

# LUMINOS-102: Lerapolturev with and without anti-PD-1 in Unresectable anti-PD-1 Refractory Melanoma

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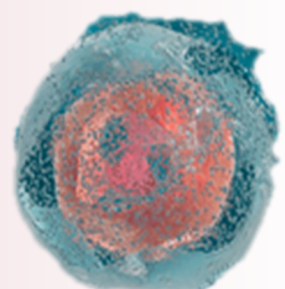
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## INTRODUCTION

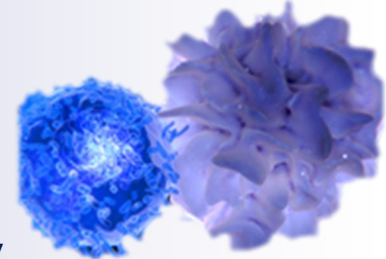
- Lerapolturev (formerly PVSRIPO) is a genetically modified version of the Sabin poliovirus vaccine designed to safely activate the immune system to treat cancer.
- Lerapolturev binds to CD155 (poliovirus receptor), a cell surface TIGIT ligand expressed on a variety of solid tumors, as well as antigen presenting cells, including dendritic cells and macrophages.

### Three Key Mechanisms of Action for Lerapolturev

Antigen Source  
**Direct tumor cell killing**

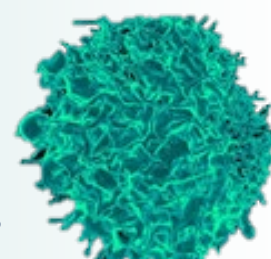


Systemic Effect  
**Immune activation** in APCs, leading to T-cell priming and anticancer immunity



Potential of Efficacy

**Recall** of polio vaccine specific T cells amplifies the immune response



## STUDY OBJECTIVES AND DESIGN

### Primary objectives

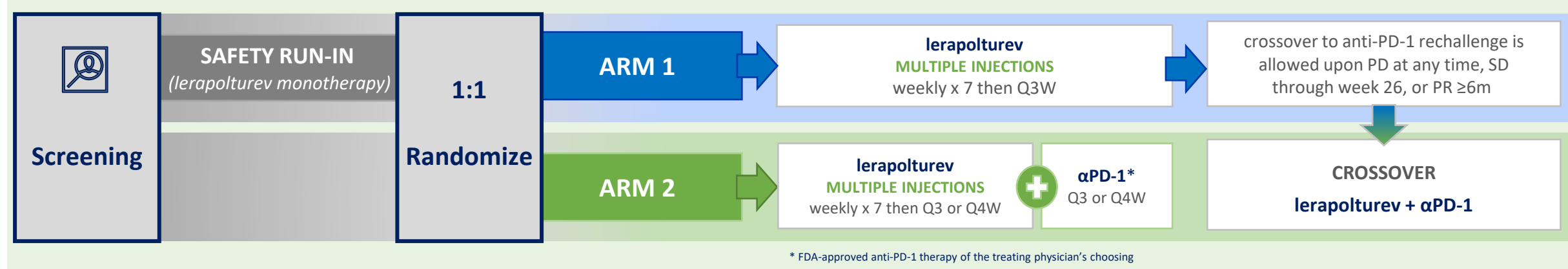
- Anti-tumor response (RECIST 1.1)
- Safety and tolerability
- Effects on the TME

### Secondary objective

- Disease control

### Exploratory objectives

- MoA and biomarkers
- Anti-tumor response (iRECIST)
- Subgroup analyses



- Population: patients with unresectable melanoma who failed prior anti-PD-1 therapy.
- Originally, participants received a single lerapolturev injection on Cycle 1 Day 1, followed by injection of up to  $6 \times 10^8$  TCID<sub>50</sub> across a maximum of 6 lesions on Cycle 1 Day 10, then repeated every 3 or 4 weeks (Dose A).
- As of March 2022, the maximum lerapolturev dose increased to  $1.6 \times 10^9$  TCID<sub>50</sub> (Dose B) across a maximum of 6 lesions weekly for 7 weeks (induction) followed by dosing every 3 or 4 weeks. 7 participants have been treated with Dose B; 3 with both Dose B and induction schedule.
- Randomization is stratified by type of anti-PD-1 resistance and baseline LDH.

## RESULTS

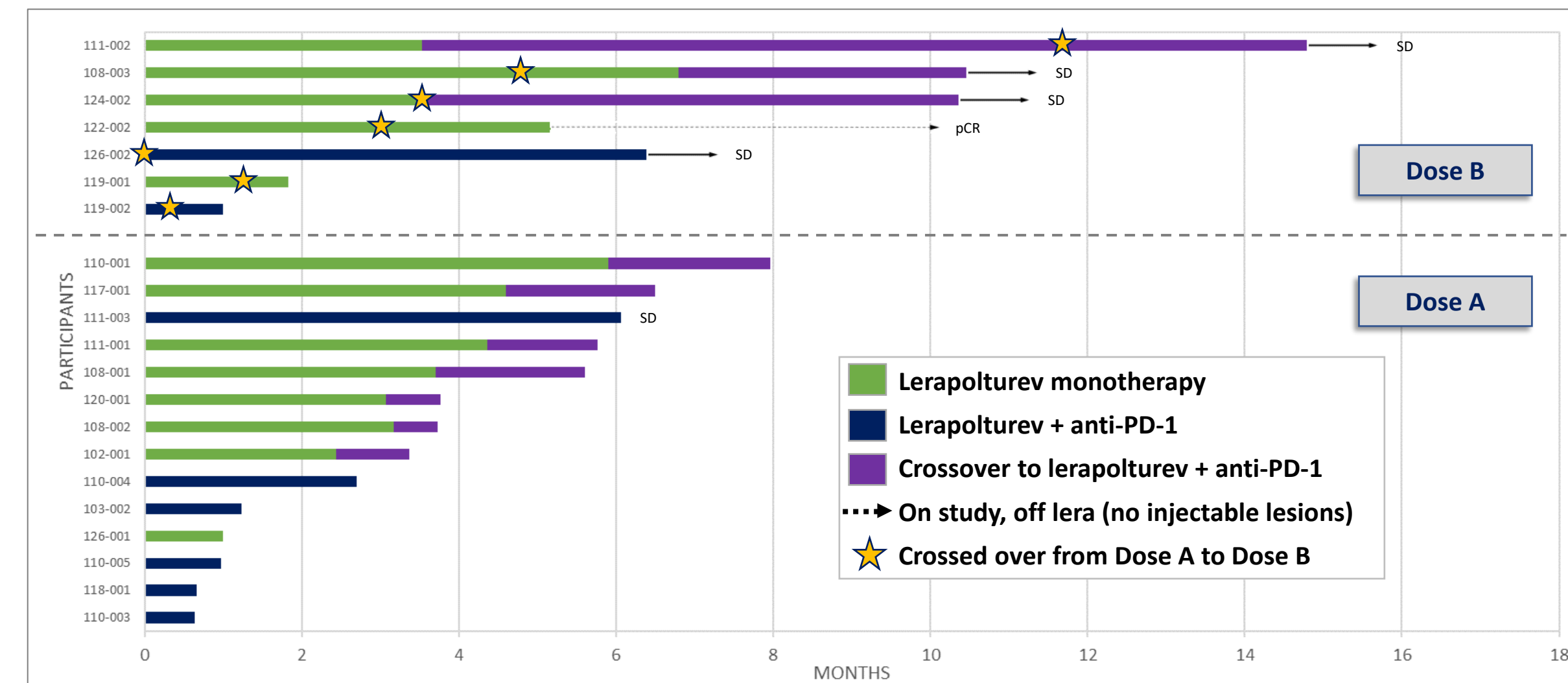
- To date, no DLTs or treatment-related SAEs have been reported after multiple lerapolturev injections per cycle.
- The only treatment related AE reported in > 1 participant was fatigue (14%, all grade 1 or 2).

**Table 1. Demography & Efficacy**

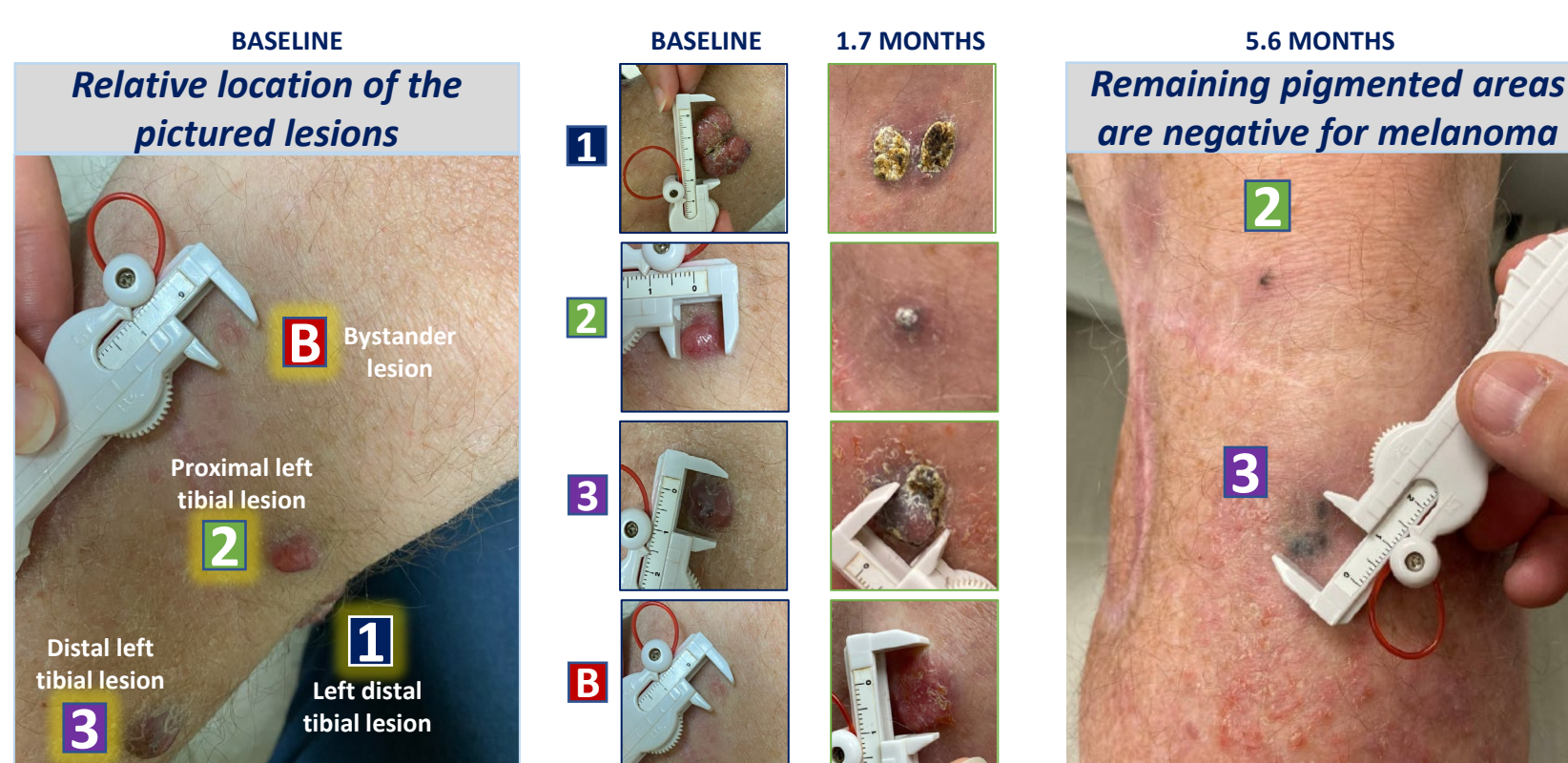
	Dose A $6 \times 10^8$ TCID <sub>50</sub>	Dose B $1.6 \times 10^9$ TCID <sub>50</sub>
Dosing		
N	14	7
Age, median (range)	63 (41, 84)	66 (25, 74)
Sex, % male / % female	50 / 50	43 / 57
Complete Response, n (%)	0	1 (14)
Clinical Benefit Rate, n (%)	1 (7)	5 (71)

## RESULTS

**Figure 1. Duration of Treatment**



**Figure 2. Participant 122-002: Lerapolturev Monotherapy**



Participant 122-002 presented with in-transit disease on the left leg after treatment with adjuvant pembrolizumab followed by ipilimumab and nivolumab. The participant was randomized to Dose A of lerapolturev monotherapy with an increase to Dose B after 3 months on study. Lesions resolved, with biopsies of remaining pigmented areas negative for melanoma after 5.6 months on study. The participant continues to be disease free as of 10 months on study.

**Figure 3. Participant 124-002: Lerapolturev & anti-PD-1**

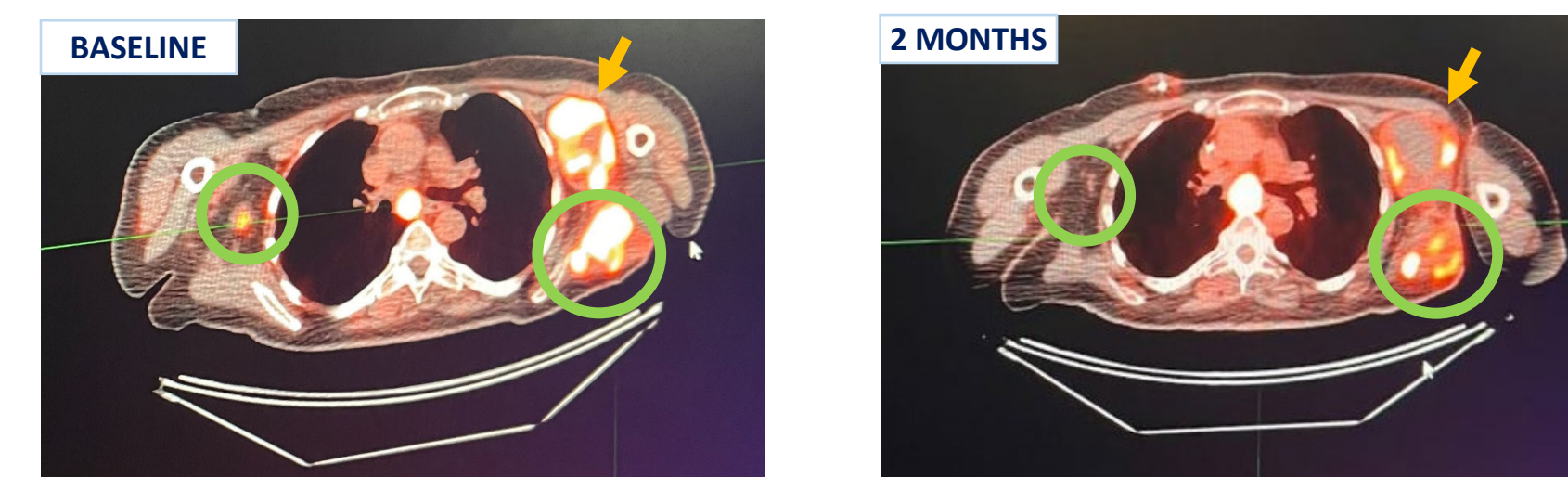


Participant 124-002 presented with Stage IV (M1b) melanoma (lesions in right neck and right lung) after previous treatment including neck dissection, adjuvant nivolumab and BRAF/MEK inhibitors. He was randomized to lerapolturev monotherapy and crossed over to lerapolturev (Dose B) + anti-PD-1 after 3.5 months on study. The non-injected lung lesion was no longer present at the 4.5-month scan, and the right neck lesion was not palpable at 5.6 months. The participant remains on study at 10.5 months.

## RESULTS

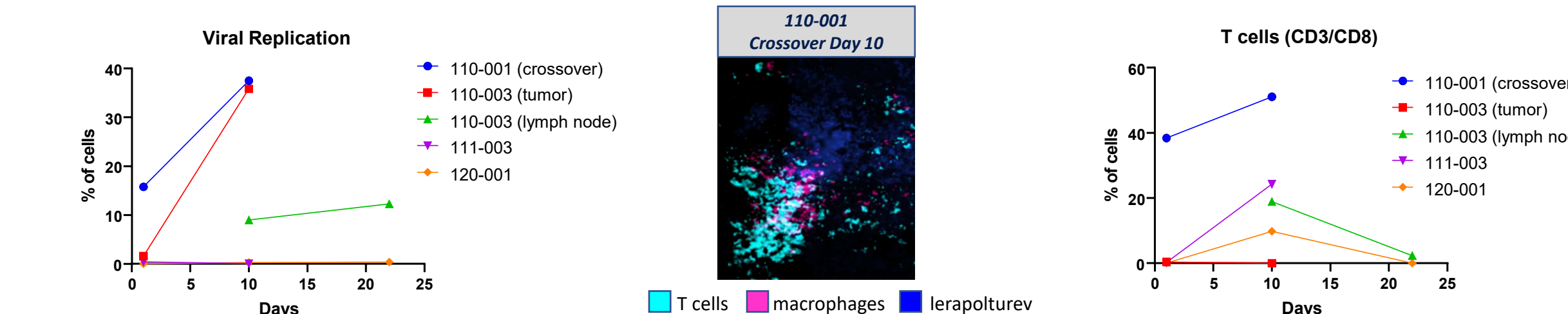
**Figure 4. Participant 126-002: Lerapolturev & anti-PD-1**

⚡ = injected lesion ○ = non-injected lesion



Participant 126-002 presented with bilateral axillary disease and a subscapular lesion after surgical resection followed by progressive disease after adjuvant nivolumab and two cycles of ipilimumab and nivolumab. She was randomized to lerapolturev (Dose B) and anti-PD-1 therapy. Overall, participant has ~24% reduction in tumor burden. One injected lesion has become edematous with PET decrease in metabolically active cells, suggesting necrosis. Non-injected lesions have decreased in size and show decreased metabolic activity. The participant remains on study at 6.4 months.

## TRANSLATIONAL: IMPORTANCE OF REPEATED DOSING



- Multiplex immunofluorescence confirms viral replication in injected lesions, mainly macrophages.
- T cell influx at 10 days, decreased at day 21 highlights importance of repeat dosing.

## CONCLUSIONS

- Intratumoral injection of lerapolturev at a dose of  $1.6 \times 10^9$  TCID<sub>50</sub> (Dose B) administered as induction (weekly x 7) followed by maintenance (every 3 or 4 weeks) is well tolerated.
- Anti-tumor responses are noted in both injected and non-injected lesions (e.g., abscopal response).
- CBR (CR/PR or >6 months of SD) of 71% in the group of participants receiving the increased dose and/or increased frequency of lerapolturev administration is encouraging.
- The LUMINOS-102 study continues to follow these participants for response and remains open to enrollment.

## ACKNOWLEDGEMENTS

- Thank you to all the investigators, clinical coordinators, and participants for your continued support.
- The study is sponsored by Istari Oncology, Inc.

**Abbreviations**  
APC, antigen-presenting cell; CBR, clinical benefit rate (CR, PR or SD ≥ 6 months); DLT, dose-limiting toxicity; FDA, Food and Drug Administration; iRECIST, immune Response Evaluation Criteria in Solid Tumors; LDH, Lactate dehydrogenase; MoA, mechanism of action; pCR, pathologic complete response; PD, progressive disease; PD-1, programmed cell death protein 1; PD-L1, programmed death ligand 1; PET, positron emission tomography; PR, partial response; PVSRIPO, Polio Vaccine Sabin Rhinovirus Poliovirus; RECIST, Response Evaluation Criteria in Solid Tumors; SAE, serious adverse event; SD, stable disease; TCID<sub>50</sub>, median tissue culture infectious dose; TME, tumor microenvironment.