



A pilot study of engineered adenovirus ONCOS-102 in combination with pembrolizumab in checkpoint inhibitor refractory advanced or unresectable melanoma

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Disclosures

Advisory boards

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- Immunocore
- Castle Biosciences

Clinical Trial Support

- Targovax
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Outline



Background and Study Design



Safety of ONCOS-102 + pembrolizumab

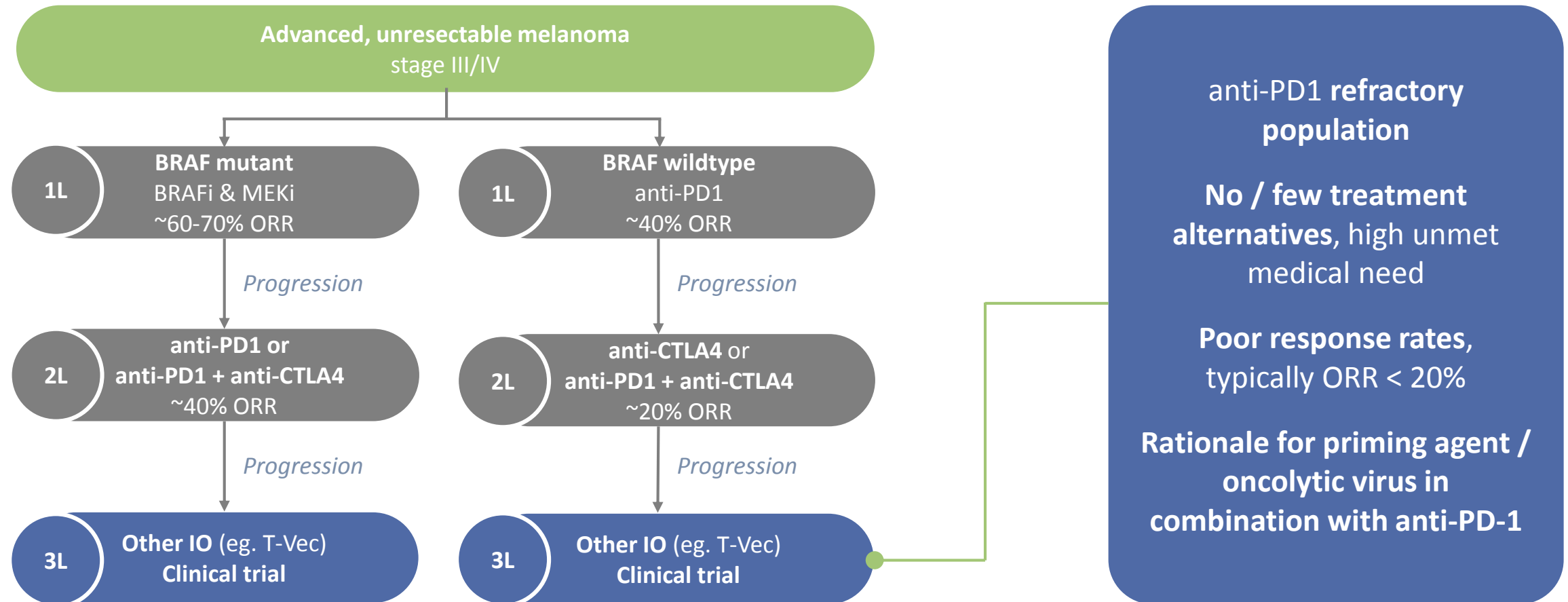


Clinical Responses in Part 1

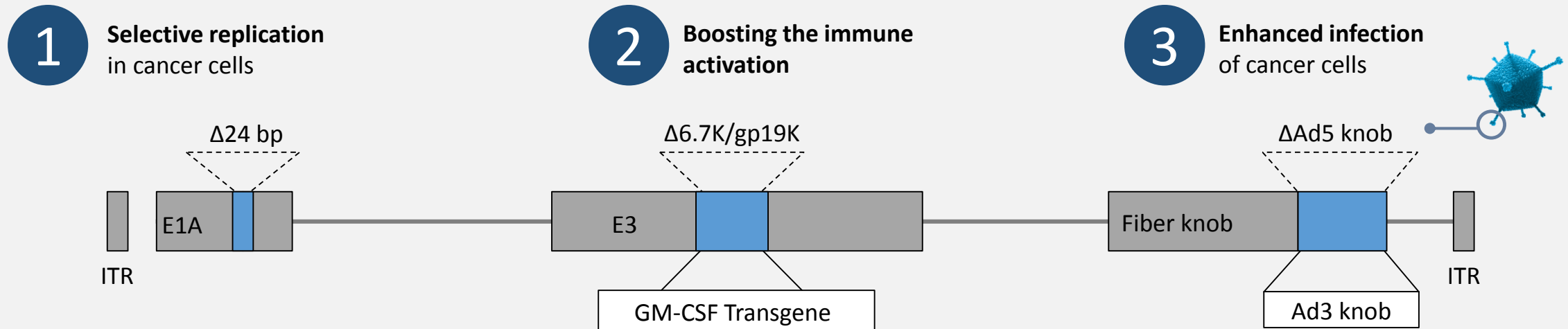
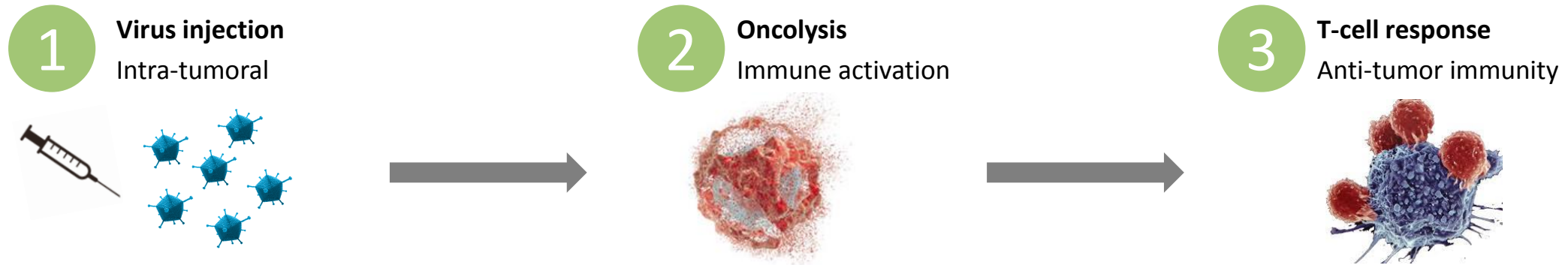


Systemic and Local Immune Responses in Part 1

Limited treatment options for anti PD-1 refractory melanoma



ONCOS-102 is an oncolytic adenovirus serotype 5 armed with a GM-CSF transgene



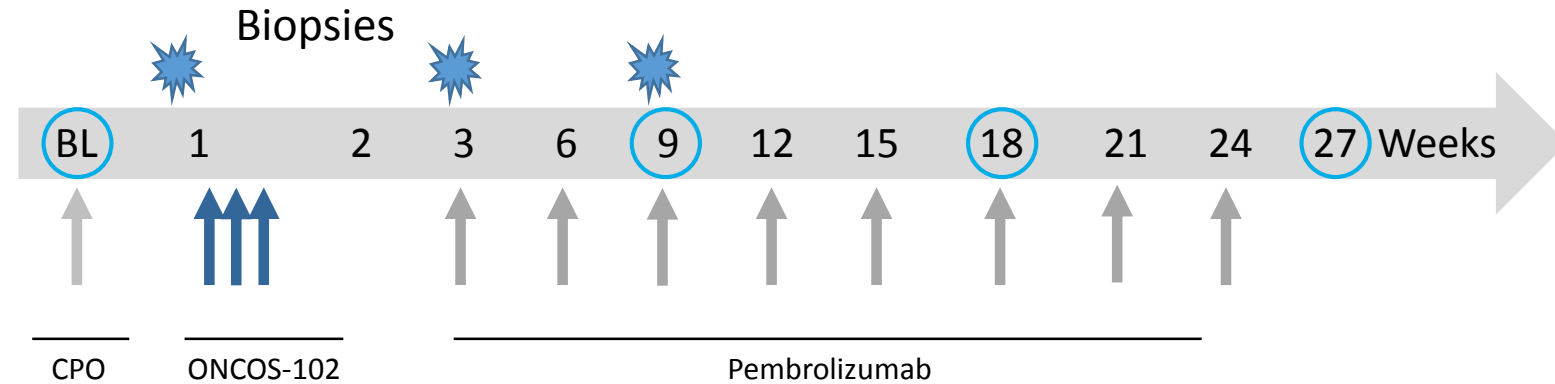
Study Design

Part 1

3x ONCOS-102

8x pembrolizumab

enrollment completed



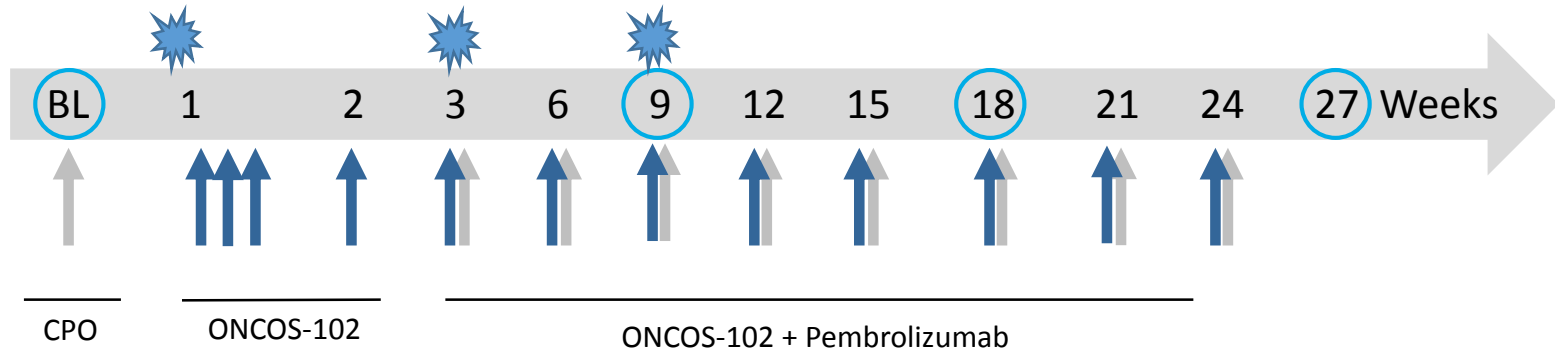
Part 2

3x ONCOS-102

8x ONCOS-102 +

pembrolizumab

enrolling



Imaging

CPO: Cyclophosphamide

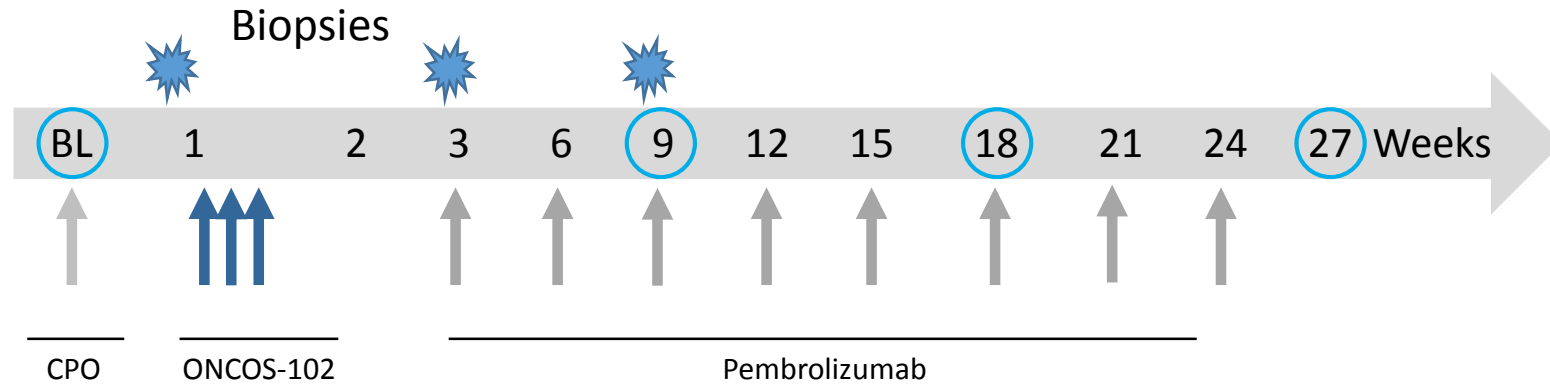
Study Design

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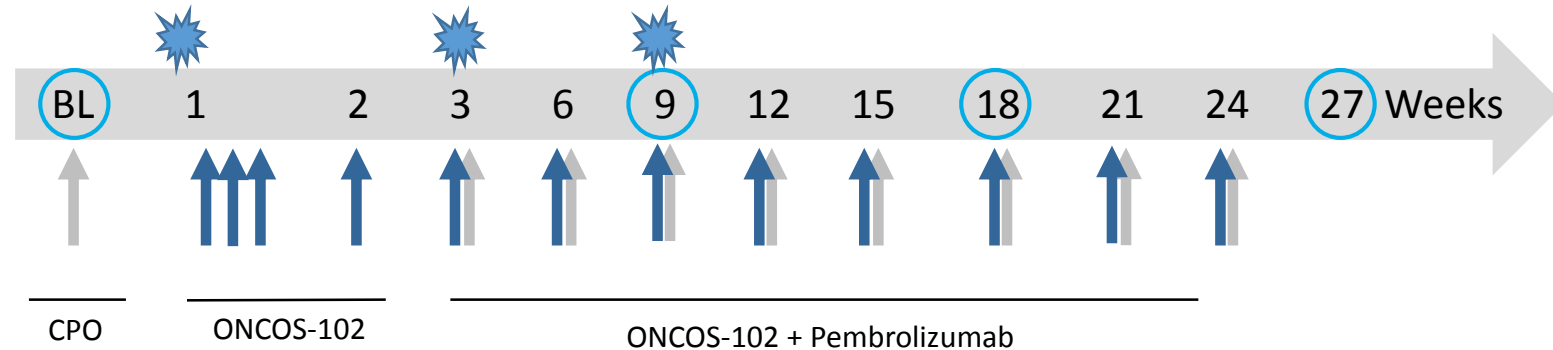
Part 2

3x ONCOS-102

8x ONCOS-102 +

pembrolizumab

enrolling



CPO: Cyclophosphamide

Demographics and prior treatment

Parameters	Number of patients (n=9)
Age (Y) median (range)	73 (40 – 87)
Gender, n	
Female	4
Male	5
Histological type	
Cutaneous	8
Acral	1
Stage at enrollment	
III	1
IIIB	2
IIIC	3
IV	2
IVM1c	1

Prior therapy	Number of patients (n=9)
Systemic Therapy	
anti-PD1 checkpoint inhibitor Pembrolizumab and/or Nivolumab	9
anti-CTLA4 checkpoint inhibitor Ipilimumab	4
Oncolytic virus Talimogene-laherparepvec	3
BRAF/MEK inhibitors Dabrafenib + Trametinib	2
TLR9 agonist CMP-001 (investigational)	1
Interleukin-2 immunotherapy	1
Surgery	7
Radiotherapy	1
Chemotherapy	1

Preliminary data

Adverse Events *

Adverse Event Preferred term	No. of events	No. of patients	CTCAE grade	Relationship to study drug
Chills	7	5	1, 2	ONCOS-102
Myalgia	6	3	1	
Pyrexia	5	3	1, 2	
Diarrhoea	4	3	1	
Nausea	3	3	1	
Alanine aminotransferase increased	2	2	1	
Fatigue	2	2	1, 2	
Vomiting	2	2	1	
Rash maculo-papular	2	2	1	
Injection site pain	2	1	1	
Injection site swelling	1	1	2	
Peripheral oedema	1	1	2	
Infectious colitis	1	1	3 **	Pembrolizumab
Productive cough	1	1	2	
Haemolytic anemia	1	1	3 **	
Diarrhoea	2	2	1,3 **	ONCOS-102 and pembrolizumab
Diabetic ketoacidosis	1	1	4 **	
Type 1 diabetes mellitus	1	1	4 **	

* AEs occurring in 2 or more
Patients or grade 2 or higher

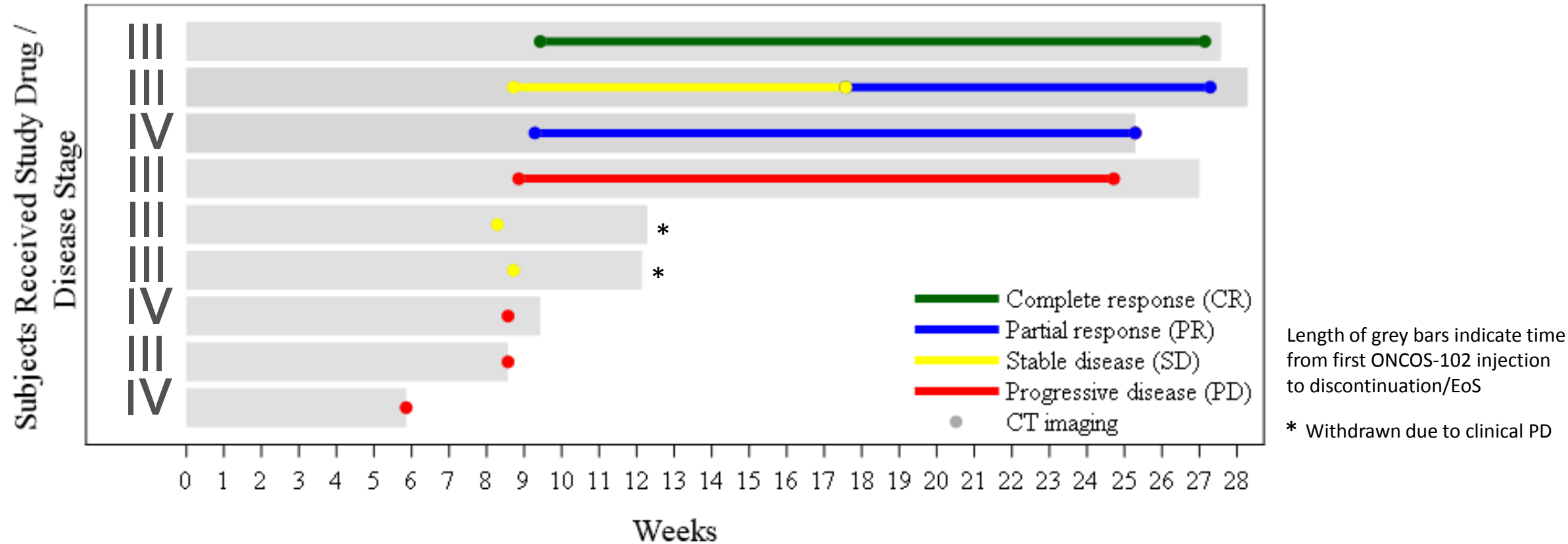
** SAEs

Total no. of AEs reported:
58 in 9 patients

Preliminary data

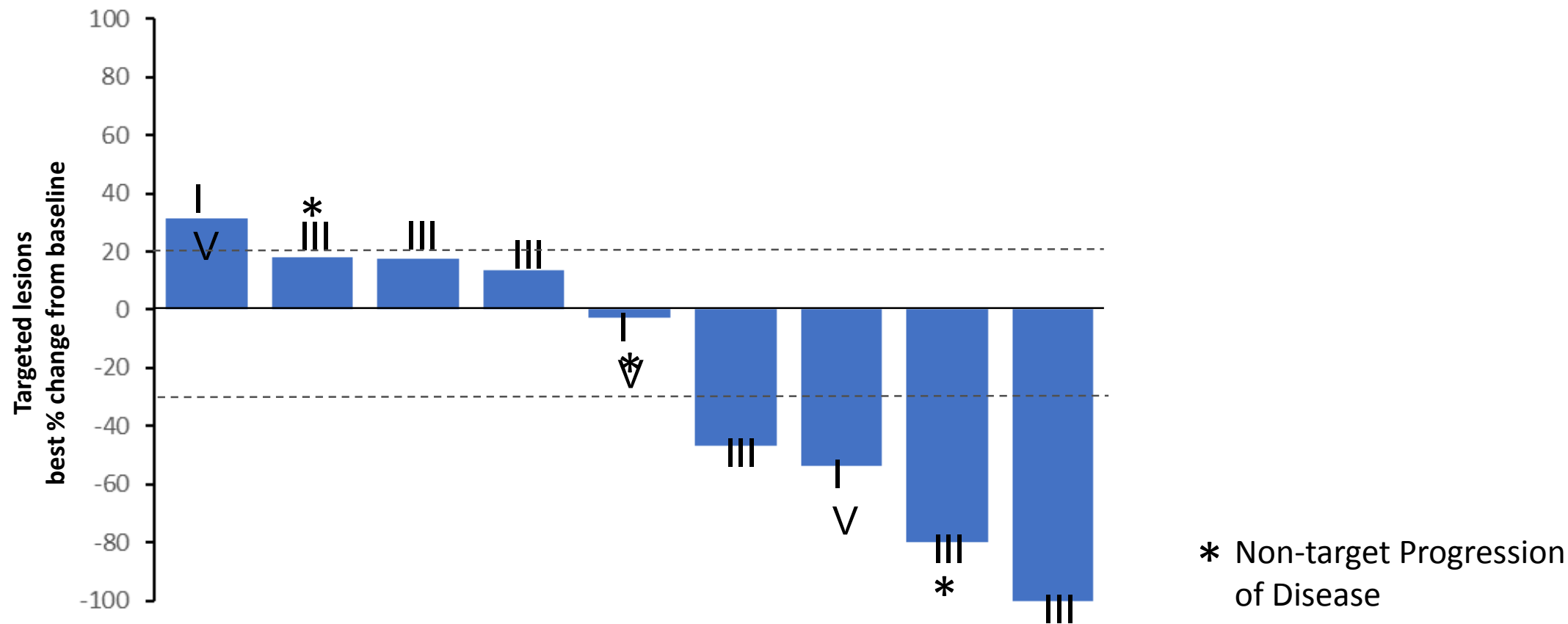
Objective Response Rate of 33% (3 of 9 pts)

RECIST 1.1



Preliminary data

Targeted lesions: best % change in tumor burden from baseline



Preliminary data

Example of response: Patient with CR

Tumor stage at enrollment: **IIIb**
T4a, N2b, M0

Prior therapies: Surgery
Ipilimumab
Dabrafenib + Trametinib
Pembrolizumab

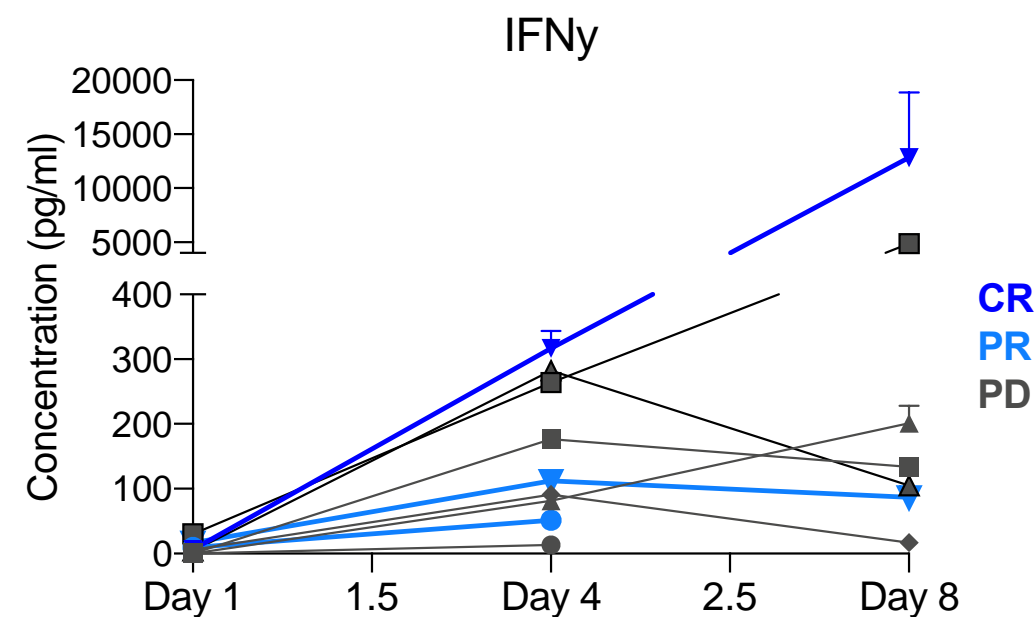
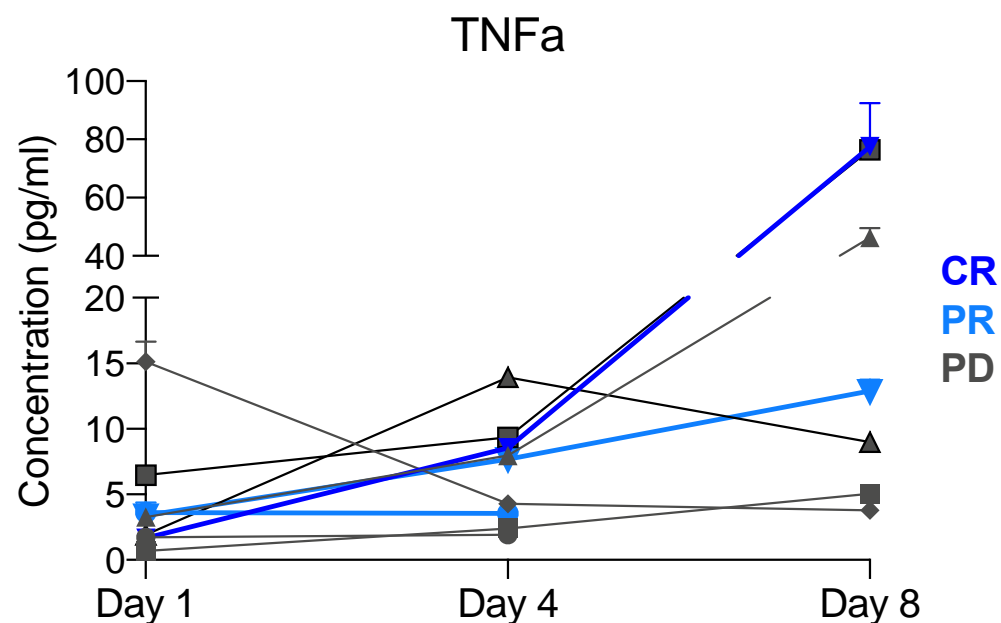
RECIST 1.1: CR



Preliminary data

Upregulation of proinflammatory cytokines in all patients

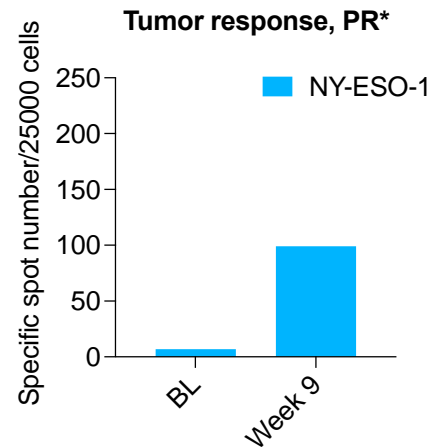
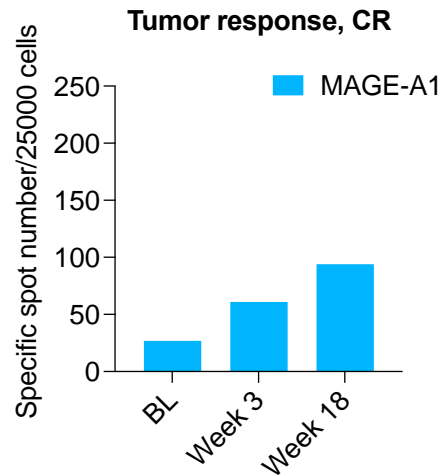
Systemic expression of proinflammatory cytokines



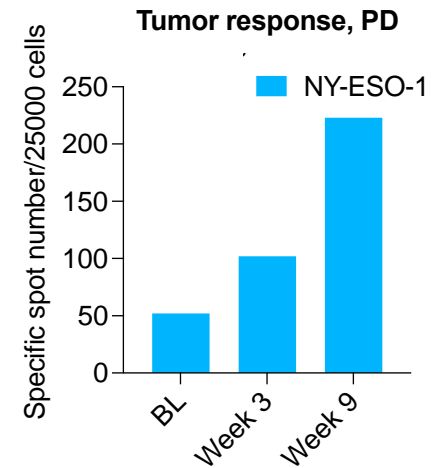
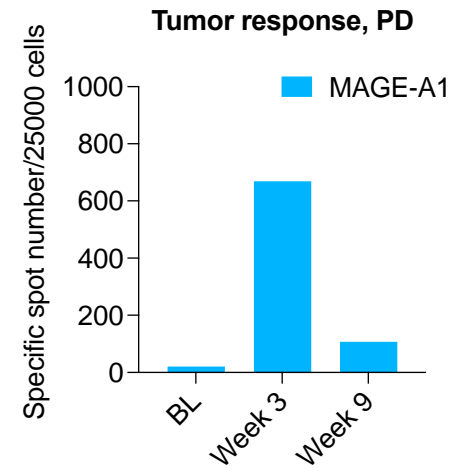
Preliminary data

Systemic increase in tumor targeting T-Cells

IFN γ ELISPOT, spot number/25,000 cells



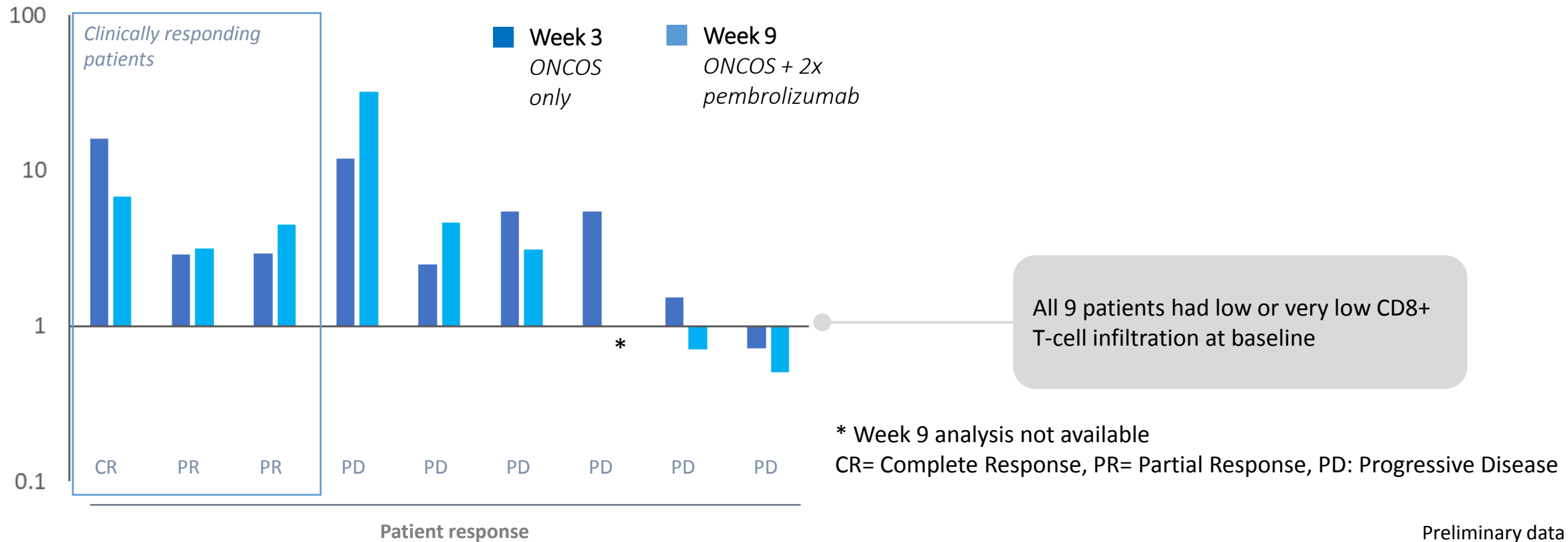
* Week 3 analysis not performed



Preliminary data

Increased T-cell infiltration in ONCOS-102 injected tumors is necessary but not sufficient for response

CD8+ T-cell tumor infiltration, -fold change from baseline



Conclusions

Sequential ONCOS-102 and pembrolizumab treatment in advanced anti-PD1 refractory melanoma patients showed:

- Acceptable safety profile; most common ONCOS-102 related adverse events were fevers, chills, and myalgias
- ORR: 3 of 9 patients (RECIST 1.1)
- Upregulation of proinflammatory cytokines
- Systemic development of anti-tumor immune responses
- Increased infiltration of CD8+ T cells in ONCOS-102 injected tumors

Part 2 of this pilot study is currently enrolling an additional 12 patients to receive 12 injections of ONCOS-102 with pembrolizumab

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