AACR American Association for Cancer Research
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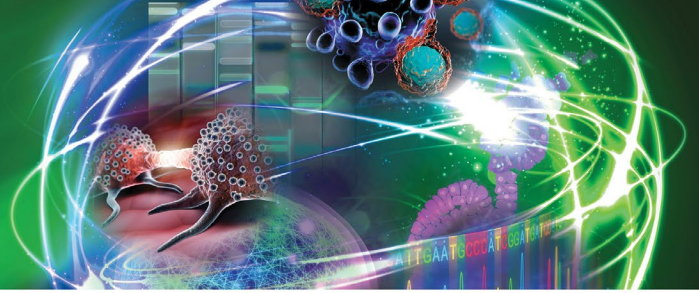

# Lifileucel (LN-144), a cryopreserved autologous tumor infiltrating lymphocyte (TIL) therapy in patients with advanced (unresectable or metastatic) melanoma: sustained duration of response at 28 month follow up

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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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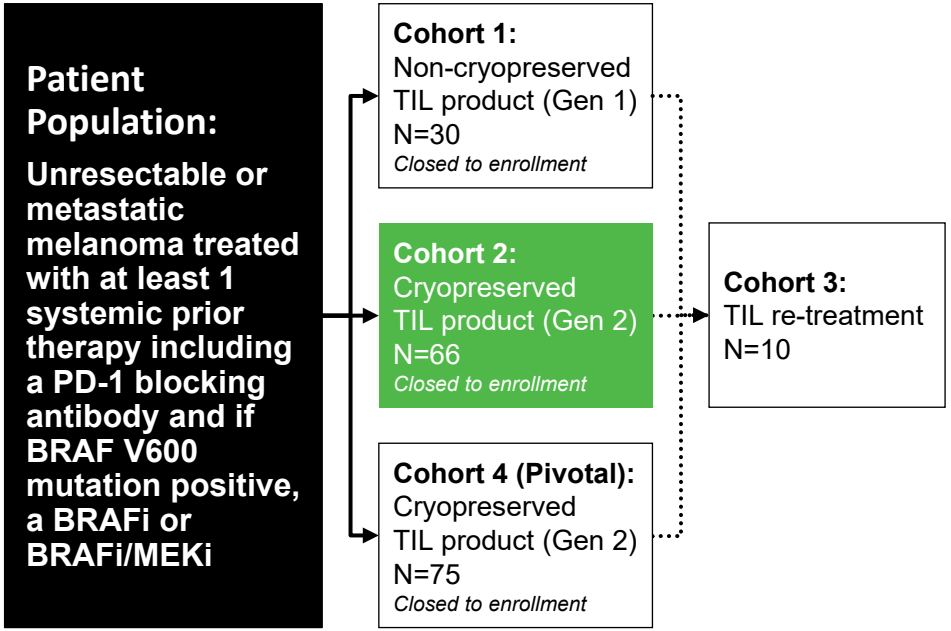
# Iovance C-144-01 Study Design



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

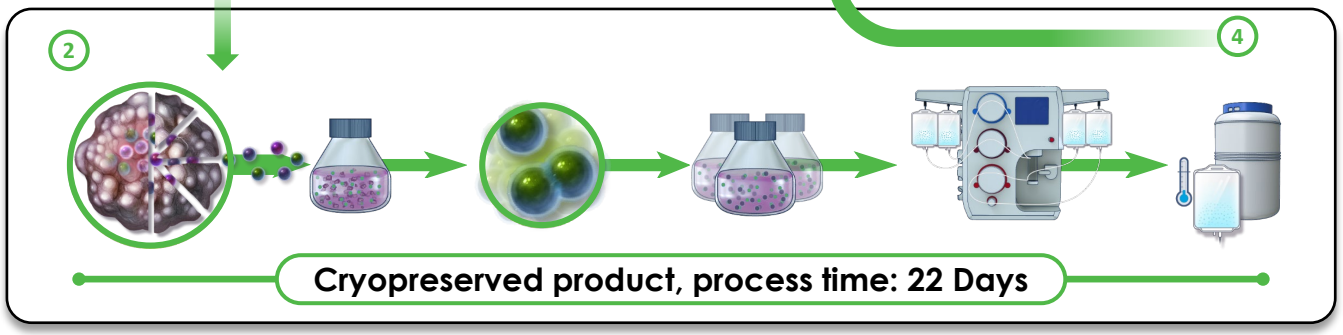
4 **Lifileucel Infusion**

- 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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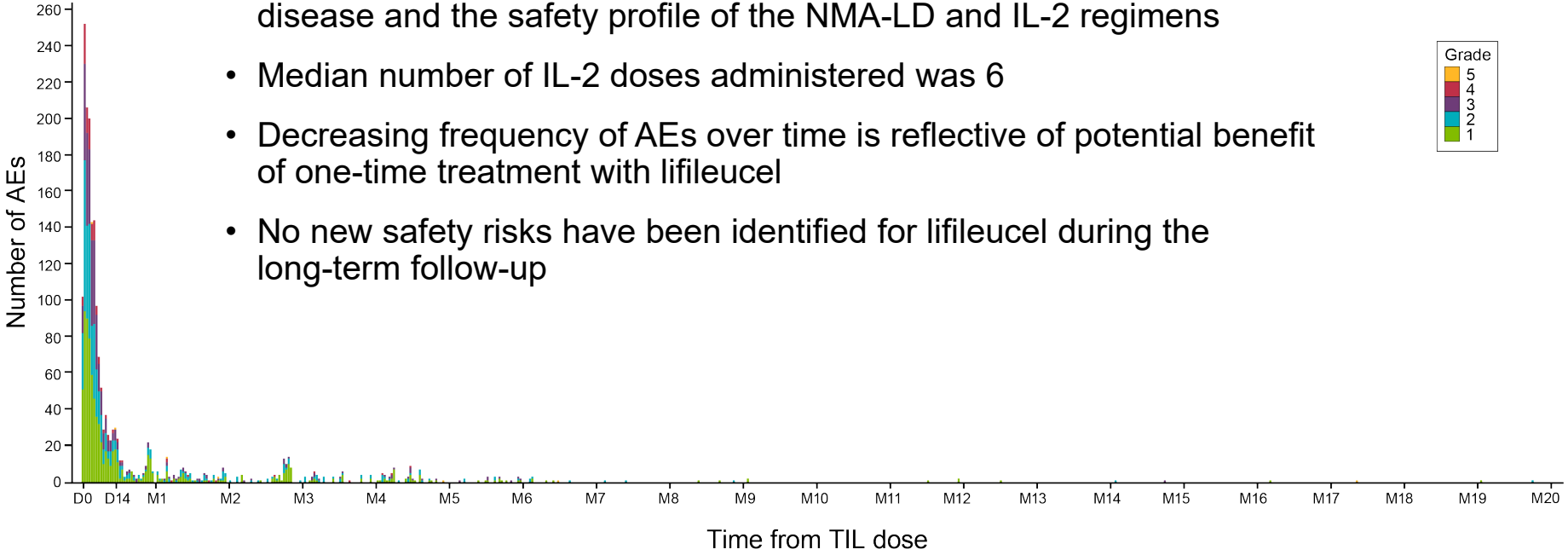
# C-144-01 Cohort 2 Safety

## *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*

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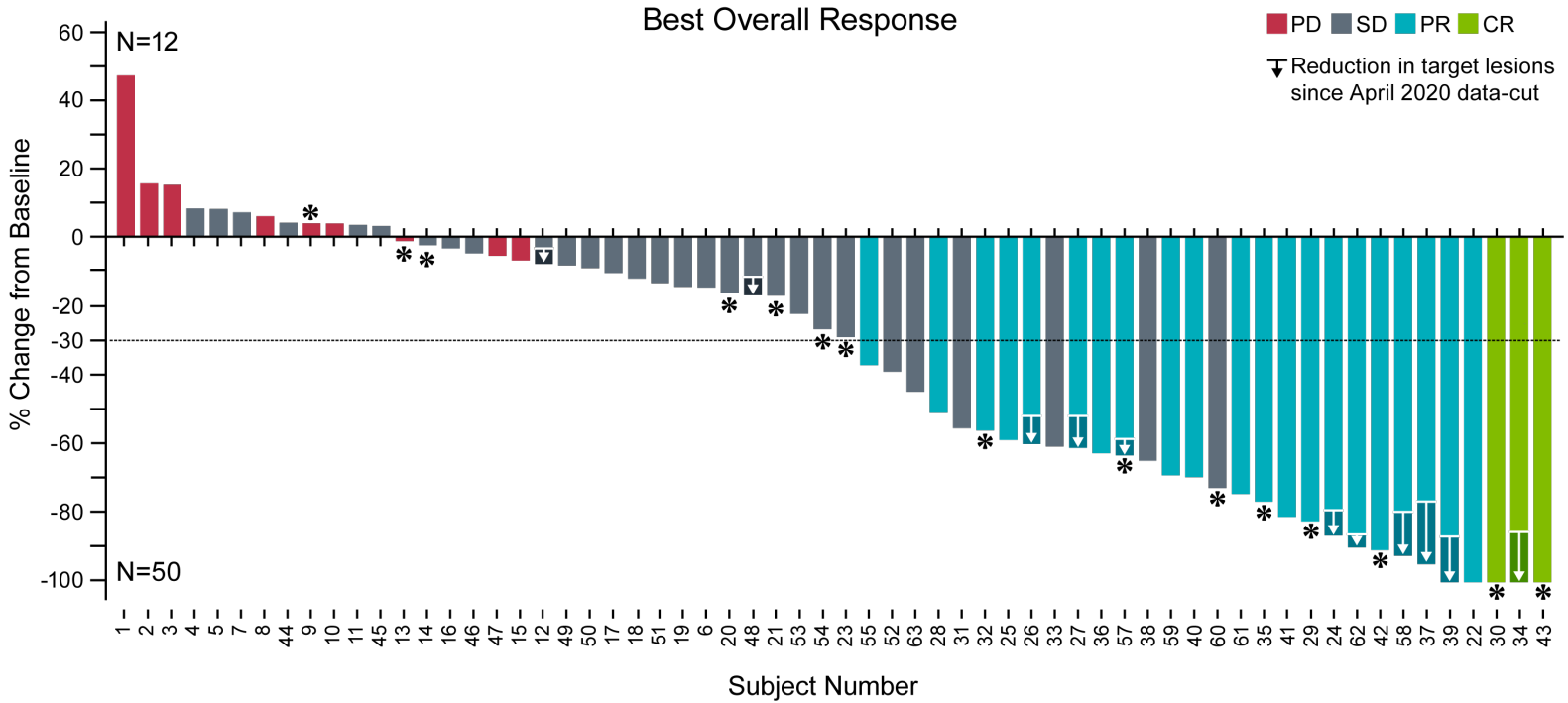
- 81% (50/62) of patients had a reduction in tumor burden
- 11 patients (17.7%) had further SOD reduction since previous data cut (23 April 2020)




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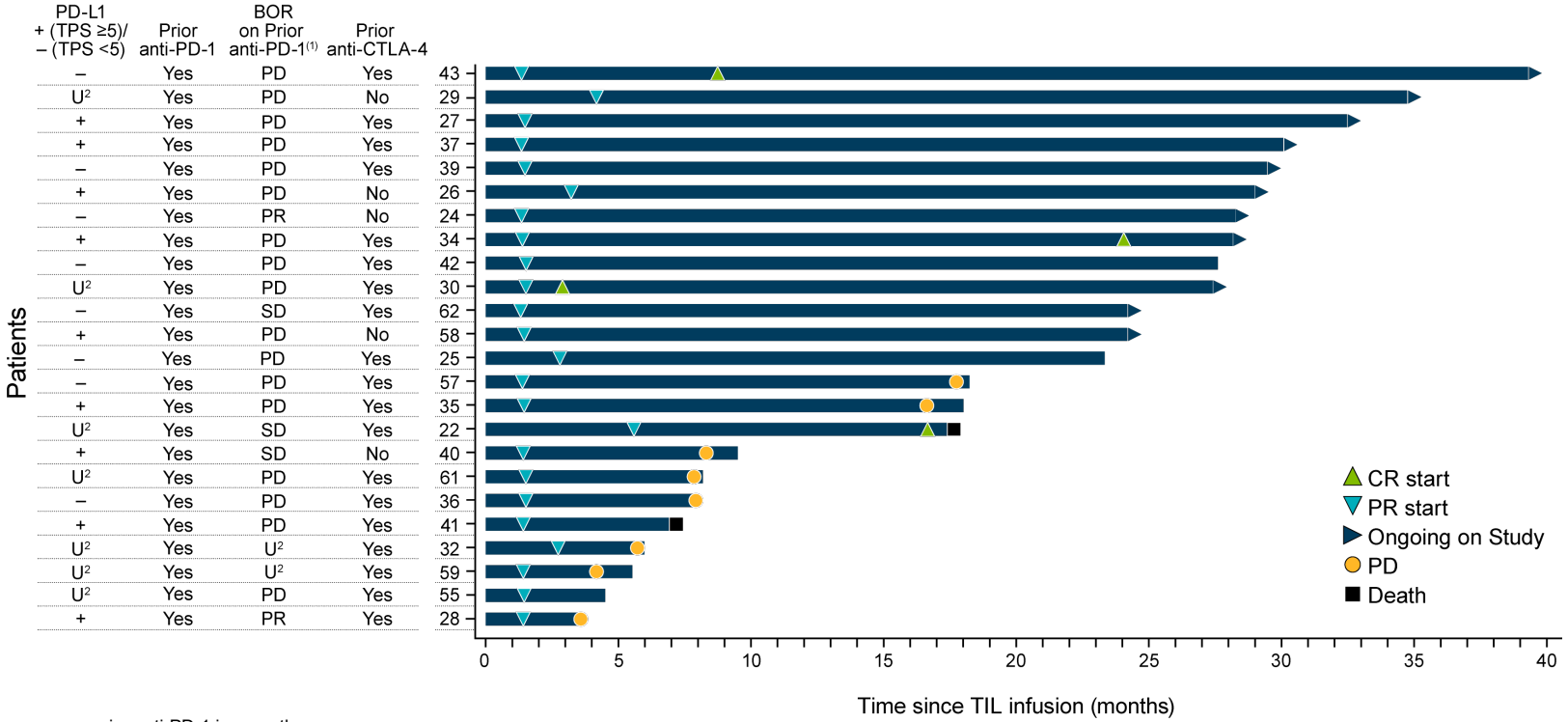
- 79% of responders had received prior ipilimumab
- One PR converted to CR after 24 months post-lifileucel




(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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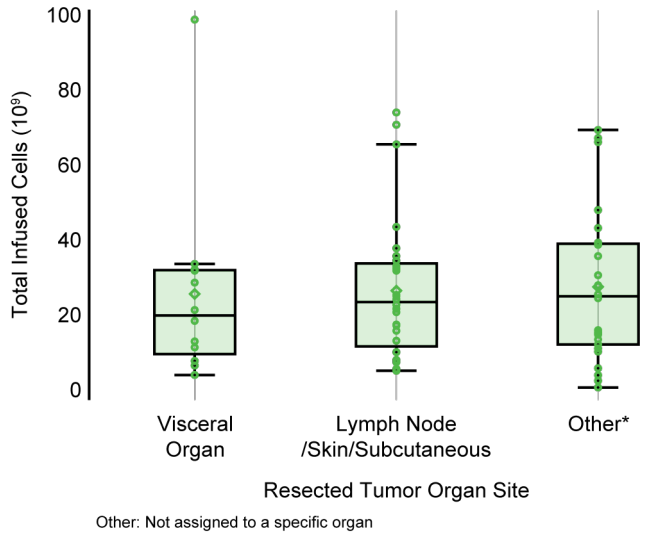
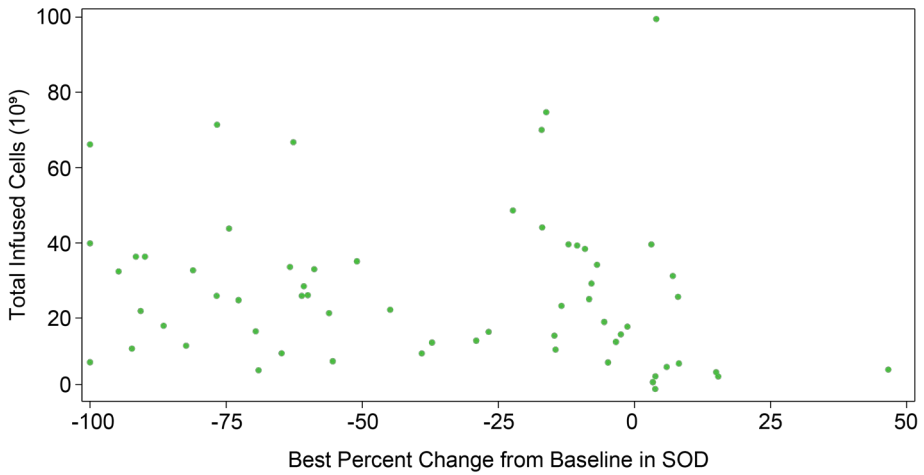
### Site of Tumor Resection




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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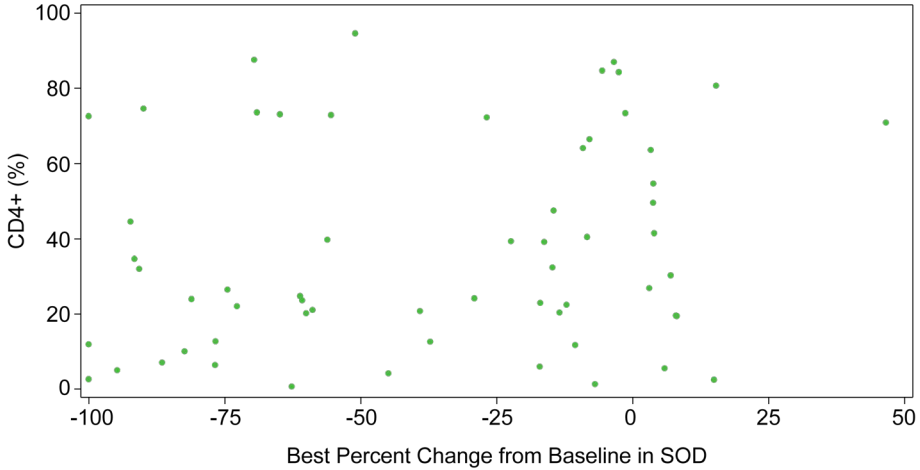
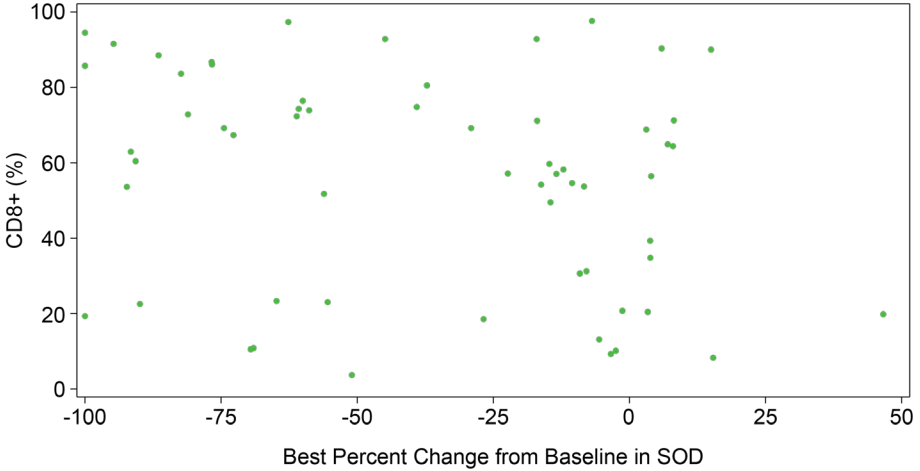
## $CD4^+$ Cell Dose




## $CD8^+$ 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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# Acknowledgments


- The authors would like to thank the patients and their families for participation in the study
- The authors would also like to acknowledge the support and dedication of all site team members from the clinical trial institutions
- The authors would like to acknowledge the Iovance team for their contributions