IOVANCE BIOTHERAPEUTICS

ADVANCING IMMUNO-ONCOLOGY

ASCO Update Call

June 6, 2021

Agenda

- **Corporate Update**: Fred Vogt, incoming Interim CEO and President
- **ASCO Updates for Lifileucel in Advanced Melanoma**: Omid Hamid, MD, Chief of Research/Immuno-Oncology, The Angeles Clinic & Research Institute
- **Financial Summary**: Jean-Marc Bellemin, CFO
- **Q&A Session**

Forward Looking Statements

Certain matters discussed in this presentation are “forward-looking statements” of Iovance Biotherapeutics, Inc, Inc. (hereinafter referred to as the “Company,” “we,” “us,” or “our”) within the meaning of the Private Securities Litigation Reform Act of 1995 (the “PSLRA”). All such written or oral statements made in this presentation, other than statements of historical fact, are forward-looking statements and are intended to be covered by the safe harbor for forward-looking statements provided by the PSLRA. Without limiting the foregoing, we may, in some cases, use terms such as “predicts,” “believes,” “potential,” “continue,” “estimates,” “anticipates,” “expects,” “plans,” “intends,” “forecast,” “guidance,” “outlook,” “may,” “could,” “might,” “will,” “should” or other words that convey uncertainty of future events or outcomes and are intended to identify forward-looking statements. Forward-looking statements are based on assumptions and assessments made in light of management’s experience and perception of historical trends, current conditions, expected future developments and other factors believed to be appropriate. Forward-looking statements in this press release are made as of the date of this press release, and we undertake no duty to update or revise any such statements, whether as a result of new information, future events or otherwise. Forward-looking statements are not guarantees of future performance and are subject to risks, uncertainties and other factors, many of which are outside of our control, that may cause actual results, levels of activity, performance, achievements and developments to be materially different from those expressed in or implied by these forward-looking statements. Important factors that could cause actual results, developments and business decisions to differ materially from forward-looking statements are described in the sections titled “Risk Factors“ in our filings with the Securities and Exchange Commission, including our most recent Annual Report on Form 10-K and Quarterly Reports on Form 10-Q, and include, but are not limited to, the following substantial known and unknown risks and uncertainties inherent in our business: the effects of the COVID-19 pandemic; risks related to the timing of and our ability to successfully develop, submit, obtain and maintain U.S. Food and Drug Administration (“FDA”) or other regulatory authority approval of, or other action with respect to, our product candidates, and our ability to successfully commercialize any product candidates for which we obtain FDA approval; preliminary and interim clinical results, which may include efficacy and safety results, from ongoing clinical trials may not be reflected in the final analyses of our ongoing clinical trials or subgroups within these trials; the risk that enrollment may need to be adjusted for our trials and cohorts within those trials based on FDA and other regulatory agency input; the new version of the protocol which further defines the patient population to include more advanced patients in our cervical cancer trial may have an adverse effect on the results reported to date; the risk that we may be required to conduct additional clinical trials or modify ongoing or future clinical trials based on feedback from the FDA or other regulatory authorities; the risk that our interpretation of the results of our clinical trials or communications with the FDA may differ from the interpretation of such results or communications by the FDA; the acceptance by the market of our product candidates and their potential reimbursement by payors, if approved; our ability or inability to manufacture our therapies using third party manufacturers or our own facility may adversely affect our potential commercial launch; the results of clinical trials with collaborators using different manufacturing processes may not be reflected in our sponsored trials; the risk that unanticipated expenses may decrease our estimated cash balances and increase our estimated capital requirements; and other factors, including general economic conditions and regulatory developments, not within our control.

2020 Accomplishments; Anticipated 2021 Milestones

	2020	2021
Regulatory	☑ Agreement with FDA on melanoma Cohort 4 clinical follow up; Cohort 2 supportive	☐ **BLA**: FDA feedback received for potency assays; additional assay data submission and interactions planned in 2H21
Clinical	☑ **Melanoma**: early pivotal Cohort 4 data and updated Cohort 2 data ☑ **Cervical**: last patient dosed in cervical pivotal cohort ☑ **NSCLC**: Moffitt TIL data; registration directed study initiated ☑ **HNSCC**: initial data for TIL + pembrolizumab	☑ **Melanoma:** TIL + pembrolizumab data at ASCO ☑ **Cervical**: last patient dosed in Cohort 2, potential to include in BLA ☐ **NSCLC:** patient dosing in IOV-LUN-202 ☑ **HNSCC:** expanding TIL + pembrolizumab in basket study
Manufacturing	☑ Gen 3 process in clinic ☑ >90% success rate in >400 patients	☑ **Melanoma**: 16-day Gen 3 process in clinic ☐ Completion of Navy Yard GMP facility (*i*CTC); start clinical manufacturing at *i*CTC

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Lifileucel Clinical Data in Advanced Melanoma

Omid Hamid, MD

Chief of Research/Immuno-Oncology,

The Angeles Clinic & Research Institute

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Lifileucel (LN-144), a Cryopreserved Autologous Tumor Infiltrating Lymphocyte (TIL) Therapy in Patients with Advanced Melanoma: Evaluation of Impact of Prior Anti–PD-1 Therapy

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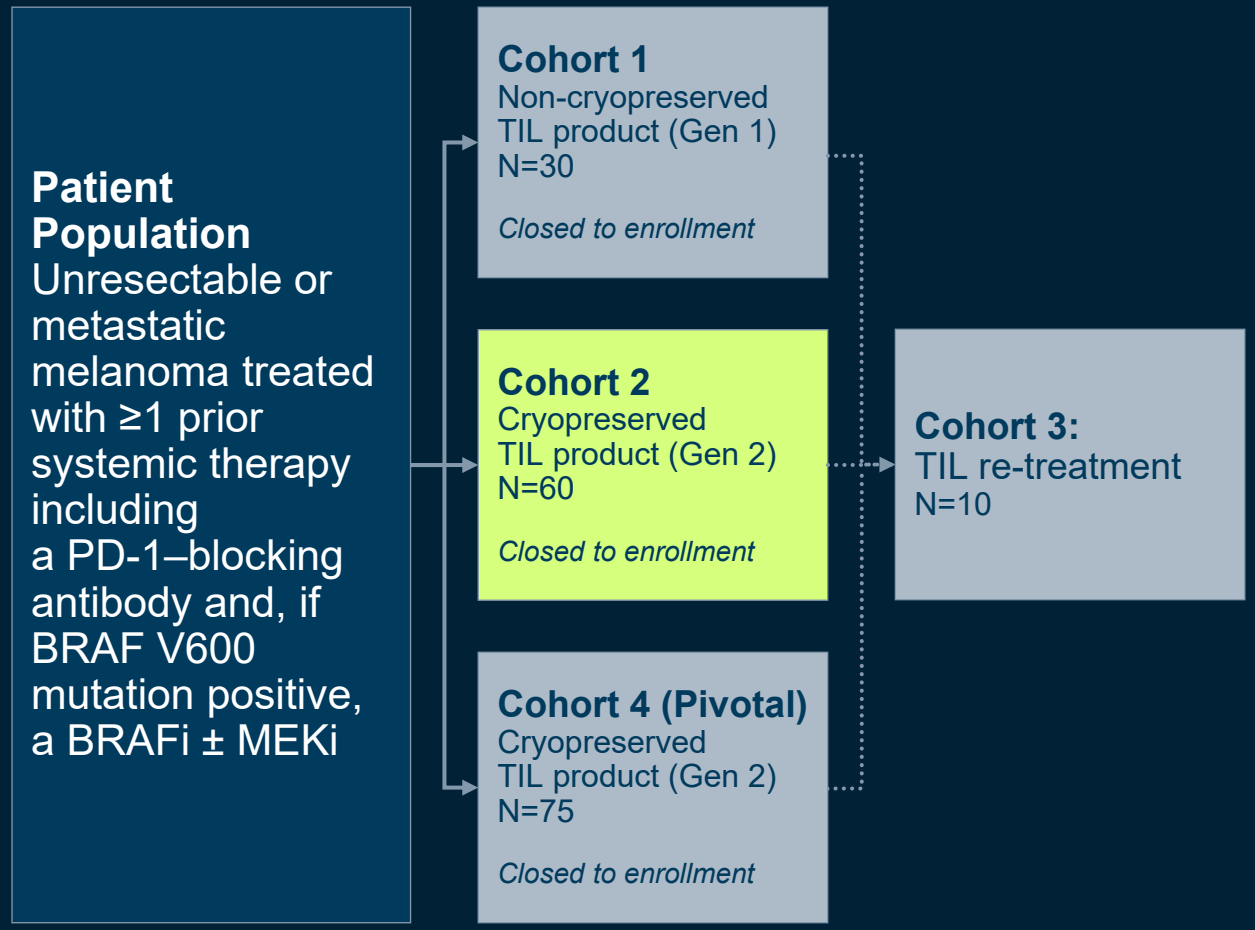
C-144-01 Study Design

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



Cohort 2 Endpoints

- Primary: Efficacy per investigator-assessed ORR using RECIST 1.1 response criteria
- Secondary: Safety and additional parameters of efficacy

Key Eligibility Criteria

- Radiographic confirmation of progression
- One tumor lesion resectable for TIL generation (~1.5 cm in diameter) and ≥1 target tumor lesion for RECIST 1.1 response assessment
- Age ≥18 years at the time of consent
- ECOG performance status of 0–1

Methods

- Patients were enrolled from April 2017 to January 2019 at 26 sites across the US and EU
- Concomitant anticancer therapy was not permitted
- Imaging-evaluable disease was required
- All responses required confirmation
- Data cutoff: 22 April 2021

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Abbreviations: BRAFi, BRAF inhibitor; ECOG, Eastern Cooperative Oncology Group; MEKi, MEK inhibitor; ORR, objective response rate; PD-1, programmed cell death protein 1; RECIST, Response Evaluation Criteria in Solid Tumors; TIL, tumor infiltrating lymphocytes.

C-144-01 Cohort 2 Baseline Patient Characteristics

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 number of prior therapies	3.3
Anti–PD-1 / Anti–PD-L1	66 (100)
Anti–CTLA-4[1]	53 (80)
Anti–PD-1 + Anti–CTLA-4	34 (52)
BRAFi/MEKi	15 (23)
Progressive Disease for ≥1 Prior Therapy, n (%)	
Anti–PD-1	65 (99)
Anti–CTLA-4	41 (77[(1)])
ECOG Performance Status, n (%)	
0	37 (56)
1	29 (44)

Characteristic	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)
LDH, n (%)	
≤ULN	39 (59)
>1 to 2 times ULN	19 (29)
> 2 times ULN	8 (12)
Target Lesions Sum of Diameter (mm)	
Mean (SD)	106 (71)
Min, Max	11, 343
Number of Target and Non-Target Lesions	
>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

Abbreviations: BRAFi, BRAF inhibitor; CTLA-4, cytotoxic T-lymphocyte antigen-4; ECOG, Easter Cooperative Oncology Group; LDH, lactate dehydrogenase; MEKi, MEK inhibitor; mm, millimeter; PD-1, programmed cell death protein-1; PD-L1, programmed death ligand-1; SD, standard deviation; TPS, tumor proportion score; ULN, upper limit of normal.

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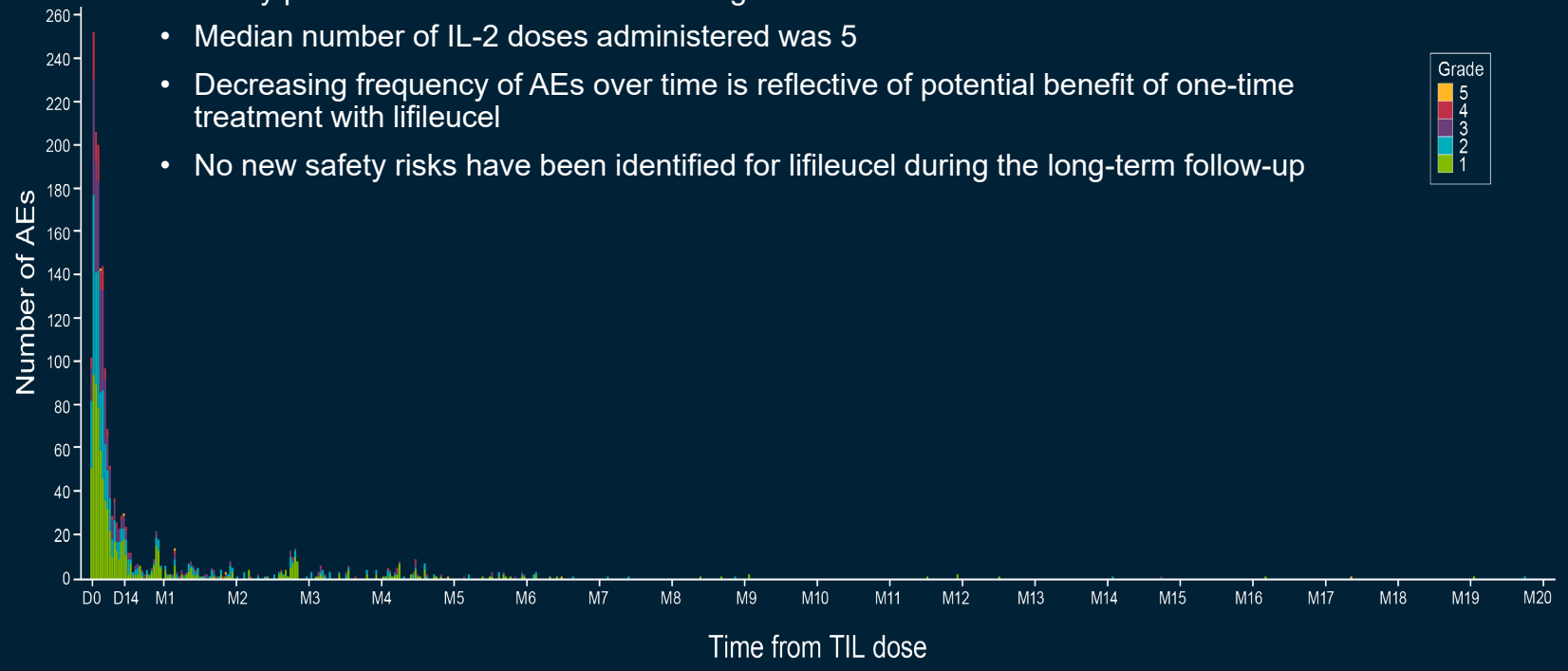
Iovance C-144-01 Cohort 2 Safety: Treatment Emergent Adverse Events (≥ 30%)

- 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 5
- 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



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 Efficacy

- After a median study follow-up of 33.1 months, median DOR was still not reached (range 2.2, 38.5+)
- 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, tumor PD-L1 expression, or time from stop of anti-PD-1/L1 to TIL infusion
  - In patients with various LDH levels or baseline tumor burden
  - In patients with liver and/or brain lesions

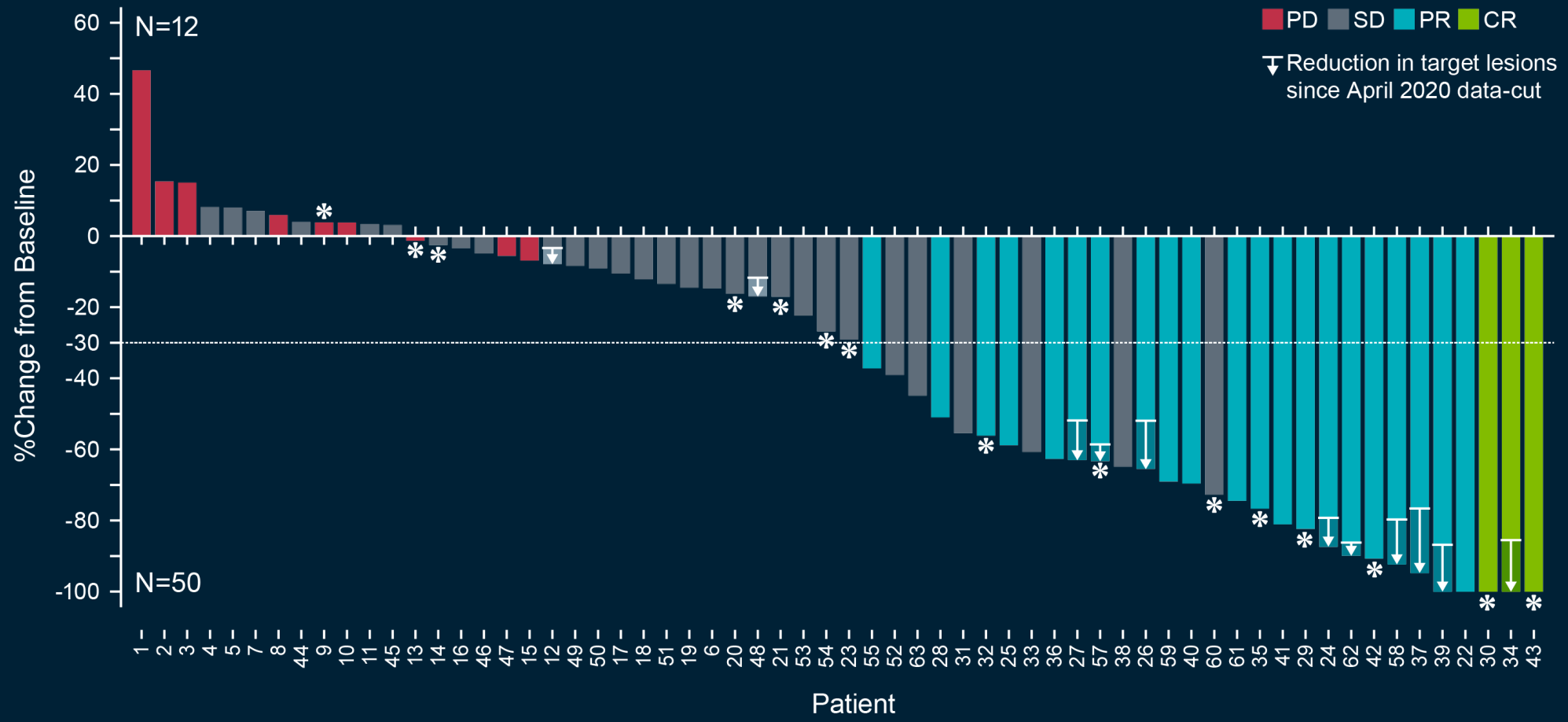
Response	Patients, n=66 N (%)
Objective Response Rate	**24 (36.4)**
Complete Response	3 (4.5)
Partial Response	21 (31.8)
Stable Disease	29 (43.9)
Progressive Disease	9 (13.6)
Non-Evaluable(1)	4 (6.1)
Disease Control Rate	53 (80.3)
Median Duration of Response	**Not Reached**
Min, Max (months)	2.2, 38.5+

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

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 April 2020 data cut



*Patients with BRAF V600 mutation
Three patients had no post-TIL disease assessment due to early death, and one due to start of new anti-cancer therapy

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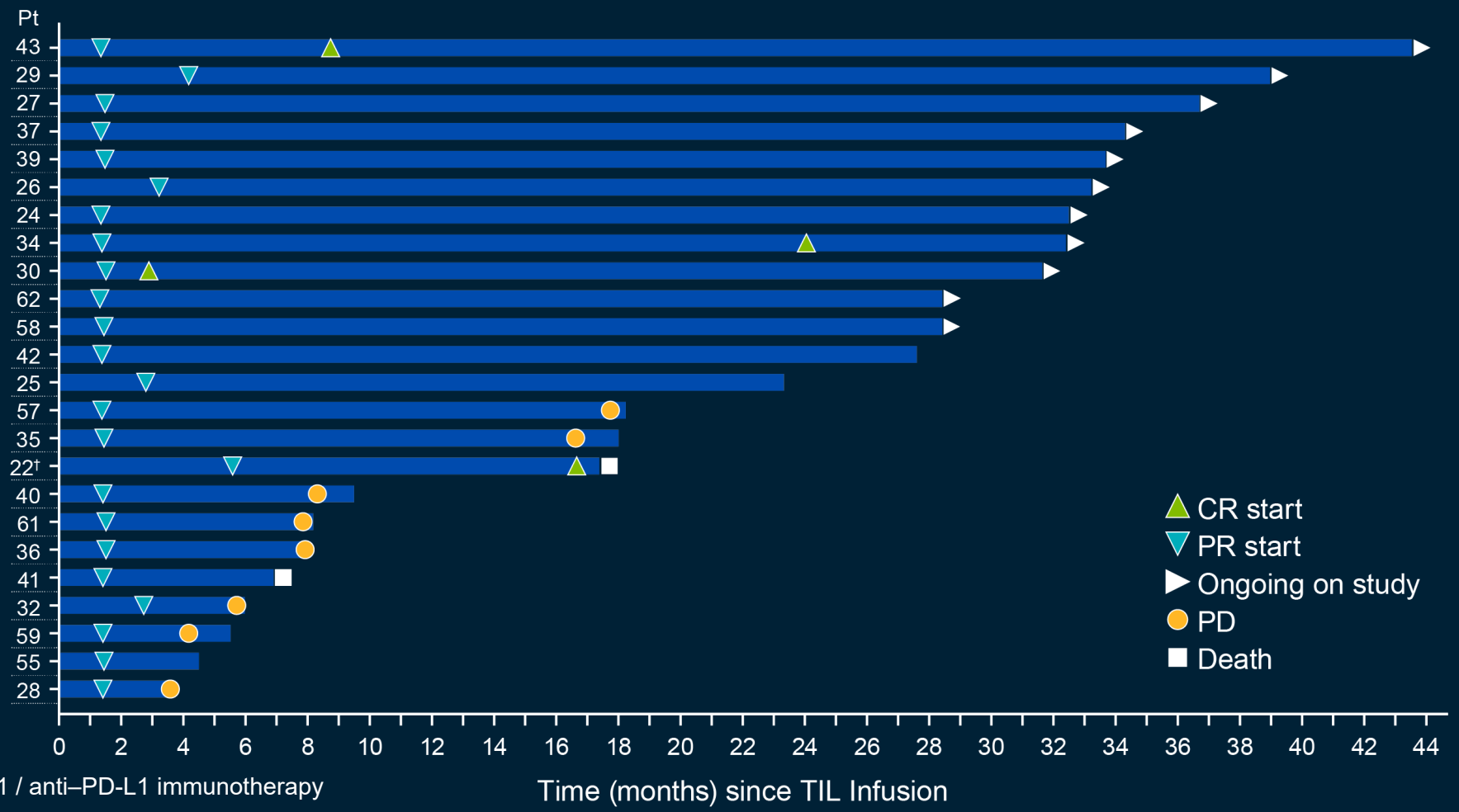
C-144-01 Cohort 2 Efficacy

Time to Response for Evaluable Patients (PR or Better)

- 79% of responders received prior ipilimumab
  - 46% of responders received prior anti–PD-1 / anti–CTLA-4 combination
- Responses continue to deepen over time
  - 17.7% of patients had deepening of response; 1 PR converted to CR after 24 months post-lifileucel

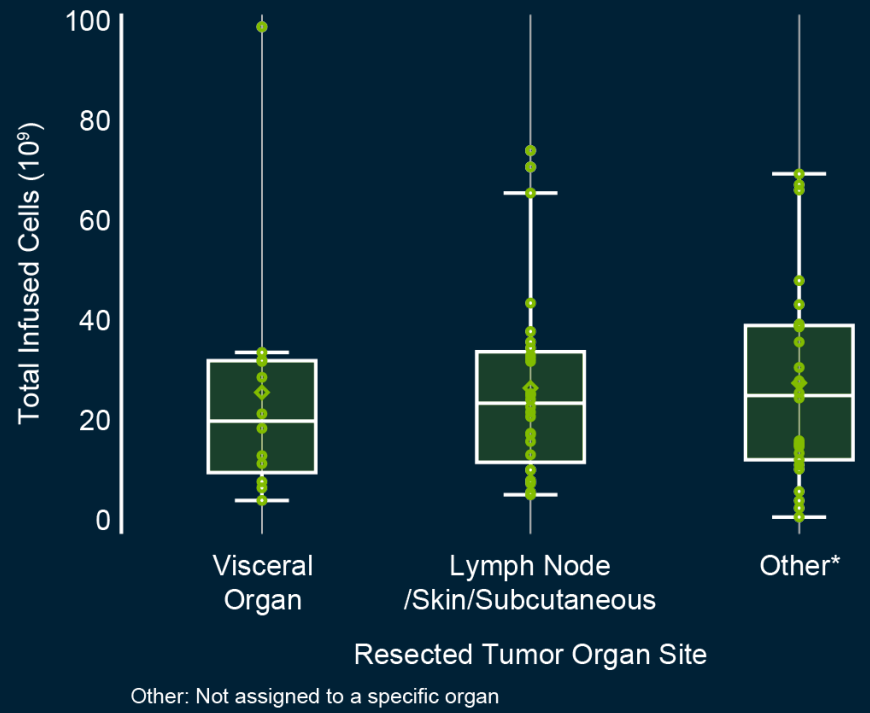


*BOR is best overall response on prior anti–PD-1 / anti–PD-L1 immunotherapy
†Patient 22 BOR is PR

C-144-01 Cohort 2 Biomarkers

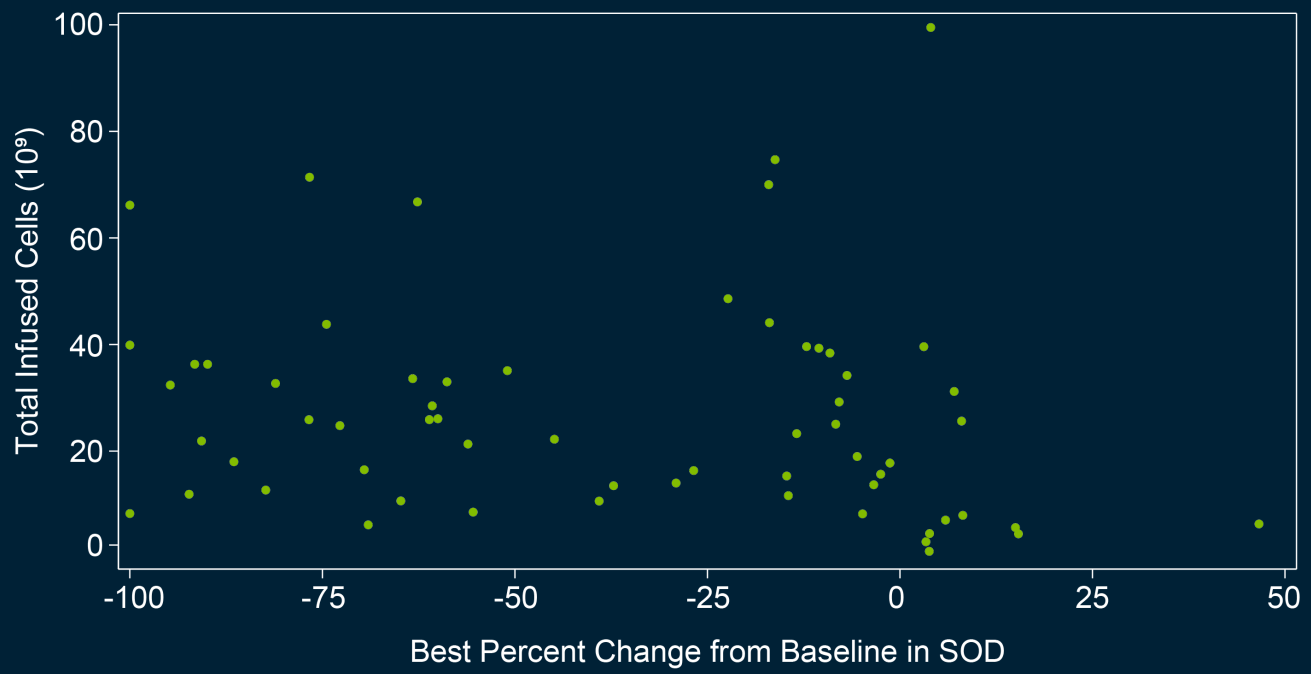
Site of Tumor Resection

Site of Tumor Resection



Other: Not assigned to a specific organ

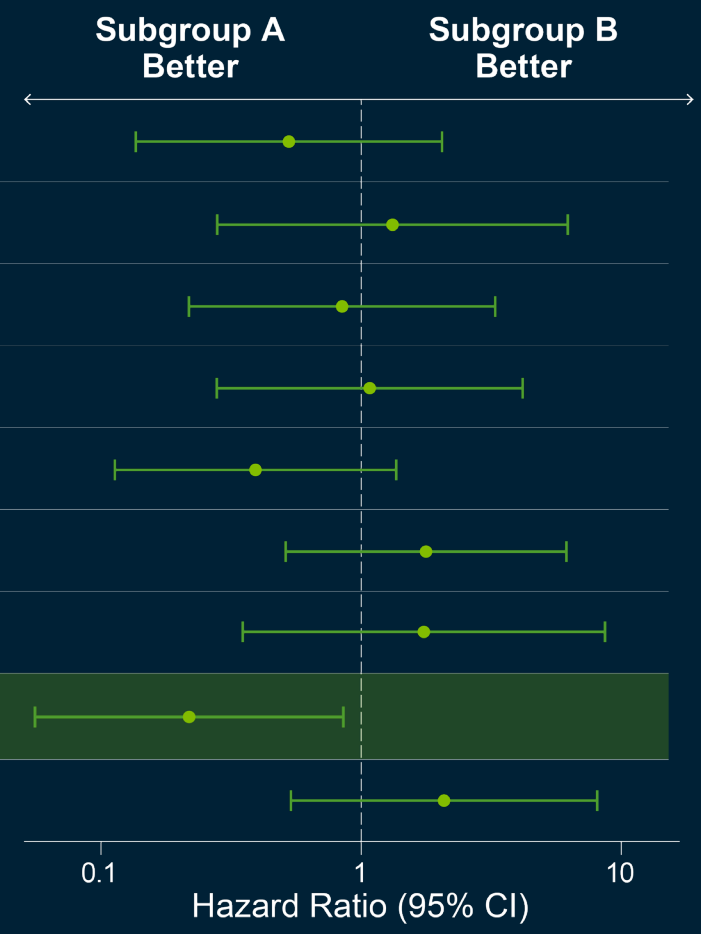
Total Cell Dose



- 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

Univariable Analyses*: DOR of Lifileucel

Parameter	Subgroup A vs B	N in Subgroup A	N in Subgroup B	HR (95% CI)
Age Group	<65 vs ≥65	19	5	0.527 (0.136, 2.046)
Prior CTLA-4 Use	Yes vs No	19	5	1.320 (0.280, 6.233)
BRAF Mutation Status	Yes vs No	7	17	0.845 (0.218, 3.278)
Baseline ECOG	0 vs ≥1	16	8	1.079 (0.279, 4.179)
Baseline LDH	≤ULN vs >ULN	15	9	0.393 (0.113, 1.364)
Baseline Brain/Liver Lesion	Yes vs No	9	15	1.776 (0.513, 6.154)
Cumulative Duration on Anti–CTLA-4	≤Median (2.10m) vs >Median	13	6	1.743 (0.350, 8.664)
Cumulative Duration on Anti–PD-1/PD-L1	**≤Median (5.06m) vs >Median**	**14**	**10**	**0.218 (0.056, 0.854)**
Baseline Target Lesion SOD	<70mm vs ≥70mm	14	10	2.083 (0.537, 8.079)



- Although cumulative duration on prior anti–PD-1 / anti–PD-L1 was not associated with achieving a response (ORR), it was associated with DOR

*Univariable Cox proportional hazards regression model was used to estimate hazard ratios with 95% confidence intervals between subgroups on DOR.

Multivariable Model*: Independent Predictors for Lifileucel DOR

- Variables from the univariable analyses were examined using the best subset approach
- Two parameters were identified:
  - Baseline LDH
  - Cumulative duration of prior anti–PD-1 / anti–PD-L1

		Responders (N=24)	
Parameter	**Comparison**	**HR (95% CI)**	***P*-value**
Baseline LDH	≤ULN vs >ULN	0.201 (0.040, 0.996)	0.049
Cumulative duration on prior anti–PD-1 / anti–PD-L1	For each 3-month decrease in exposure to prior anti–PD-1 / anti–PD-L1	0.715 (0.518, 0.987)	0.041
	For each 6-month decrease in exposure to prior anti–PD-1 / anti–PD-L1	0.511 (0.268, 0.974)	

› For each 6-month decrease in exposure to prior anti–PD-1 / anti–PD-L1, the median DOR to lifileucel will be nearly doubled†

*Cox proportional hazards regression model.
†Assuming the data follow exponential distribution.

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 33.1 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
- Prior anti–PD-1 therapy:
  - Shorter duration of prior anti–PD-1 therapy maximizes DOR to lifileucel treatment
  - All newly diagnosed patients should be closely monitored for progression on anti–PD-1 therapy
  - ❯ **Early intervention with lifileucel at the time of initial progression on anti–PD-1 agents may maximize benefit**

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Safety and efficacy of lifileucel (LN-144), an autologous tumor-infiltrating lymphocyte cell therapy, in combination with pembrolizumab for immune checkpoint inhibitor–naïve patients with advanced melanoma

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Methods

Study Design

- IOV-COM-202 is a prospective, open-label, multicohort, nonrandomized, multicenter Phase 2 study evaluating TIL cell therapy in multiple settings and indications
- We report on Cohort 1A, which is enrolling patients with ICI-naïve advanced melanoma (unresectable or metastatic) for treatment with a combination of lifileucel + pembrolizumab

Cohort 1A Patients

- Key eligibility criteria include age ≥18 years, ICI-naïve, ≤3 lines of prior systemic therapy, ECOG PS 0–1, ≥1 resectable lesion (~1.5 cm in diameter) for lifileucel manufacturing, and ≥1 measurable lesion post-resection for response assessment

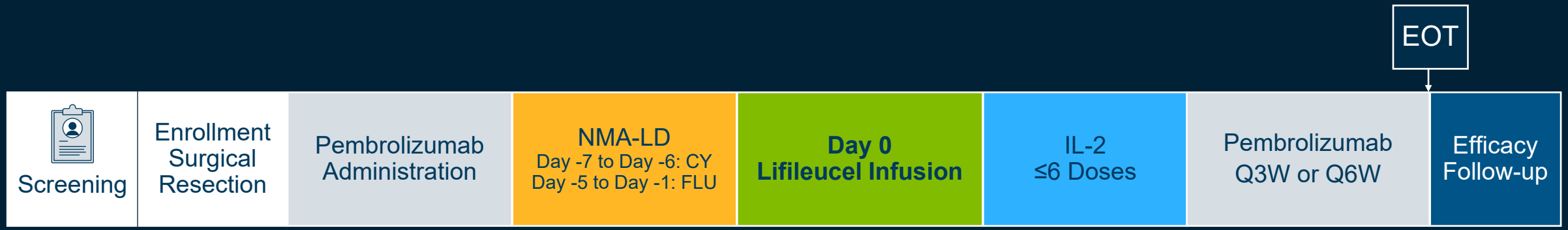
Primary Endpoints

- Efficacy, defined as investigator-assessed objective response rate (ORR) per RECIST 1.1
- Safety, as measured by incidence of Grade ≥3 treatment-emergent adverse events (TEAEs)

Data cutoff: 29 April 2021

Abbreviations: ECOG PS, Eastern Cooperative Oncology Group performance status; ICI, immune checkpoint inhibitor; ORR, objective response rate; RECIST, Response Evaluation Criteria in Solid Tumors.

Cohort 1A Patient Treatment Schema



Abbreviations: EOT, end of treatment; IL-2, interleukin-2; NMA-LD, non-myeloablative lymphodepletion.

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Baseline Patient Characteristics

Characteristic	Cohort 1A (N=7)
Gender, n (%)	
Female	1 (14.3)
Male	6 (85.7)
Age, years	
Median	52.0
Min, max	34, 59
Number of Systemic Prior Therapies, n (%)	
0	5 (71.4)
1	2 (28.6)
Systemic Prior Therapy Type, n (%)	
Chemotherapy	1 (14.3)
Targeted therapy (BRAFi/MEKi)	1 (14.3)
Immunotherapy	0
Other*	1 (14.3)
Baseline ECOG Performance Status, n (%)	
0	5 (71.4)
1	2 (28.6)
Stage, n (%)	
IIIC	1 (14.3)
IV (metastatic)	6 (85.7)

Characteristic	Cohort 1A (N=7)
BRAF Status, n (%)	
Mutated V600E or V600K	1 (14.3)
Wild type	3 (42.9)
Unknown	1 (14.3)
Other†	2 (28.6)
Tumor PD-L1 Expression, n (%)	
PD-L1 positive (TPS ≥5%)	4 (57.1)
PD-L1 negative (TPS <5%)	2 (28.6)
Missing	1 (14.3)
Baseline LDH, n (%)	
<ULN	4 (57.1)
1–2 × ULN	2 (28.6)
>2 × ULN	1 (14.3)
Target Lesions Sum of Diameters (mm)	
Mean	111.4
Min, max	32, 355
Baseline Number of Target and Non-Target Lesions	
>3, n (%)	6 (85.7)
Mean (SD)	4.9 (1.4)
Liver and/or brain lesions, n (%)	5 (71.4)

At baseline:

- Patients had high tumor burden: 111.4 mm mean target lesion sum of diameters
- 42.9% of patients had elevated LDH
- 85.7% of patients had >3 lesions

Please refer to Poster 9537 for full safety data

*1 patient received prednisone as part of chemotherapy regimen.
†2 patients with BRAF mutations other than V600E or V600K: 1 with T599_V600insT mutation and 1 with L584F mutation.
Abbreviations: BRAFi/MEKi, BRAF inhibitor ± MEK inhibitor; ECOG PS, Eastern Cooperative Oncology Group performance status; LDH, lactate dehydrogenase; PD-L1, programmed death ligand 1.

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Efficacy

Response (RECIST 1.1), n (%)	Cohort 1A (N=7)
Objective Response Rate	**6 (85.7)**
Complete Response*	3 (42.9)
Partial Response	3 (42.9)
Stable Disease	1 (14.3)
Progressive Disease	0
Non-evaluable	0
Disease Control Rate	7 (100)

- 85.7% of patients responded to combination treatment with lifileucel + pembrolizumab
- Median number of TIL infused was 27.3 × 10^9
- Median follow-up was 8.2 months

*Includes 1 unconfirmed CR; patient had not yet reached confirmatory CR assessment at the time of the data-cut, but had previously achieved PR.
Abbreviations: RECIST, Response Evaluation Criteria in Solid Tumors; TIL, tumor-infiltrating lymphocytes.

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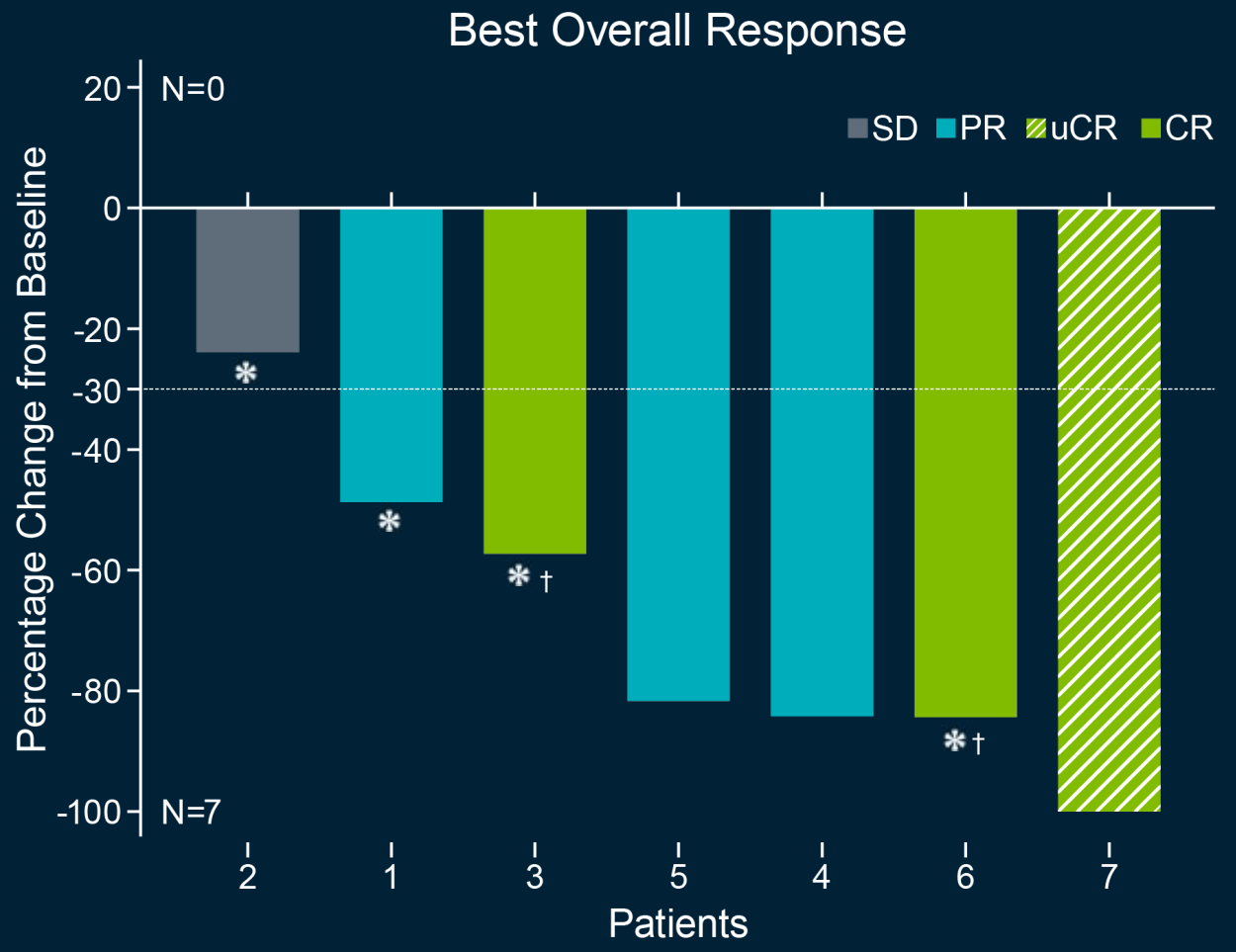
Best Percentage Change from Baseline in Target Lesion Sum of Diameters for All Evaluable Patients



- Median number of pembrolizumab doses was 10

*Patients with BRAF V600 mutation
†The overall response of CR was based on investigator assessment of a negative FDG-PET scan
Abbreviations: CR, complete response; PR, partial response; SD, stable disease.

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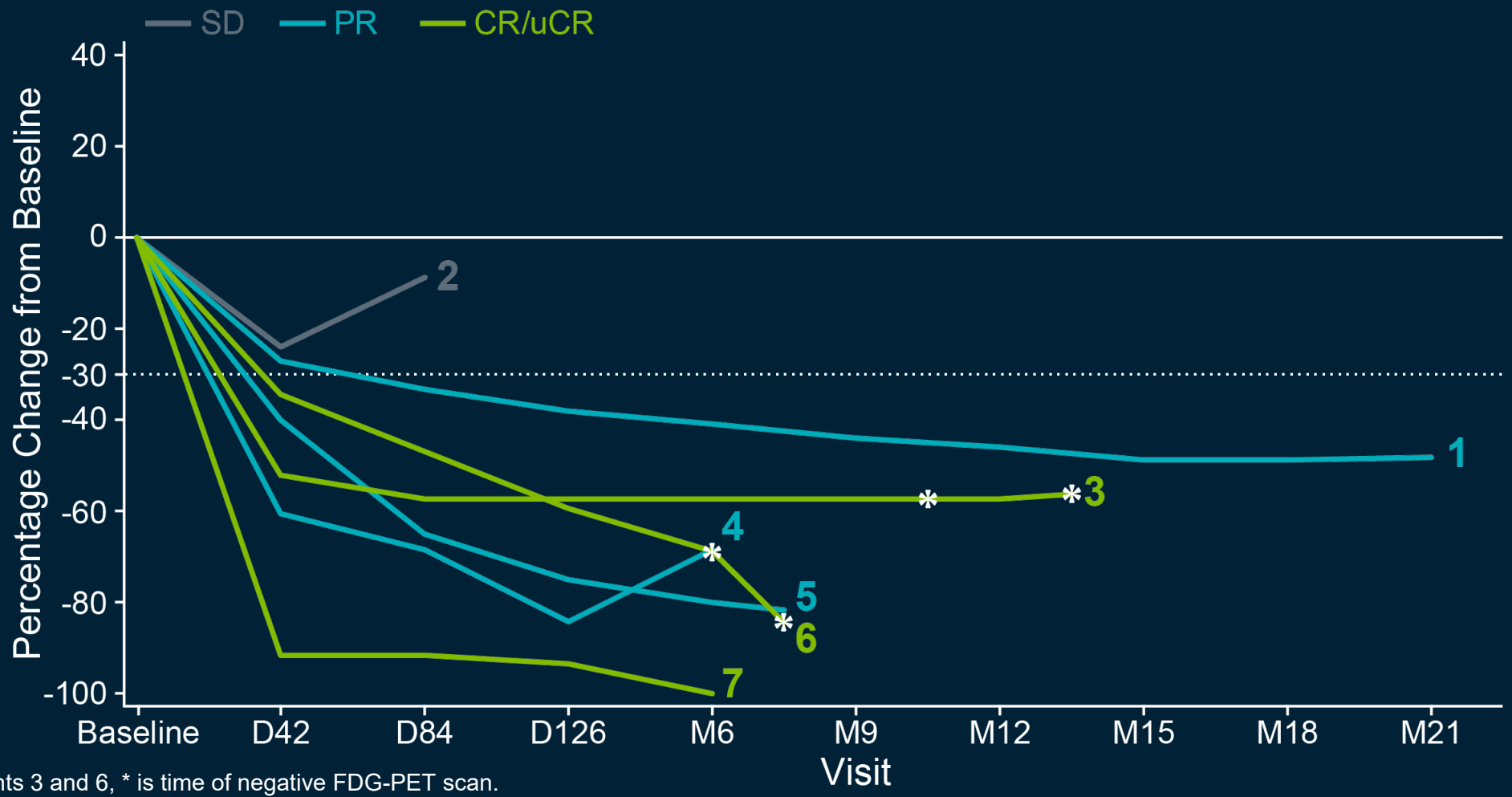
Percentage Change from Baseline in Target Lesion Sum of Diameters Over Time for All Evaluable Patients



For patients 3 and 6, * is time of negative FDG-PET scan.

Abbreviations: CR, complete response; PR, partial response; SD, stable disease.

Patients with CRs

Patient ID	BRAF Status	Prior Therapies	BOR on Study	Visit	Imaging Scan Method	Target Lesion SOD (mm)	Response at Visit
3	Other	None	CR	Baseline	CT	96	-
				Day 42	CT	46	PR
				Day 84	CT	41	PR
				Day 126	CT	41	PR
				Month 6	CT	41	PR
				Month 9	CT	41	PR
				Unscheduled 1 (Month 10.5)	PET/CT	41	CR
				Month 12	CT	41	CR
				Unscheduled 2 (Month 13)	PET/CT	42	CR
6	V600E	Dabrafenib / Trametinib (duration: ~5.2 y, best response PR, discontinued for PD)	CR	Baseline	CT	32	-
				Day 42	CT	21	PR
				Day 84	CT	17	PR
				Day 126	CT	13	PR
				Month 6	PET/CT	10	CR
				Unscheduled 1 (Month 7)	PET/CT	5	CR
7	Wild type	None	uCR	Baseline	CT	107	-
				Day 42	CT	9	PR
				Day 84	CT	9	PR
				Day 126	CT	7	PR
				Month 6	CT	0	CR

Abbreviations: BOR, best overall response; CR, complete response; CT, computed tomography; PET, positron emission tomography; PR, partial response; SOD, sum of diameters; uCR, unconfirmed complete response.

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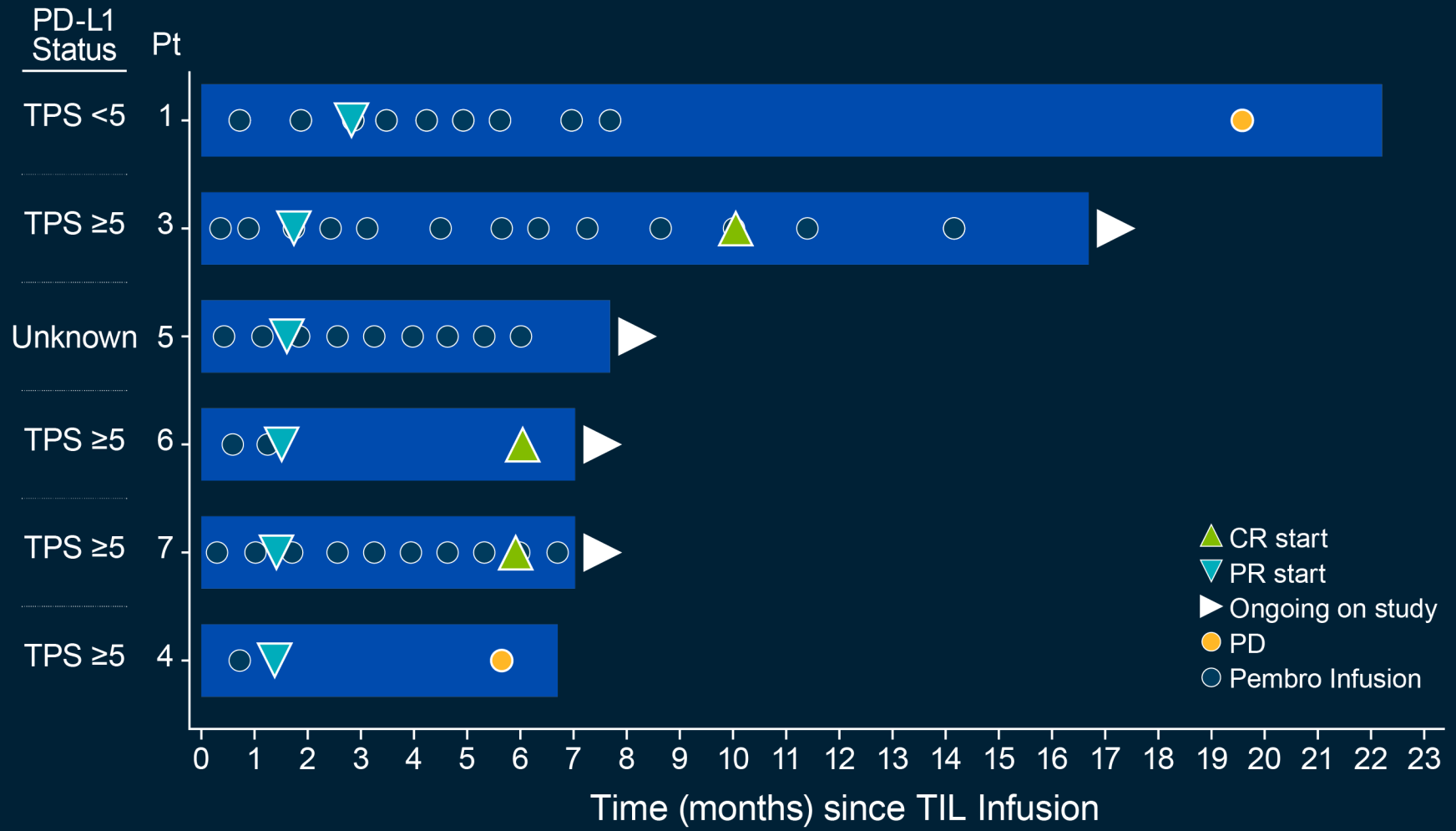
Time to First Response, Duration of Response, and Time on Efficacy Assessment for Confirmed Responders Who Achieved PR or Better



Abbreviations: CR, complete response; PD, progressive disease; PD-L1, programmed death ligand 1; PR, partial response; SD, stable disease.

Conclusions

- Early data suggest the response rate for lifileucel + pembrolizumab may be additive in patients with ICI-naïve advanced melanoma:
  - ORR was 85.7%
  - CR/uCR was 42.9%
  - Responses deepened over time
- Patients, although anti–PD-1 / anti–PD-L1 naïve, had high disease burden at baseline
- In patients with ICI-naïve advanced melanoma, lifileucel can be safely combined with pembrolizumab

These encouraging data confirm the potential feasibility and activity of the combination of lifileucel + pembrolizumab in early-line treatment of patients with advanced melanoma

Abbreviations: CR, complete response; ICI, immune checkpoint inhibitor; ORR, objective response rate; PD-L1, programmed death ligand 1; PR, partial response.

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Financial Summary

Jean-Marc Bellemin

CFO

Well Capitalized in Pursuit of TIL Commercialization

March 31, 2021	In millions (unaudited)
Common shares outstanding	149.3
Preferred shares outstanding	2.8[1]
Options	12.6
Cash, cash equivalents, short-term investments, restricted cash	$610.2[2]
Anticipated cash runway sufficient into 2023	

[1] Preferred shares are shown on an as-converted basis.
[2] Includes Restricted Cash of $5.5 million and $42.9 million in net proceeds through ATM offering as of end March 31st.

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Q&A

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Thank You!