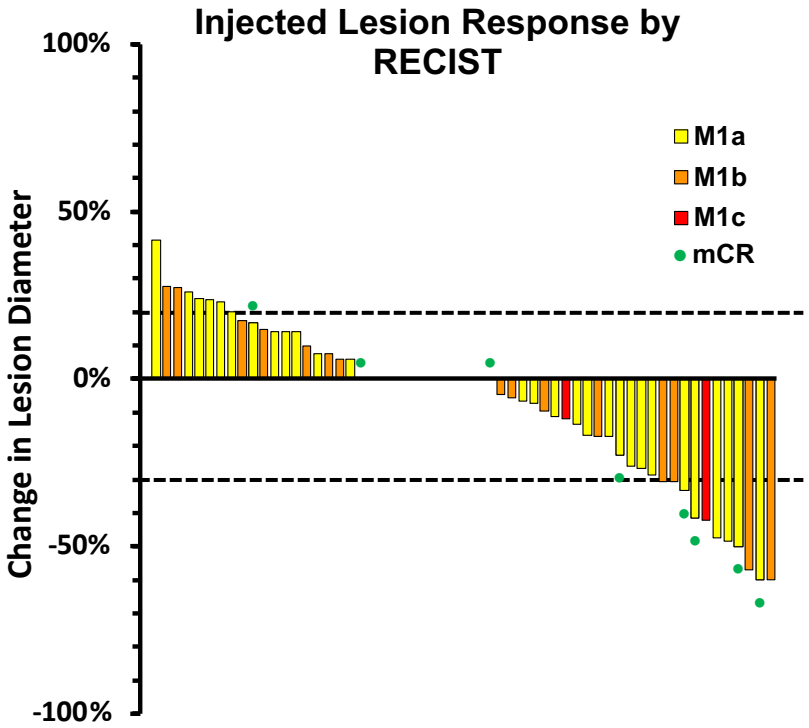
(3) Qin et al. Colon cancer cell treatment with rose bengal generates a protective immune response via immunogenic cell death. Cell Death and Disease 8, e2584, 2017.

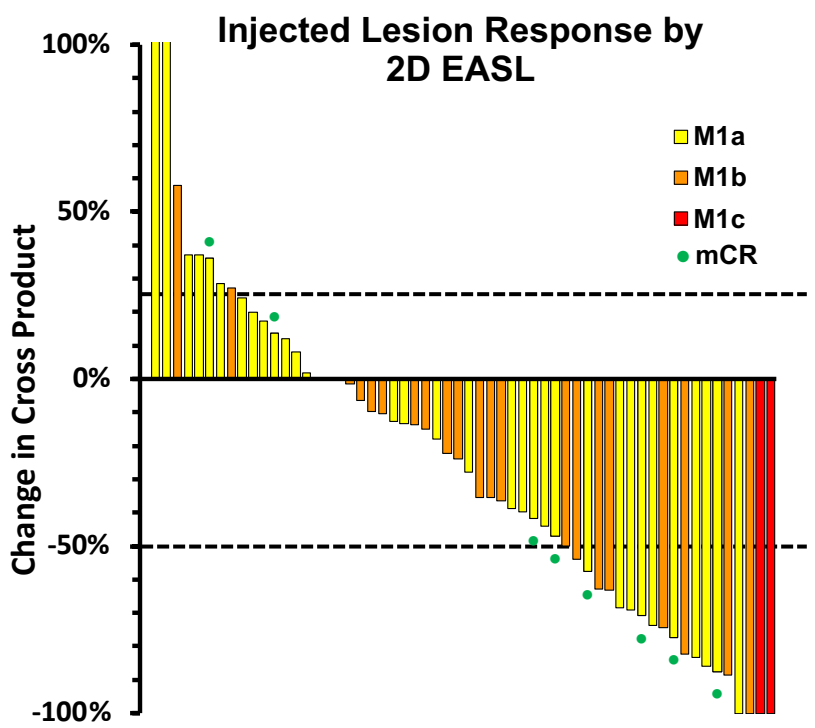
(4) Liu et al. T cell mediated immunity after combination therapy with intralesional PV-10 and blockade of the PD-1/PD-L1 pathway in a murine melanoma model. PLoS One 13, e0196033, 2018.

Patient Characteristics

Category	All Patients (N)	PET-CT (N)	mCR (N)
No. Patients	23	9	4
Age, median (range)	64 (32–80)	66 (51–72)	68 (56–70)
Gender			
Male	12	3	2
Female	11	6	2
M-category			
M1a (largest diameter ≤ 3.0 cm)	14	6	4
M1b (largest diameter 3.1–8.0 cm)	8	3	0
M1c (largest diameter ≥ 8.1 cm)	1	0	0
Sites of metastatic disease			
Hepatic only	12	3	2
Hepatic + extra-hepatic	11	6	2
Prior lines of therapy			
0	10	3	2
1	11	4	1
2+	2	2	2
Prior treatment			
Immunotherapy	12	5	2
Study treatment			
PV-10 only	6	2	1
PV-10 + PD-1	6	2	0
PV-10 + PD-1 + CTLA-4	11	5	3
PV-10 treatment cycles, median (range)	2.0 (1–6)	2.0 (1–3)	1.5 (1–3)
Lesions injected, median (range)	2.0 (1–11)	2.0 (1–6)	2.0 (1–3)

Best Response of Injected Lesions



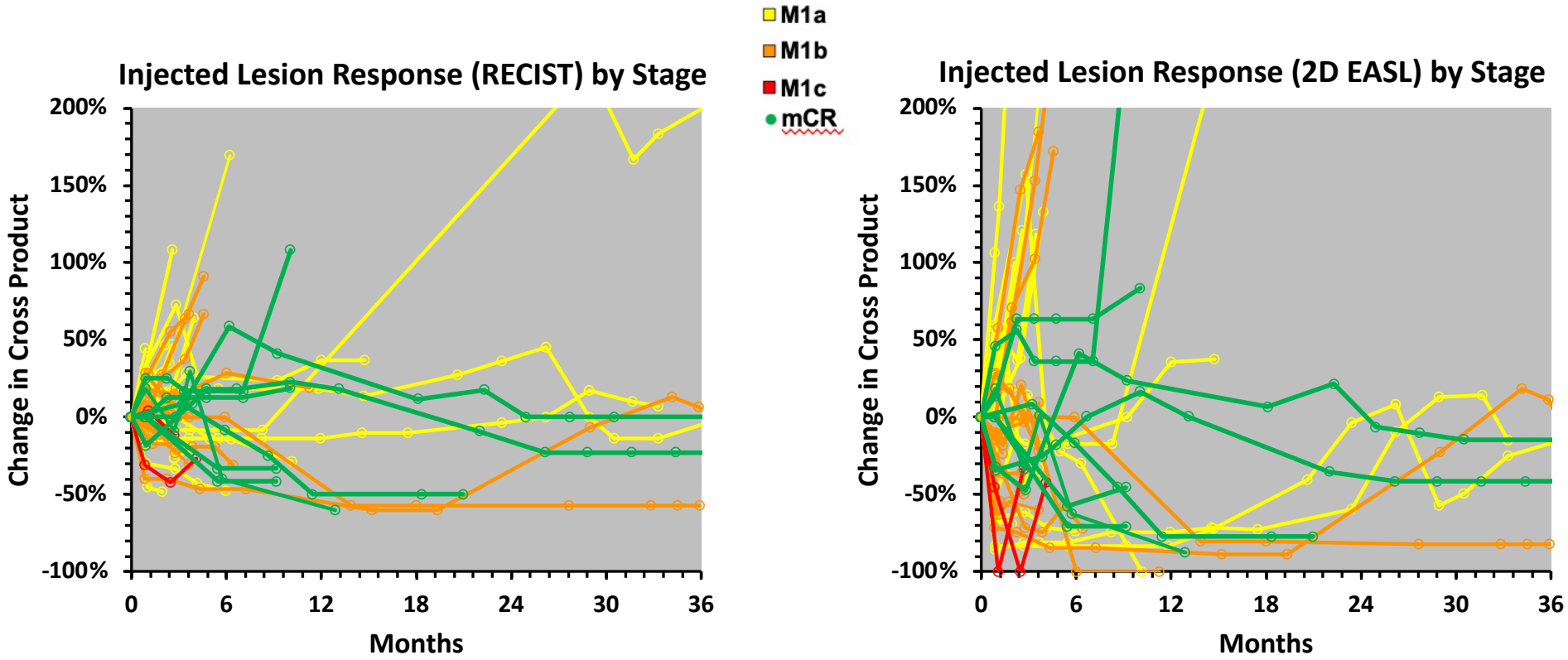


Best Overall Response (Injected Lesions)	RECIST	2D EASL
No. Lesions Evaluated	59	58*
Objective responses	11 (19%)	20 (34%)
Complete response	0 (0%)	4 (7%)
Partial response	11 (19%)	16 (28%)
Stable disease	39 (66%)	30 (52%)
Progressive disease	9 (15%)	8 (14%)

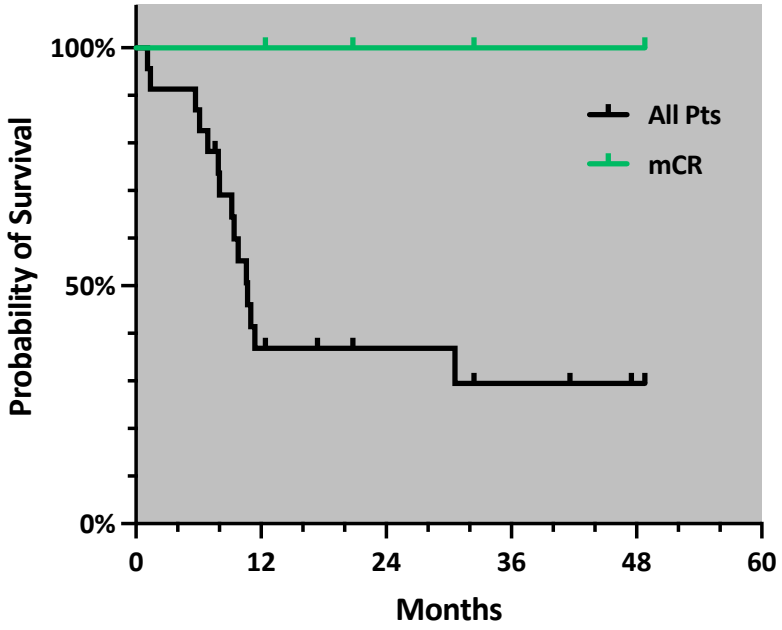
* One lesion not evaluable by 2D EASL (baseline cross product of zero).

- Metabolic complete responses (mCR) on PETCT in 8 of 59 tumors

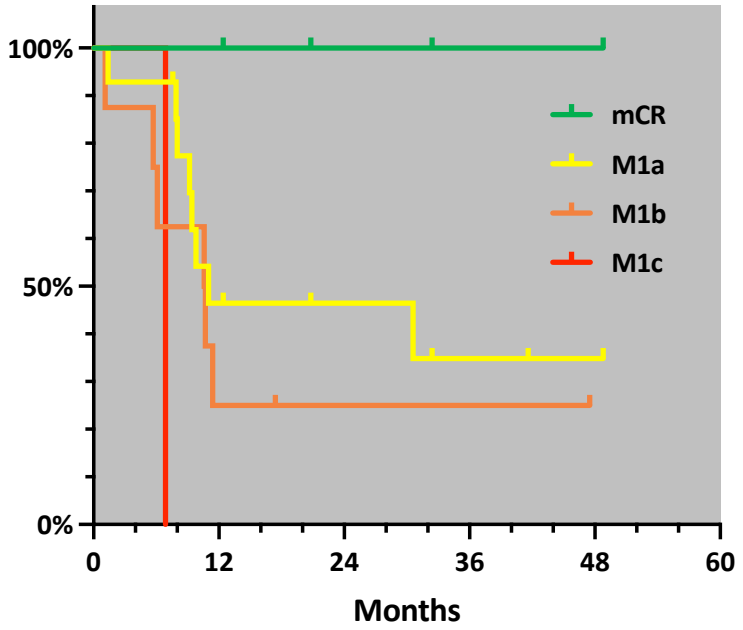
Temporal Response of Injected Lesions



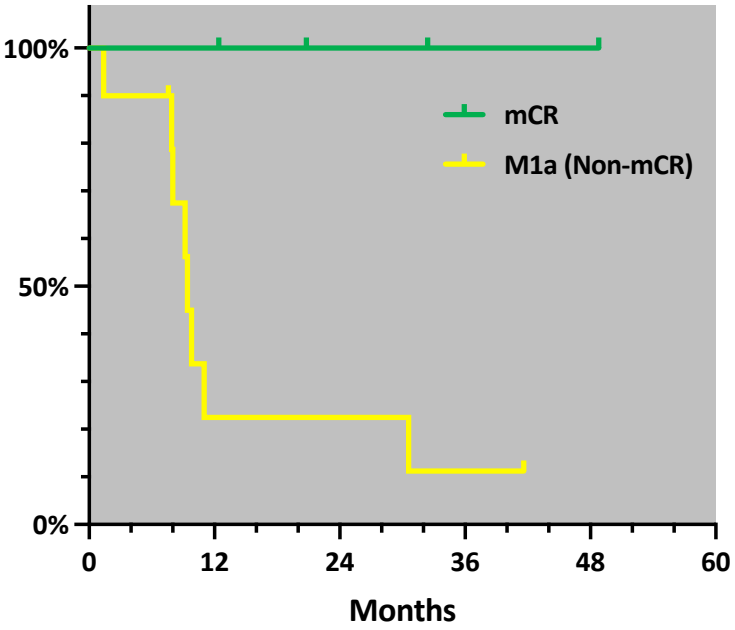
Overall Survival from Initiation of PV-10



- mOS = 10.7 months (All pts)
- mOS not reached (mCR pts)



- mOS = 11.0 months (M1a pts)
- mOS = 10.7 months (M1b pts)
- mOS = 6.9 months (M1c pts)
- mOS not reached (mCR pts)



- mOS = 9.4 months (M1a, Non-mCR)
- mOS not reached (mCR pts)

Conclusions

- PV-10 can induce mCR in both injected (adscopal) and non-injected (abscopal)
- CT may underestimate the effect of PV-10 in injected tumors
- 2D EASL is more sensitive than RECIST to changes in injected lesions
- PET-CT may be a useful tool for assessing response in metastatic uveal melanoma patients*

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