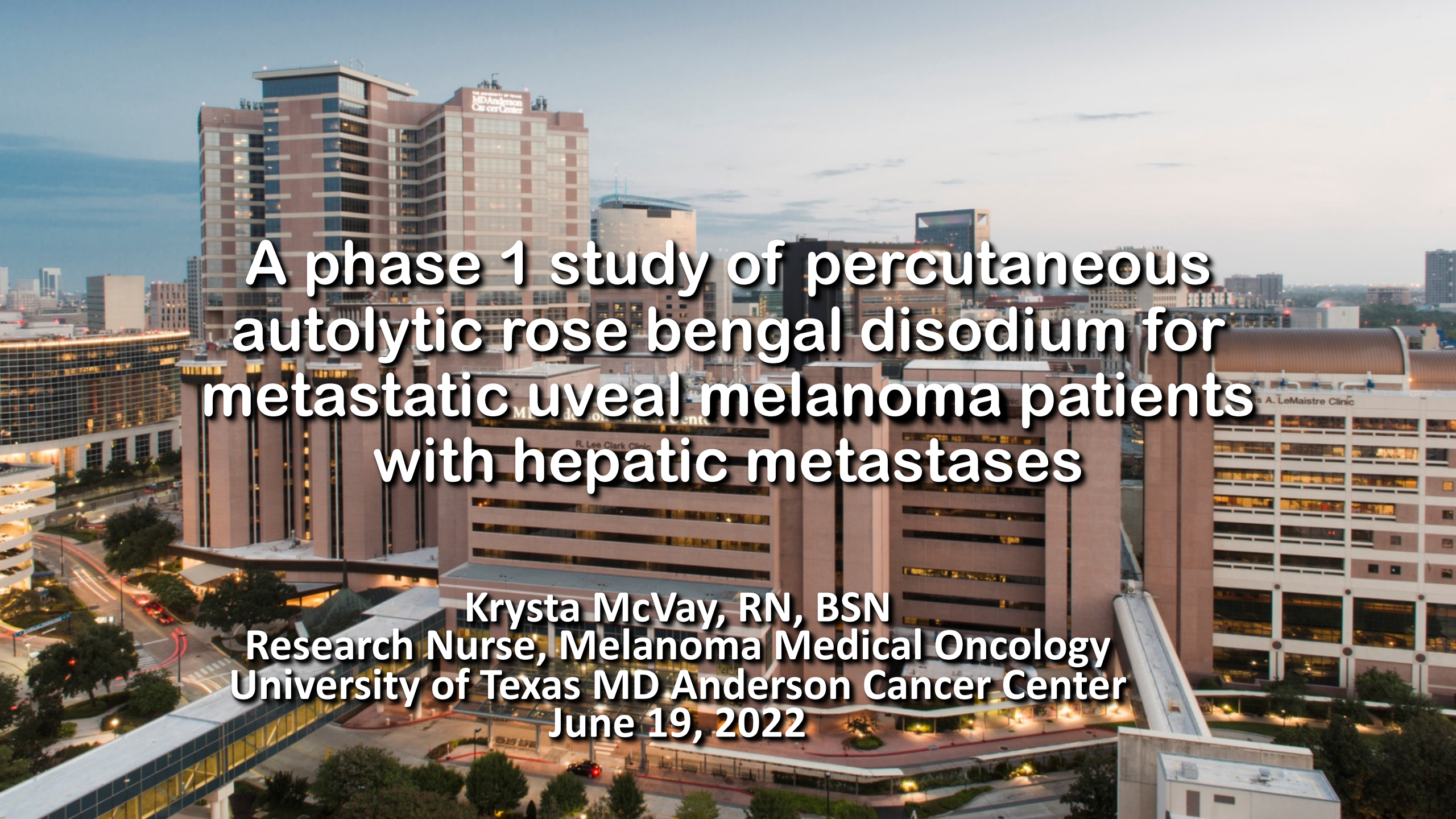

A phase 1 study of percutaneous autolytic rose bengal disodium for metastatic uveal melanoma patients with hepatic metastases

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Disclosures

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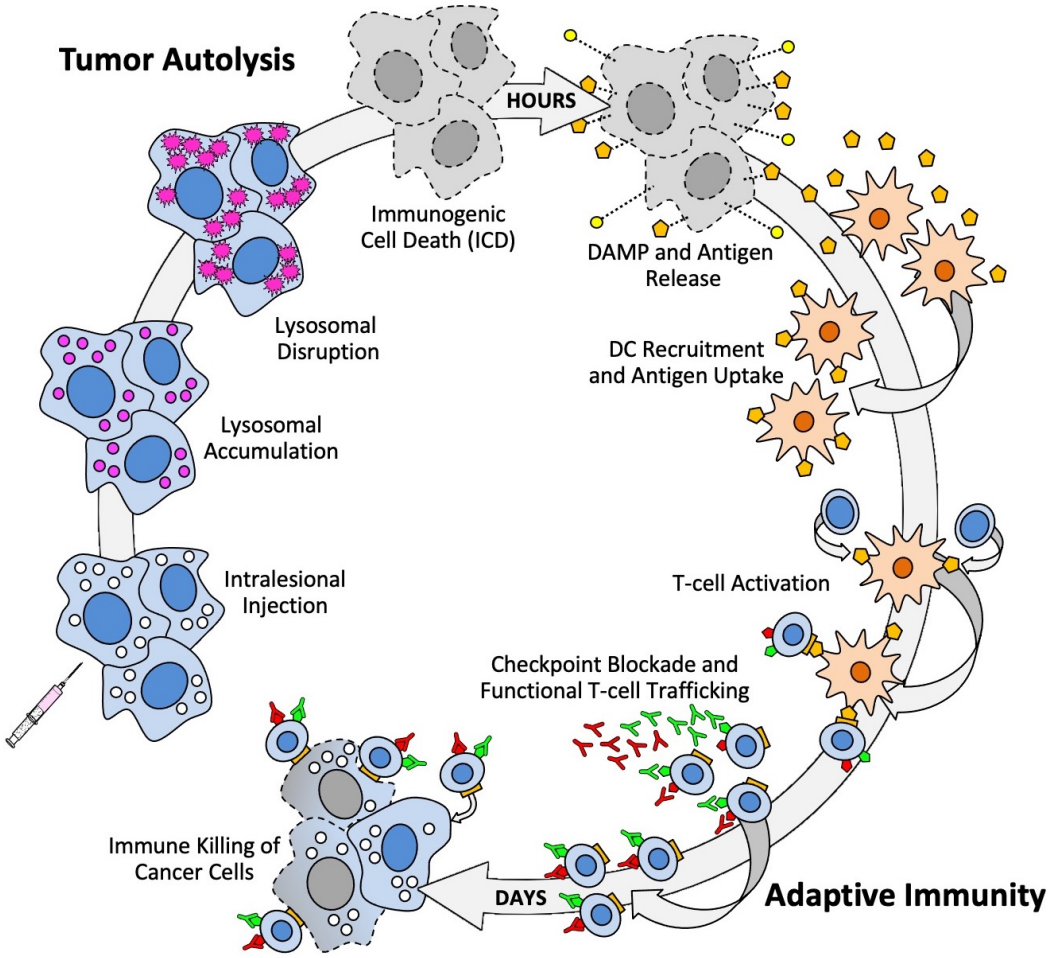
Background



- 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

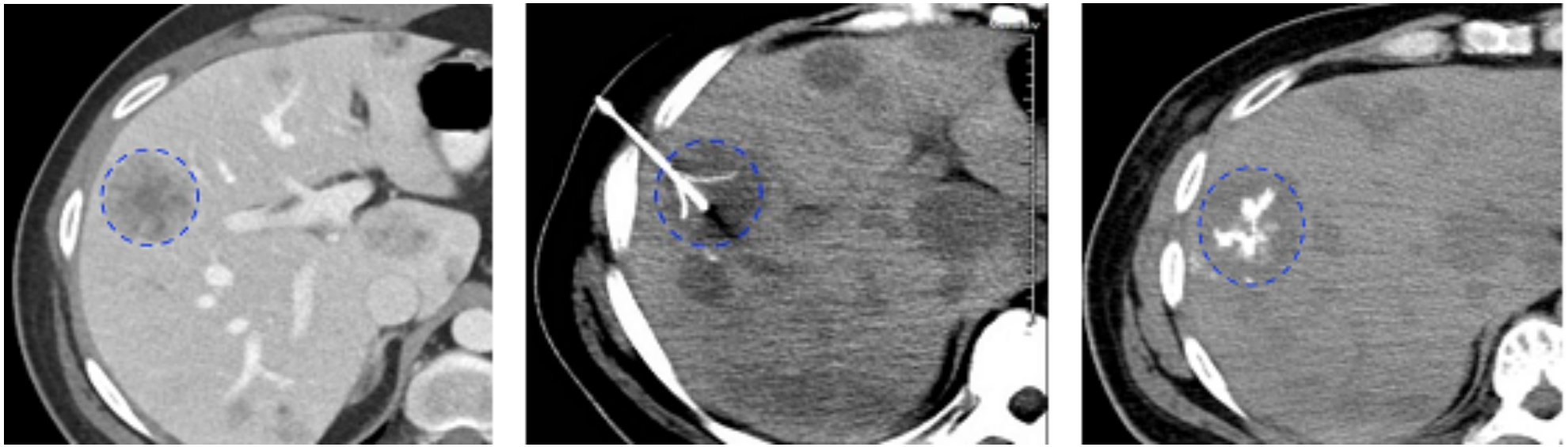
(1) Wachter et al. Functional Imaging of Photosensitizers using Multiphoton Microscopy. Proceedings of SPIE 4620, 143, 2002.

(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.

Intralesional PV-10

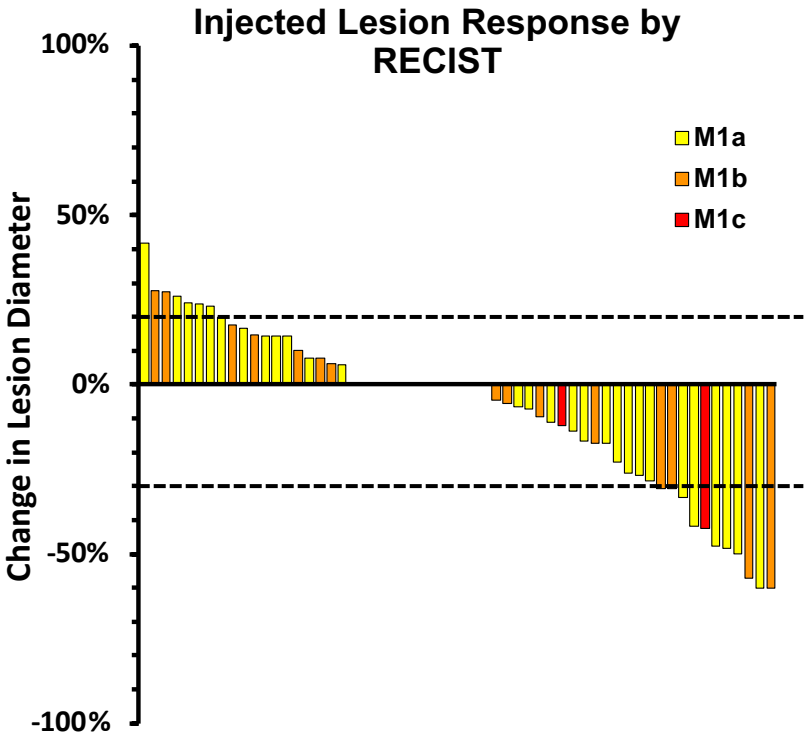


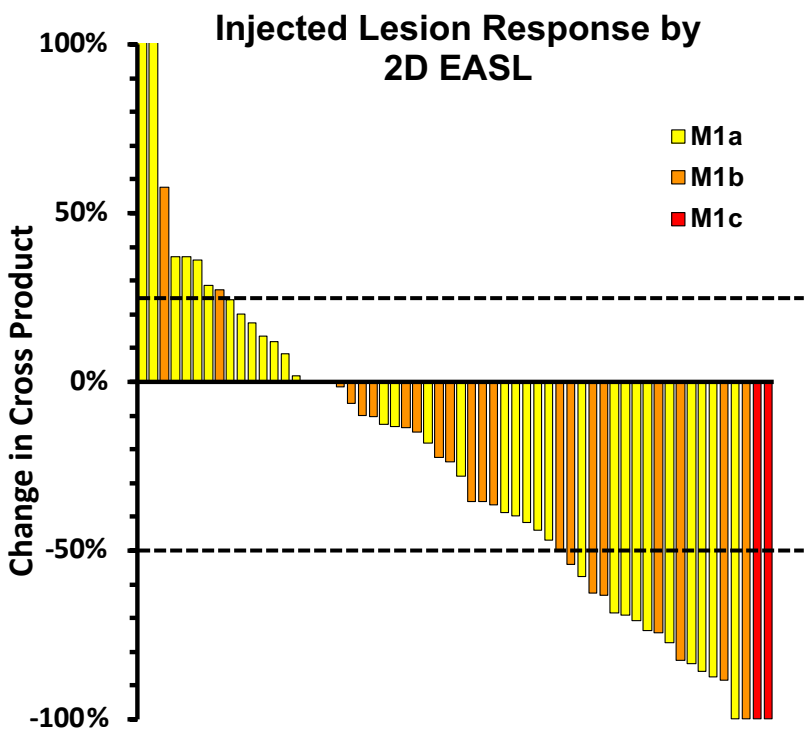
Source: Sapna P. Patel et al., SIR 2020

Patient Characteristics

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

Best Response of Injected Lesions

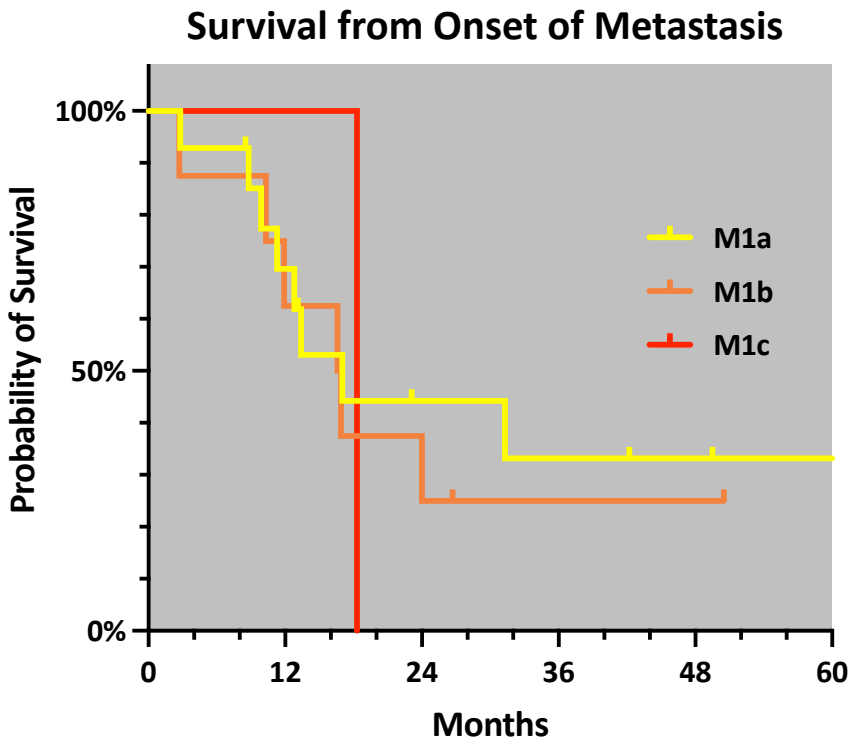




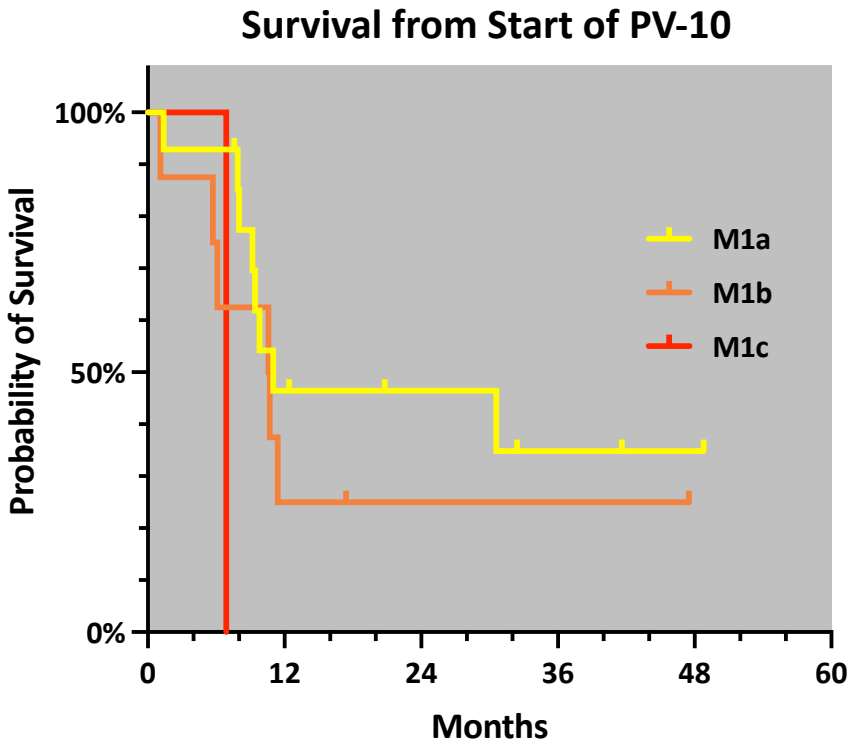
Best Overall Response (Injected Lesions)	RECIST	2D EASL
No. Lesions Evaluated	59	58*
Objective responses	11 (19%)	20 (34%)
Complete response	0 (0%)	4 (7%)
Partial response	11 (19%)	16 (28%)
Stable disease	39 (66%)	30 (52%)
Progressive disease	9 (15%)	8 (14%)

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

Overall Survival

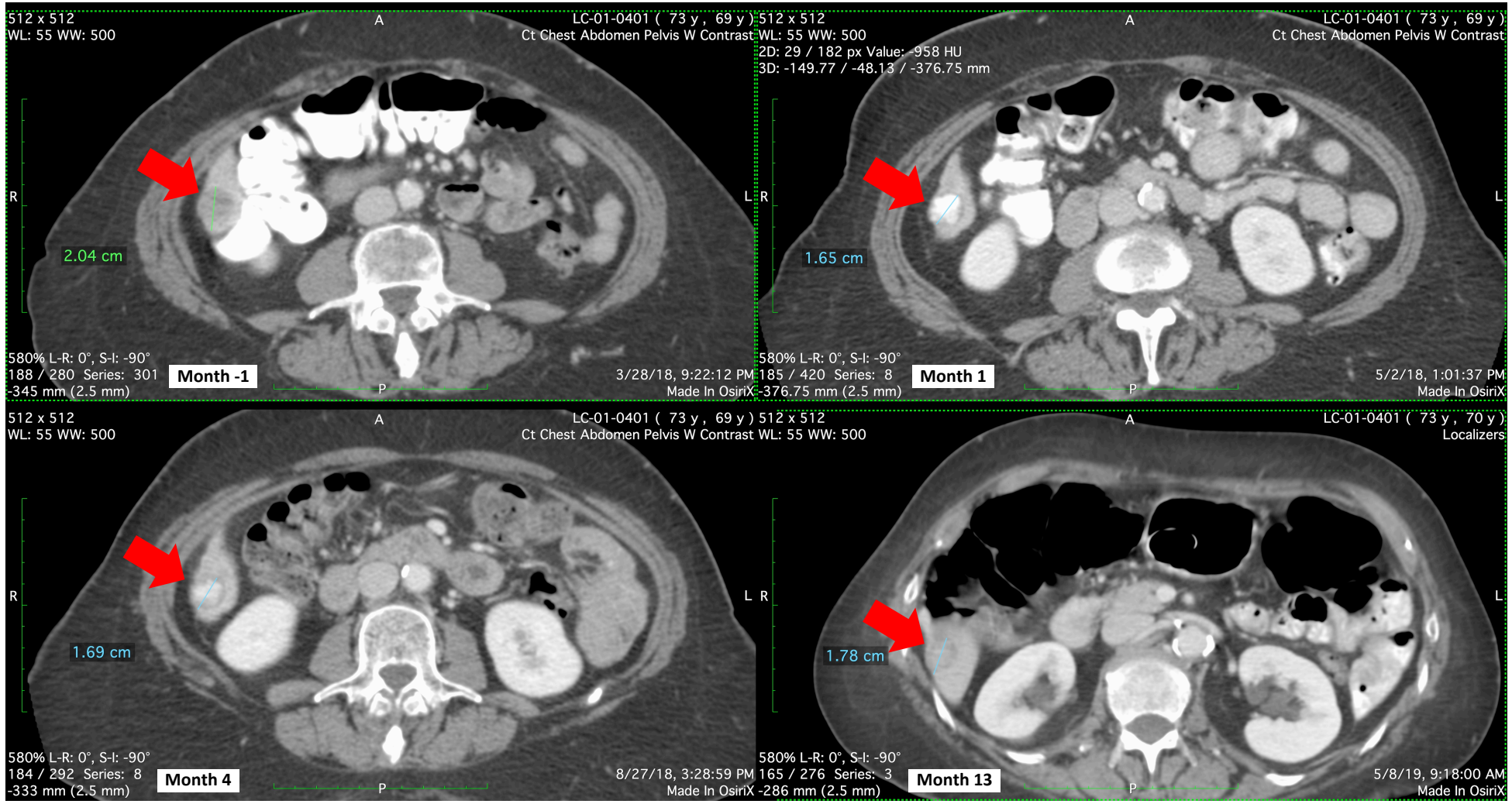


- mOS = 17.0 months (M1a pts)
- mOS = 16.8 months (M1b pts)
- mOS = 19.3 months (M1c pts)



- mOS = 11.0 months (M1a pts)
- mOS = 10.7 months (M1b pts)
- mOS = 6.9 months (M1c pts)

Retention of PV-10



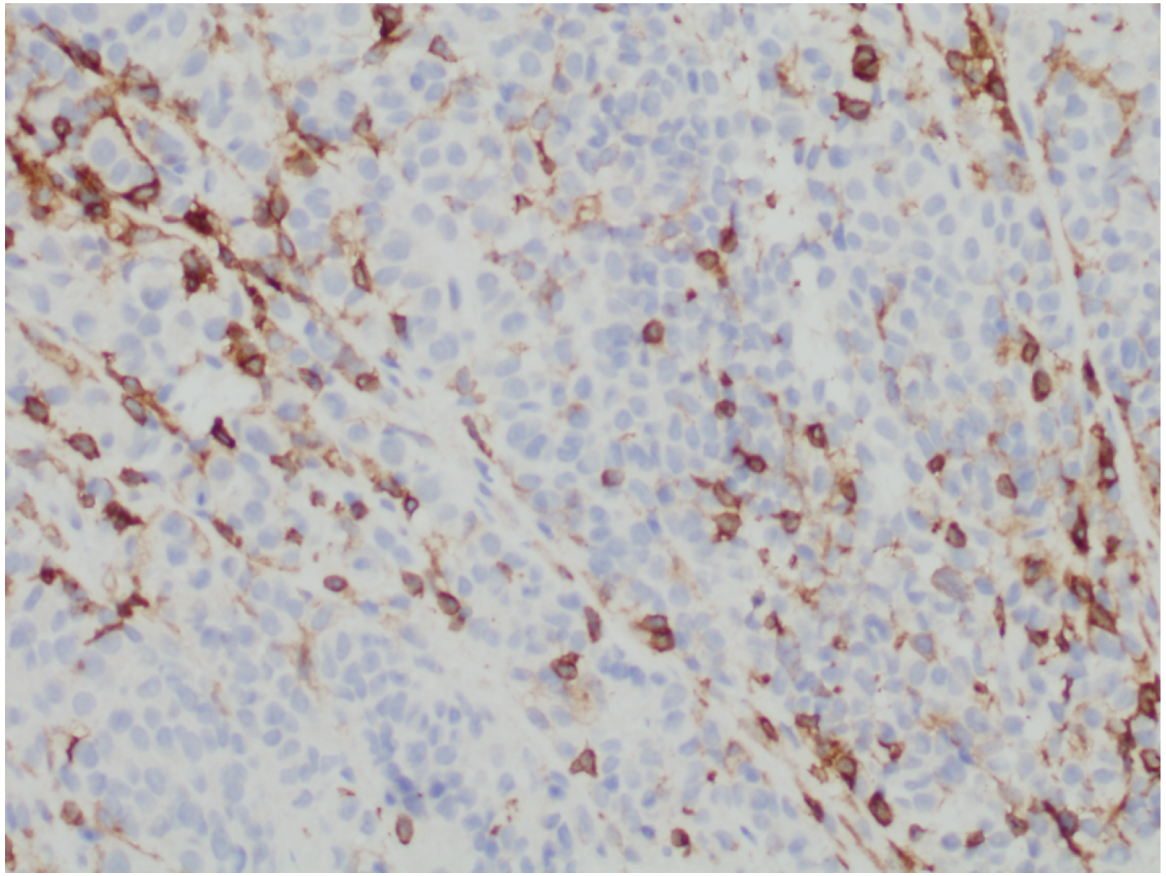
Subject 0401 (Month -1, 1, 4 and 13)

Adverse Events (Grade 3 or Higher)

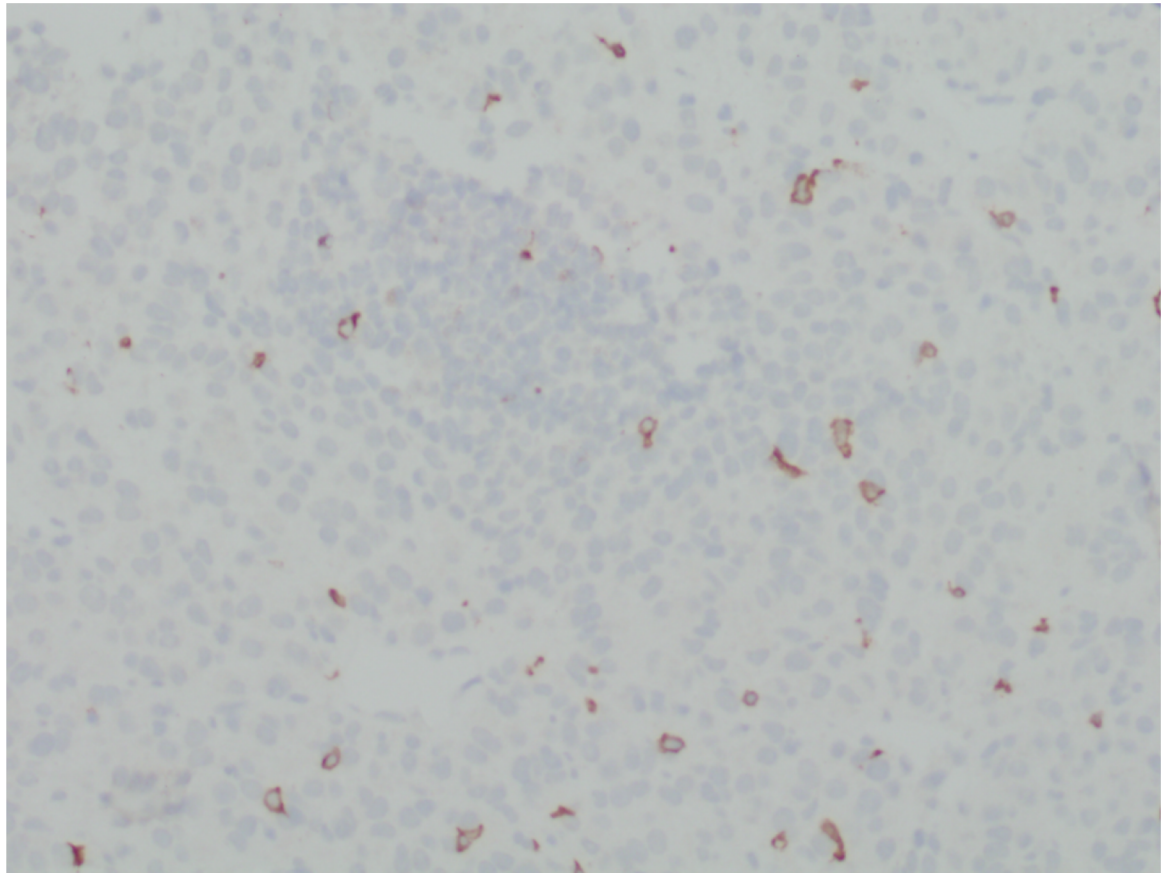
System Organ Class Preferred Term	Grade 3 (N)	Grade 4 (N)	Grade 5 (N)	Grade 3 or Higher (N)
Blood and Lymphatic System Disorders				
Haemolytic Uraemic Syndrome	1	0	0	1
Thrombocytopenia	1	0	0	1
General Disorders and Administration Site Conditions				
Injection Site Pain	3	0	0	3
Investigations				
Alanine Aminotransferase Increased	3	2	0	5
Aspartate Aminotransferase Increased	3	2	0	5
Blood Bilirubin Increased	1	1	0	2
Blood Creatinine Increased	1	0	0	1
Gamma-Glutamyl transferase Increased	1	0	0	1
Lymphocyte Count Decreased	1	0	0	1
Nervous System Disorders				
Presyncope	1	0	0	0
Renal and Urinary Disorders				
Acute Kidney Injury	1	0	0	0
Respiratory, Thoracic and Mediastinal Disorders				
Hypoxia	2	0	0	2
Vascular Disorders				
Hypertension	1	0	0	0

System Organ Class and Preferred Term are based on the MedDRA® version 25.0 terminology dictionary.
Includes all CTCAE Grade 3 and higher AEs at least possibly related to study treatment.
If a patient experienced an AE more than once during the study the greatest severity is presented.

Correlative studies – IHC for CD4+ and CD8+ cells



CD4 IHC at 20x magnification



CD8 IHC 20x magnification

Conclusions

- Intralesional image-guided PV-10 is safe and tolerable in metastatic uveal melanoma patients with liver metastasis

- The majority of injected lesions exhibited stable or better response; only 15% of patients experienced progression of disease in their injected tumor(s)

- 2D EASL is more sensitive than RECIST 1.1 to changes in injected lesions

- Adverse events are uncommon and transient

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Thank You

Thank you to patients, families, and caregivers

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