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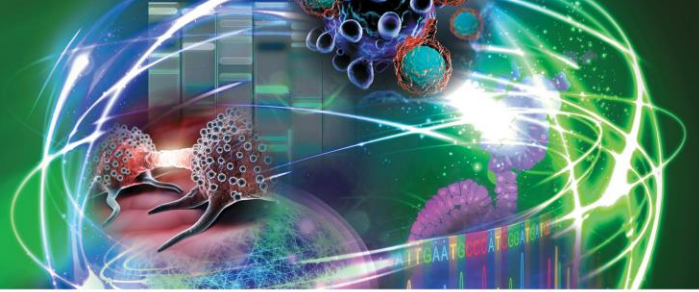

Lifileucel (LN-144), a cryopreserved autologous tumor infiltrating lymphocyte (TIL) therapy in patients with advanced (unresectable or metastatic) melanoma: sustained duration of response at 28 month follow up

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Disclosure Information

Jason Alan Chesney, MD, PhD

I have the following financial relationships to disclose:

Consultant for: Amgen

Research Funding from: Iovance Biotherapeutics, Amgen, Bristol Myers Squibb

Iovance C-144-01

Background

- There are currently no approved agents for patients with metastatic melanoma whose disease progresses while on or after treatment with immune checkpoint inhibitors (ICI) and BRAF/MEK inhibitors (BRAFi/MEKi) if BRAF V600 mutant
- In advanced melanoma patients who are either primary refractory or develop resistance to ICI, retreatment with ICI or treatment with chemotherapy yields a poor response:
  - ORR 4%-10%[1-2] and mOS ~7-8 months[3-4]
- Adoptive cell therapy utilizing tumor-infiltrating lymphocytes (TIL) has demonstrated antitumor efficacy with durable long-term responses in heavily pretreated patients[5]
- **C-144-01** (NCT02360579) is a global Phase 2, open-label, multicohort, multicenter study:
  - Investigational agent: centrally manufactured and cryopreserved autologous TIL product, lifileucel (LN-144)
  - Patient population: unresectable or metastatic melanoma who have progressed on checkpoint inhibitors and BRAF/MEK inhibitors (if BRAF mutant)
  - Manufacturing method: central manufacturing of cryopreserved TIL, in a 22-day process

[1] Larkin J, Minor D, D'Angelo S, et al. Overall Survival in Patients With Advanced Melanoma Who Received Nivolumab Versus Investigator's Choice Chemotherapy in CheckMate 037: A Randomized, Controlled, Open-Label Phase III Trial. *J Clin Oncol.* 2018;36:383-90.
[2] Keytruda (pembrolizumab) prescribing information. Whitehouse Station, NJ: Merck & Co., Inc.; 2019.
[3] Goldinger SM, Lo S, Hassel JC, et al. The utility of chemotherapy after immunotherapy failure in metastatic melanoma: A multicenter case series. *J Clin Oncol*. 2018;36:e21588-e.
[4] Kirchberger MC, Hauschild A, Schuler G, Heinzerling L. Combined low-dose ipilimumab and pembrolizumab after sequential ipilimumab and pembrolizumab failure in advanced melanoma. *Eur J Cancer.* 2016;65:182-4.
[5] Rosenberg SA, Yang JC, Sherry RM, et al. Durable complete responses in heavily pretreated patients with metastatic melanoma using T-cell transfer immunotherapy. *Clin Cancer Res.* 2011;17:4550-7.

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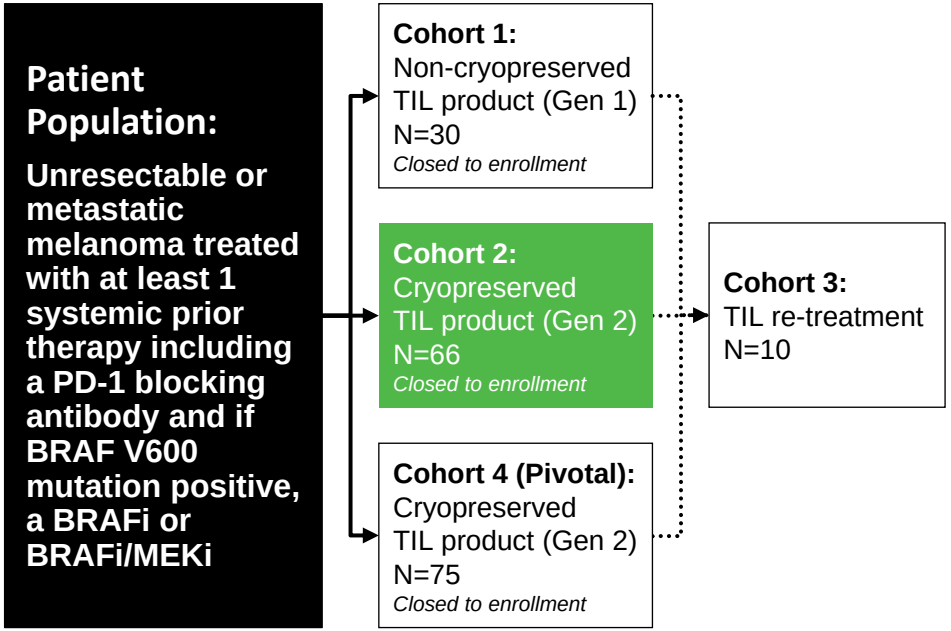
Iovance C-144-01 Study Design

Phase 2, multicenter study to assess the efficacy and safety of autologous Tumor Infiltrating Lymphocytes (lifileucel) for treatment of patients with metastatic melanoma (NCT02360579)



Cohort 2 Endpoints:

- Primary: Efficacy defined as investigator-assessed Objective Response Rate (ORR) following RECIST 1.1
- Secondary: Safety and additional parameters of Efficacy

Other Key Eligibility Criteria:

- One tumor lesion resectable for TIL generation (~1.5 cm in diameter) and ≥ one tumor lesion as target for RECIST 1.1 assessment
- Age ≥ 18 years at the time of consent
- ECOG Performance Status of 0-1

Methods:

- Data Extract: 14 December 2020 for Cohort 2

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C-144-01 Cohort 2 Patient Characteristics

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CHARACTERISTICS	Cohort 2, N=66
Gender, n (%)	
Female	27 (41)
Male	39 (59)
Age, years	
Median	55
Min, Max	20, 79
Prior therapies, n (%)	
Mean # prior therapies	3.3
anti-PD-1 / anti-PD-L1	66 (100)
anti-CTLA-4	53 (80)
BRAFi/MEKi	15 (23)
Progressive Disease for at least 1 prior therapy, n (%)	
anti-PD-1 / anti-PD-L1	65 (99)
anti-CTLA-4	41 (77[(1)])
Baseline ECOG score, n (%)	
0	37 (56)
1	29 (44)

CHARACTERISTICS	Cohort 2, N=66
BRAF Status, n (%)	
Mutated V600E or V600K	17 (26)
Wild Type	45 (68)
Unknown	3 (5)
Other	1 (2)
Tumor PD-L1 expression, n (%)	
PD-L1 Positive (TPS ≥ 5%)	23 (35)
PD-L1 Negative (TPS < 5%)	26 (39)
Baseline LDH (U/L)	
Median	244
1-2 times ULN, n (%)	19 (29)
> 2 times ULN, n (%)	8 (12)
Target Lesions Sum of Diameter (mm)	
Mean (SD)	106 (71)
Min, Max	11, 343
Number of Target and Non-Target Lesions (at Baseline)	
>3, n (%)	51 (77)
Mean (SD)	6 (2.7)
Liver and/or Brain Lesions, n (%)	28 (42)

Cohort 2 patients have:

- 3.3 mean prior therapies, ranging from 1-9
- High tumor burden at baseline

(1) % is calculated based on number of patients who received prior anti-CTLA-4

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Study Overview and Procedures

1 **Patient Intake**

2 **Tumor Tissue Procurement**

- Surgical resection of a tumor lesion (~1.5 cm in diameter)
- Shipped to a Central GMP facility

Tumor resection sites include **skin, lymph nodes, liver, lung, peritoneal, musculo-skeletal, breast, and other organs**

3 **Non-myeloablative Lymphodepletion (NMA-LD)**

- NMA-LD: cyclophosphamide followed by fludarabine

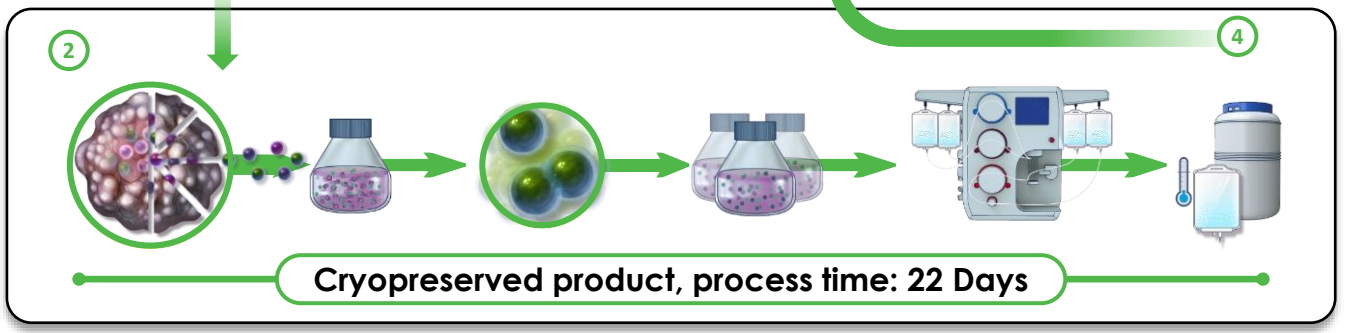
4 **Lifileucel Infusion**

- One time treatment
- Lifileucel is a rejuvenated and expanded TIL product

5 **IL-2 Administration**

- Up to 6 doses

6 **Discharge**



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Iovance C-144-01 Cohort 2 Safety

Treatment Emergent Adverse Events (≥ 30%)

PREFERRED TERM	Cohort 2 (N=66)		
	Any Grade, n (%)	Grade 3/4, n (%)	Grade 5, n (%)
Number of patients reporting at least one Treatment-Emergent AE	66 (100)	64 (97.0)	2 (3.0)*
Thrombocytopenia	59 (89.4)	54 (81.8)	0
Chills	53 (80.3)	4 (6.1)	0
Anemia	45 (68.2)	37 (56.1)	0
Pyrexia	39 (59.1)	11 (16.7)	0
Neutropenia	37 (56.1)	26 (39.4)	0
Febrile neutropenia	36 (54.5)	36 (54.5)	0
Hypophosphatemia	30 (45.5)	23 (34.8)	0
Leukopenia	28 (42.4)	23 (34.8)	0
Fatigue	26 (39.4)	1 (1.5)	0
Hypotension	24 (36.4)	7 (10.6)	0
Lymphopenia	23 (34.8)	21 (31.8)	0
Tachycardia	23 (34.8)	1 (1.5)	0

*One death was due to intra-abdominal hemorrhage considered possibly related to TIL, second was due to acute respiratory failure assessed as not related to TIL per Investigator assessment.
- Patients with multiple events for a given preferred term are counted only once using the maximum grade under each preferred term
- Treatment-Emergent Adverse Events refer to all AEs starting on or after the first dose date of TIL up to 30 days

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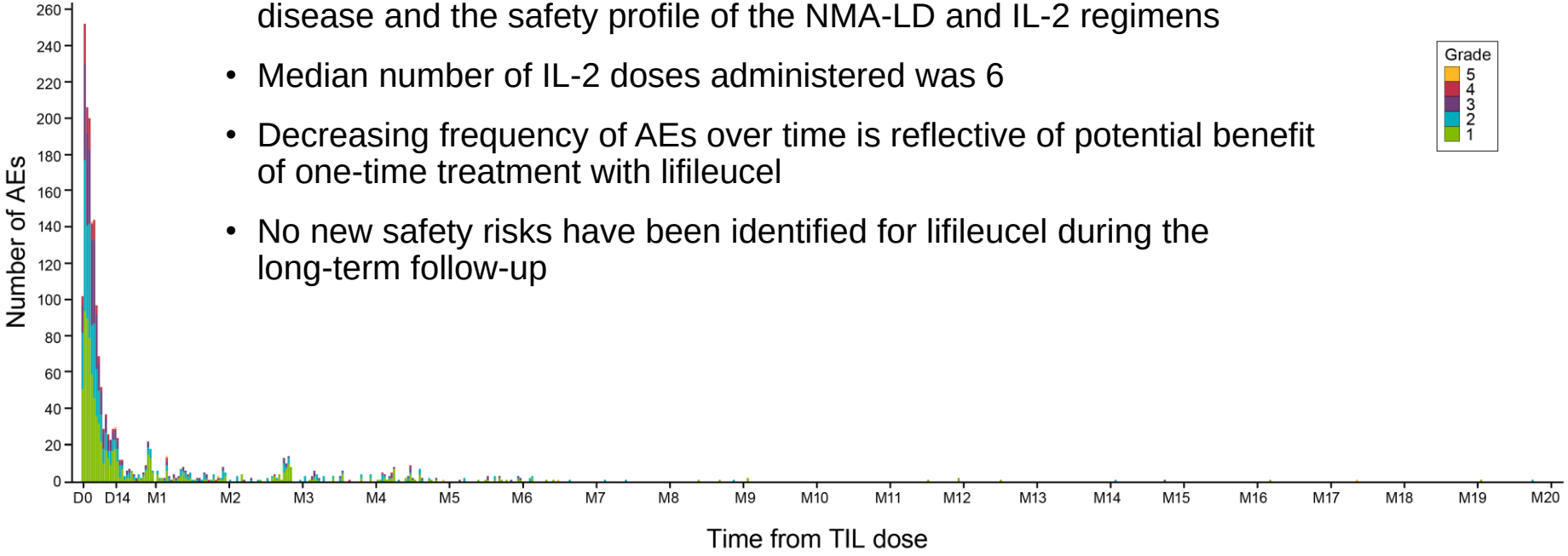
C-144-01 Cohort 2 Safety

Adverse Events over Time

- The adverse event profile was consistent with the underlying advanced disease and the safety profile of the NMA-LD and IL-2 regimens
- Median number of IL-2 doses administered was 6
- Decreasing frequency of AEs over time is reflective of potential benefit of one-time treatment with lifileucel
- No new safety risks have been identified for lifileucel during the long-term follow-up



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C-144-01 Cohort 2 Efficacy

RESPONSE	PATIENTS, N=66 n (%)
Objective Response Rate	**24 (36.4)**
Complete Response	3 (4.5)
Partial Response	21 (31.8)
Stable Disease	29 (43.9)
Progressive Disease	9 (13.6)
Non-Evaluable(1)	4 (6.1)
Disease Control Rate	53 (80.3)
Median Duration of Response	**Not Reached**
Min, Max (months)	2.2, 35.2+

- After a median study follow-up of 28.1 months, median DOR was still not reached (range 2.2, 35.2+)
- Mean number of TIL cells infused: 27.3 x 10^9
- Responses were demonstrated:
  - In patients who received prior anti-CTLA-4 or BRAF/MEK inhibitors
  - Regardless of BRAF mutational status
  - Regardless of Tumor PD-L1 expression
  - In patients with various LDH levels
  - In patients with various baseline tumor burden
  - In patients with liver and/or brain lesions
  - Regardless of time from stop of anti-PD-1/L1 to TIL infusion

(1) Not evaluable (NE) due to not reaching first assessment

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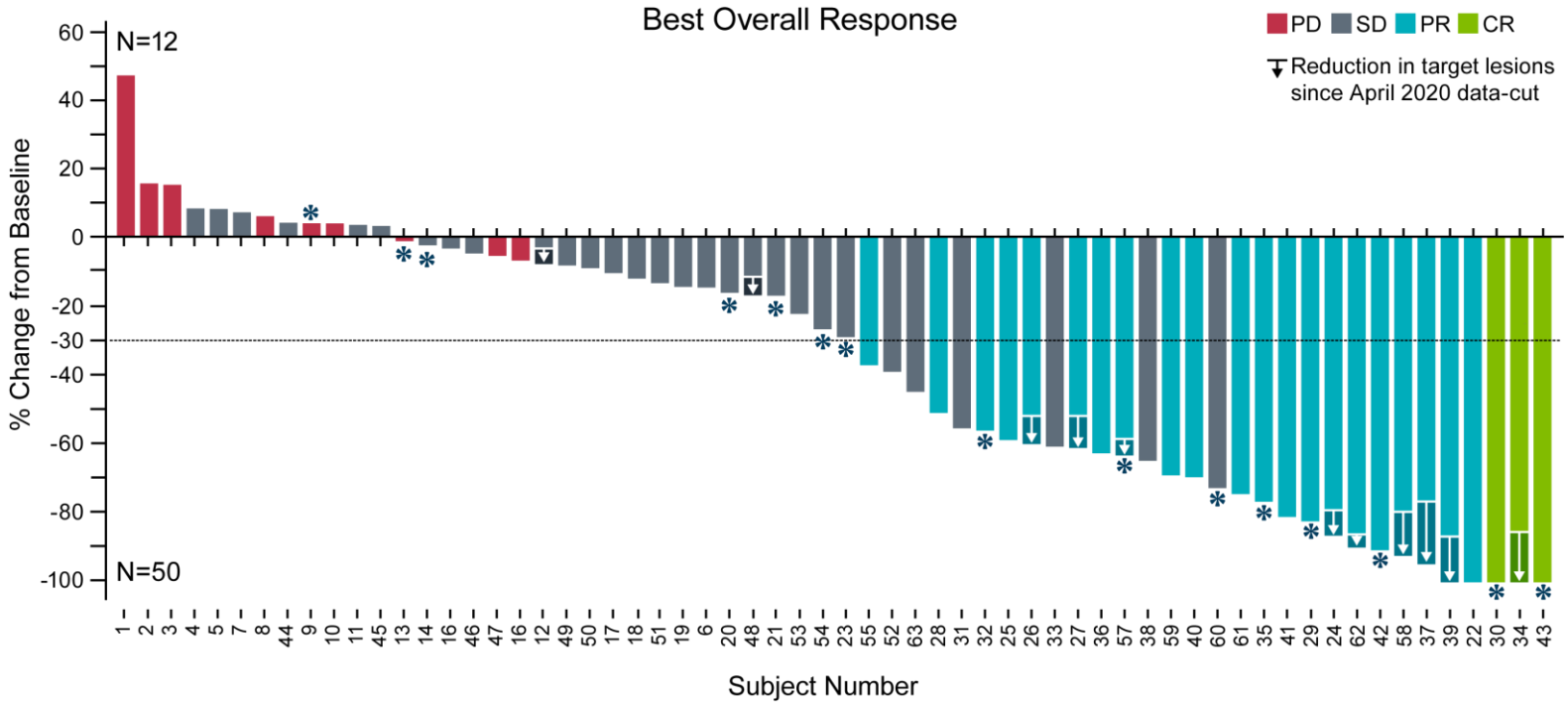
C-144-01 Cohort 2 Efficacy

Best Overall Response

- 81% (50/62) of patients had a reduction in tumor burden
- 11 patients (17.7%) had further SOD reduction since previous data cut (23 April 2020)



* Patients with BRAF V600 mutation

Three subjects had no post TIL disease assessment due to early death, and one due to start of new anti-cancer therapy

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C-144-01 Cohort 2 Efficacy

Time to Response for Evaluable Patients (PR or Better)

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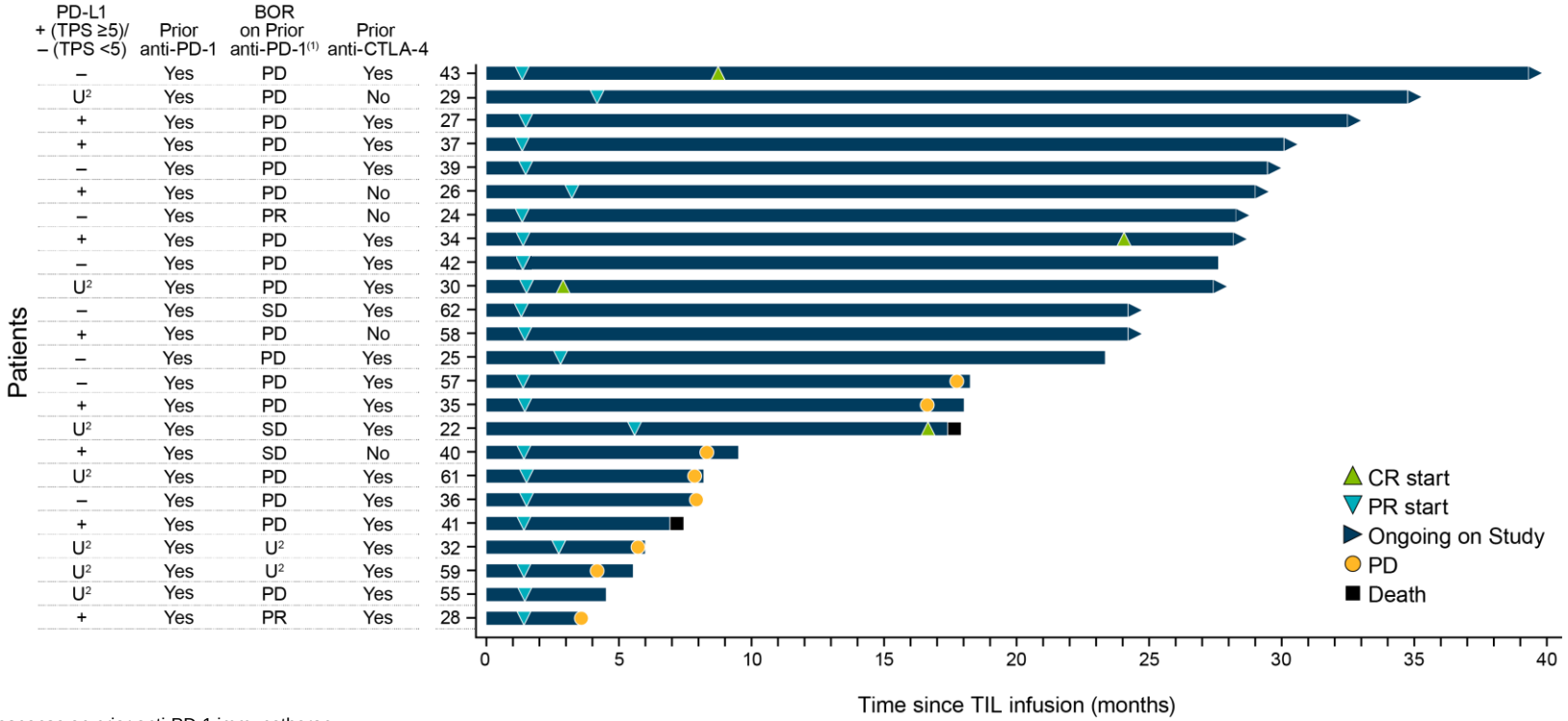
- 79% of responders had received prior ipilimumab
- One PR converted to CR after 24 months post-lifileucel



(1) BOR is best overall response on prior anti-PD-1 immunotherapy
(2) U: unknown
(3) Patient 22 BOR is PR

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C-144-01 Cohort 2 Biomarkers

Site of Tumor Resection

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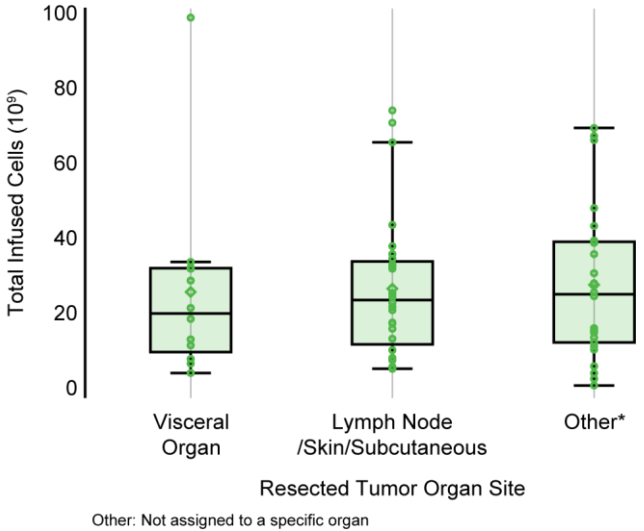
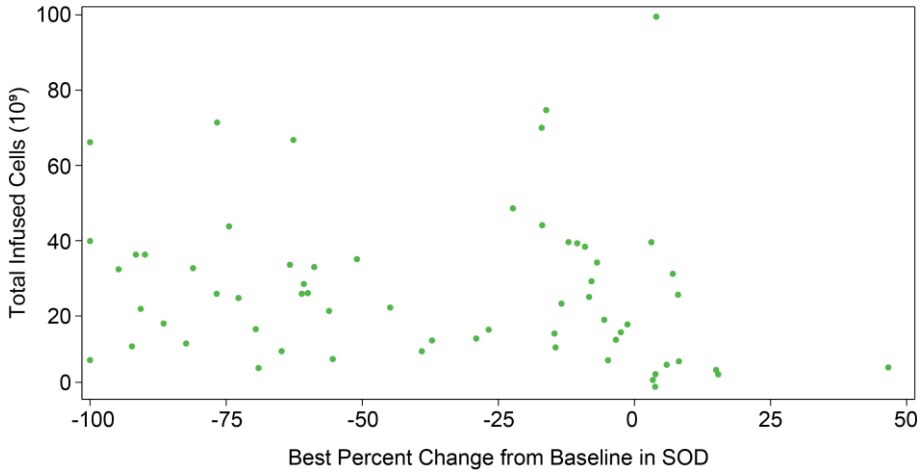
Site of Tumor Resection



Other: Not assigned to a specific organ

Total Cell Dose



- Appropriate amount of TIL was manufactured from tumors regardless of location of resection
- Target lesion SOD reductions were seen across the range of TIL total cell dose

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C-144-01 Cohort 2 Biomarkers

Infused Cell Dose

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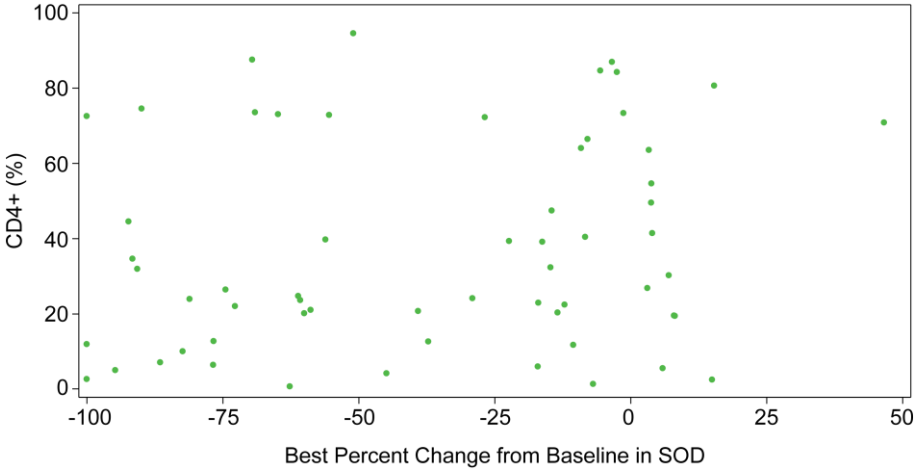
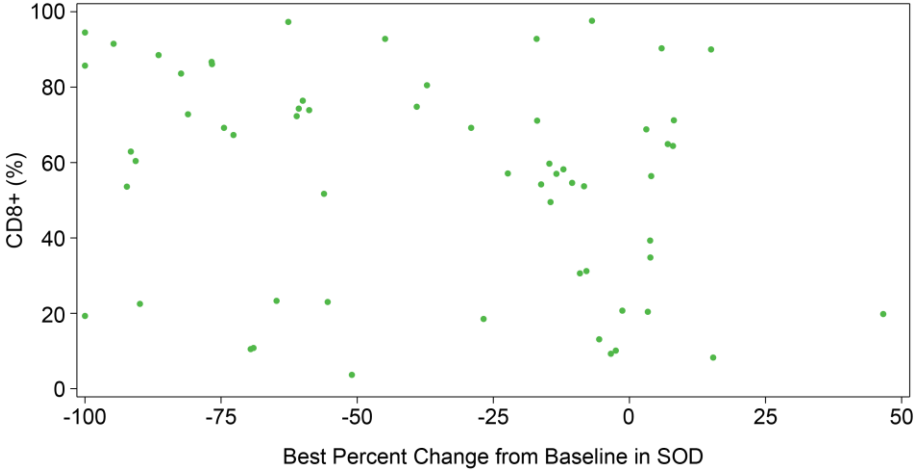
$CD4^+$ Cell Dose



$CD8^+$ Cell Dose



Target lesion SOD reductions were seen across the range of TIL $CD4^+$ and $CD8^+$ cell dose

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C-144-01 Cohort 2

Conclusions

- In heavily pretreated metastatic melanoma patients who progressed on multiple prior therapies, including anti-PD-1 and BRAFi/MEKi, if BRAFV600 mutant, lifileucel treatment resulted in:
  - 36.4% ORR
  - Median DOR not reached at 28.1 months of median study follow up
- Responses deepened over time:
  - 11 patients (17.7%) demonstrated further reduction in SOD since prior data cut in April 2020
  - One patient converted from PR to CR at 24 months post lifileucel infusion
- Lifileucel was successfully manufactured regardless of the organ site of the resected tumor
- Target lesion SOD reductions were not associated with total cell doses, or with $CD4^+$ or $CD8^+$ cell doses
- Lifileucel has demonstrated efficacy and durability of response for patients with metastatic melanoma and represents a viable therapeutic option warranting further investigation

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