



ADVANCING IMMUNO-ONCOLOGY

Tumor Infiltrating Lymphocyte Cell Therapy for Treatment of Solid Tumors

April 2021

Forward Looking Statements

Certain matters discussed in this presentation are “forward-looking statements” of Iovance Biotherapeutics, 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.

Iovance: Developing to commercialize TIL Cell Therapy

400+ Patients Treated with Iovance TIL Using Proprietary Process



Platform

- Leading cell therapy platform in solid tumors
- Clinical data in multiple indications
- Consistent GMP manufacturing process across solid tumors
- Next gen research in selected and genetically modified TIL



Pipeline

- Pivotal programs in metastatic melanoma and advanced cervical cancers
- Registration-supporting study in non-small cell lung carcinoma (NSCLC)
- Combinations with immune-checkpoint inhibitors in earlier lines
- Academic collaborations in new indications



Assets

- ~\$635M cash (12/31/20)
- Global rights to all programs, IP and technology
- Iovance manufacturing facility (iCTC)



Partners



MDAnderson
Cancer Network™



Yale
CANCER
CENTER



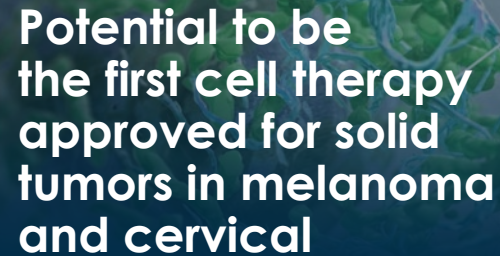
Investment Highlights

Leading cell therapy company focused on treatment of solid tumors



Large market opportunity & strong unmet need

- Initial focus in post-checkpoint solid tumors
- Expansion into combinations and earlier lines of therapy
- Five company-sponsored programs in melanoma, cervical, head & neck, NSCLC, and chronic lymphocytic leukemia (CLL) indications



Potential to be the first cell therapy approved for solid tumors in melanoma and cervical

- Accelerated path to approval in melanoma and cervical cancer
- BLA submission expected 2021
- Melanoma: RMAT, Orphan Drug, and Fast Track
- Cervical: BTDR, Orphan Drug, and Fast Track



Efficient & scalable proprietary manufacturing

- US and EU capacity with contract manufacturers
- Iovance Cell Therapy Center (iCTC) under construction in Philadelphia
- Rapid 22-day Gen 2 manufacturing with 90%+ success rate
- 400+ patients treated with Iovance proprietary process

2020 Accomplishments; Anticipated 2021 Milestones

	2020	2021
Regulatory	<input checked="" type="checkbox"/> Agreement with FDA on melanoma Cohort 4 clinical follow up; Cohort 2 supportive	<input type="checkbox"/> BLA: Continue work on potency assay to support submission of a BLA to FDA for lifileucel
	<input checked="" type="checkbox"/> Additional work on potency assays	
Clinical	<input checked="" type="checkbox"/> Melanoma: early pivotal Cohort 4 data and updated Cohort 2 data	<input checked="" type="checkbox"/> Cervical: Complete enrollment into Cohort 2, under consideration for inclusion in the BLA
	<input checked="" type="checkbox"/> Cervical: last patient dosed in cervical pivotal cohort	<input checked="" type="checkbox"/> NSCLC: Add a new cohort in the basket study; combine TIL + ipilimumab/nivolumab
	<input checked="" type="checkbox"/> NSCLC: Moffitt TIL data; registration directed study initiated	<input type="checkbox"/> NSCLC: Start patient dosing in IOV-LUN-202
	<input checked="" type="checkbox"/> HNSCC: initial data for TIL + pembrolizumab	<input checked="" type="checkbox"/> HNSCC: Expanding the HNSCC TIL + pembrolizumab in basket study (as part of moving TIL in earlier lines); Close C-145-03 HNSCC single therapy
Manufacturing	<input checked="" type="checkbox"/> Gen 3 process in clinic	<input checked="" type="checkbox"/> Melanoma: Initiate administration of 16-day Gen 3 process in clinic in the basket study
	<input checked="" type="checkbox"/> >90% success rate in >400 patients	<input type="checkbox"/> Completion of Navy Yard GMP facility (<i>i</i> CTC); start clinical manufacturing at <i>i</i> CTC

Key Highlights for Melanoma Cohort 2 Data

2019: Melanoma Data update at SITC⁽¹⁾

Melanoma Cohort 2 showed

36.4% ORR

by investigator and

34.8% ORR

as read by independent review committee (IRC) (N=66)

Jan 2021: Updated Melanoma Data

Median DOR still not reached at 28.1 months of median study follow up⁽²⁾

April 2021: Updated Cohort 2 Data to at AACR Plenary Session⁽³⁾

⁽¹⁾ Sarnaik et al., SITC 2019

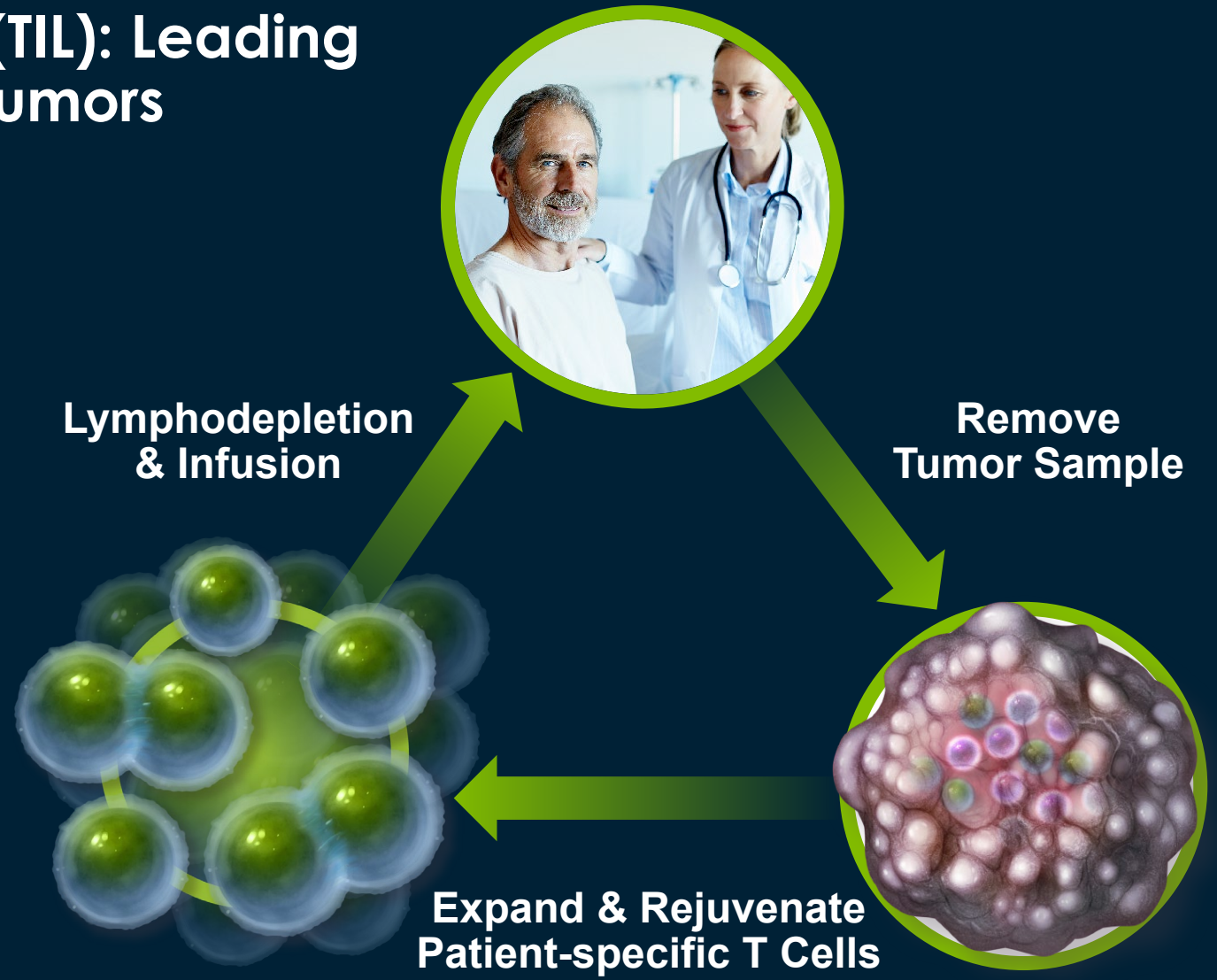
⁽²⁾ Investigator assessed, data extract 14 Dec 2020

⁽³⁾ Chesney, et. al. AACR 2021. Abstract #5329. Presentation #CT008

Tumor Infiltrating Lymphocytes (TIL): Leading Platform for Treatment of Solid Tumors

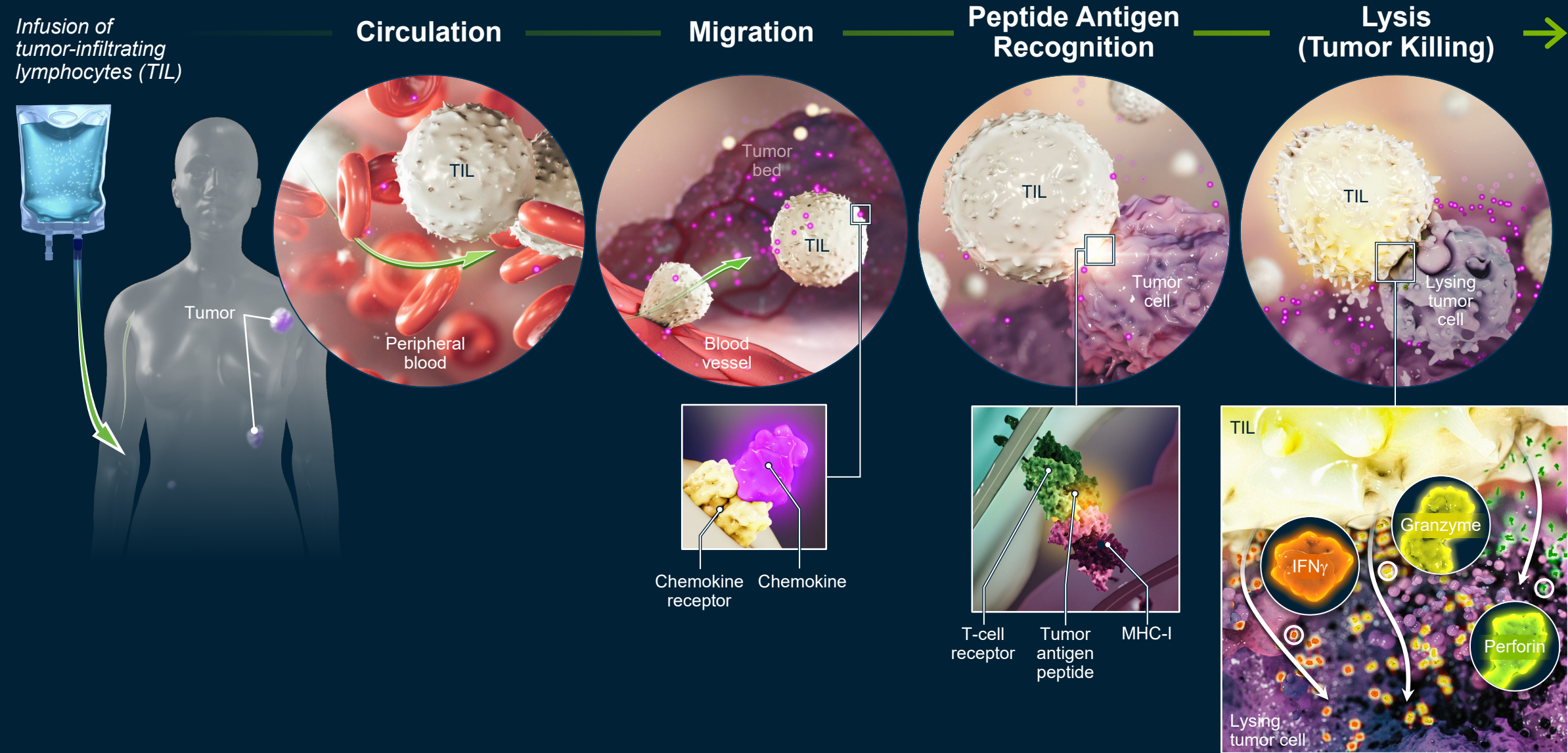
TIL – Unique Mechanism of Action

- Highly personalized
- One-time therapy
- Patient's own immune system amplified and rejuvenated ⁽¹⁾



⁽¹⁾ Simpson-Abelson et al., ESMO 2020

TIL Mechanism of Action



Competitive Advantages of TIL in Solid Tumors

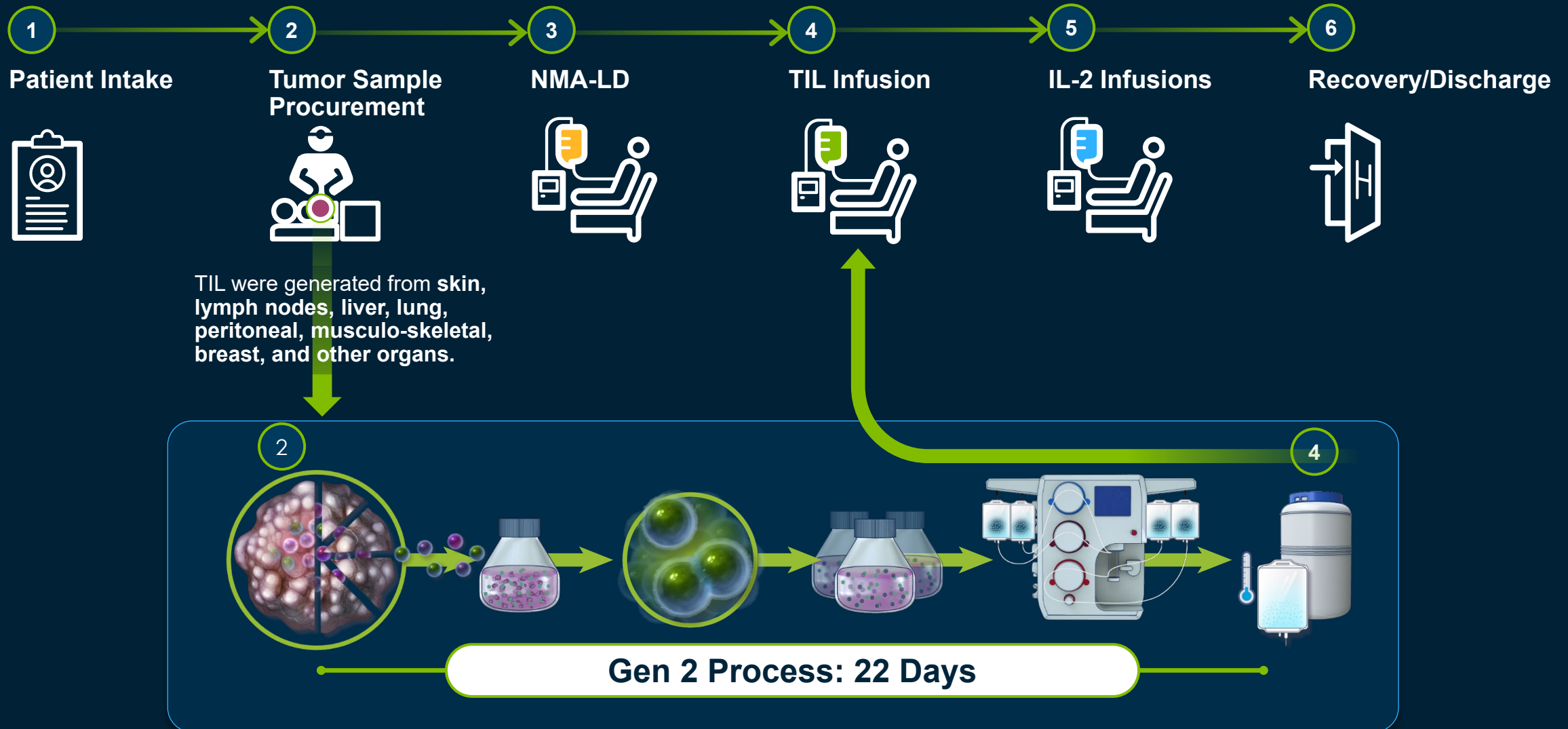
Checkpoints	TCR	CAR-T (Liquid tumors)	TIL (Solid tumors)
Target multiple tumor antigens	Target only single tumor antigen	Mainly target only single/ surface tumor antigen	Target multiple tumor antigens
Long maintenance period	One-time treatment	One-time treatment	One-time treatment
Utility in several solid tumors	Few solid tumors treated so far	No examples of successful utility in solid tumors	Available data in: melanoma, cervical, head & neck, and lung cancers
Potential long-term irreversible toxicities	Potential on-target, off-tissue effects	Potentially immunogenic: cytokine release syndrome	No unexpected off tumor tissue effects found to date
Off-the-shelf	Autologous	Autologous	Autologous



TIL target a diverse array of cancer antigens; we believe this approach represents a **highly differentiated, personalized, and targeted immunotherapy**

Manufacturing Process

Iovance Streamlined 22-Day GMP Manufacturing Process



Iovance Cell Therapy Center: iCTC



- Build-to-suit custom facility in Philadelphia, PA
- ~136,000 ft², \$85M investment
- First set of clean rooms occupied
- Clinical supply planned in 2021
- Commercial GMP planned in 2022
- Significant reduction in COGS expected

First Set of Cleanrooms (Flex Suite) Complete



Establishing Leadership in TIL Cell Therapy for Solid Tumors

Clinical, Manufacturing, and Regulatory

Registration & Commercialization

2011

TIL therapy conducted by Steven Rosenberg/NCI published promising results in melanoma^(1,2)

2016

Melanoma: First patient dosed for Gen 1 lifileucel

Gen 2 manufacturing developed and transferred to CMOs

2017

Melanoma: FDA Fast Track designation for lifileucel received

Cervical and head and neck studies began

2018

Melanoma: Lifileucel Cohort 2 clinical data (N=47, 38% ORR by investigator)

Melanoma: FDA RMAT designation for lifileucel in advanced melanoma received

Melanoma: FDA EOP2 meeting for lifileucel held

2019

Melanoma: First patient dosed in registrational cohort

Melanoma: IRC data from Cohort 2 presented (35% ORR)

Cervical: FDA Fast Track and BTDR received, EOP2 held

2020

Melanoma: Last patient dosed in pivotal cohort 4

Cervical: Last patient dosed in the pivotal Cohort 1

NSCLC: Moffitt TIL shows durable CRs in post-PD1 NSCLC

HNSCC: First TIL + pembro data at SITC

2021

Melanoma: Continue discussions with US FDA about potency assays

Cervical: Fully enroll Cohort 2. Meet with FDA to discuss the program.

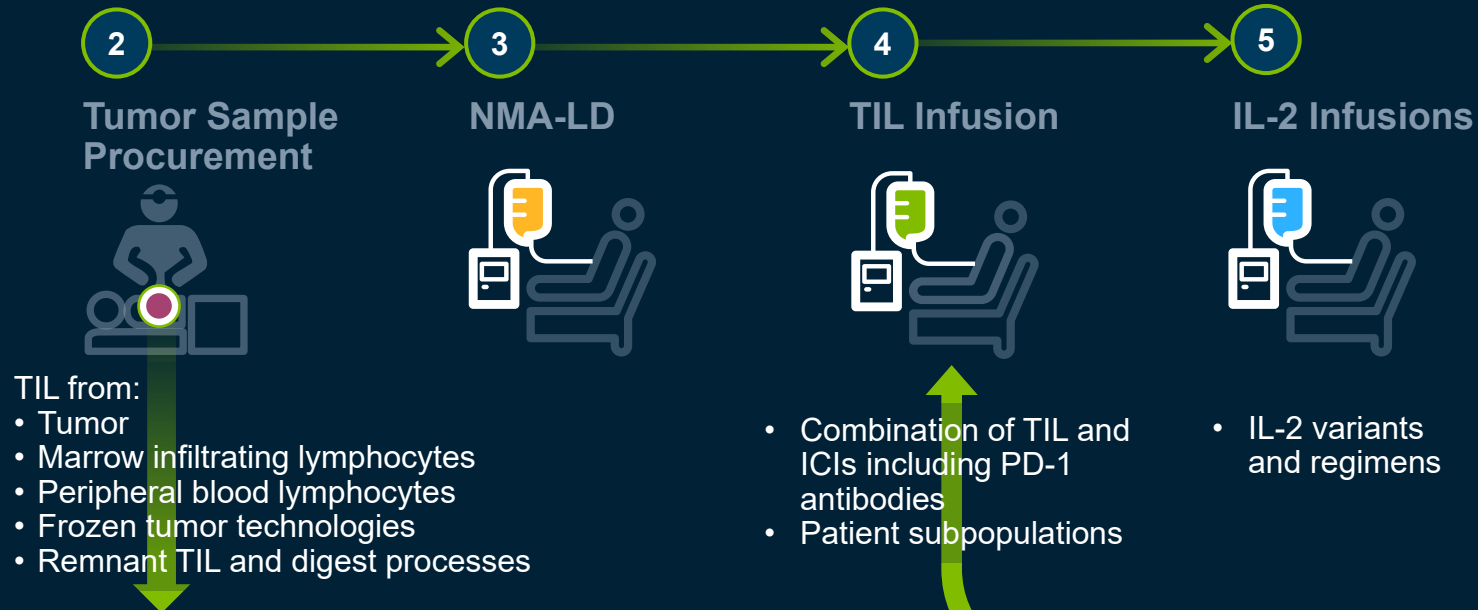
NSCLC and head and neck: New Cohort for NSCLC with TIL + ipi/nivo; expansion of head and neck combination with TIL+ pembro cohort

Pre-BLA meeting with FDA
BLA submission for lifileucel

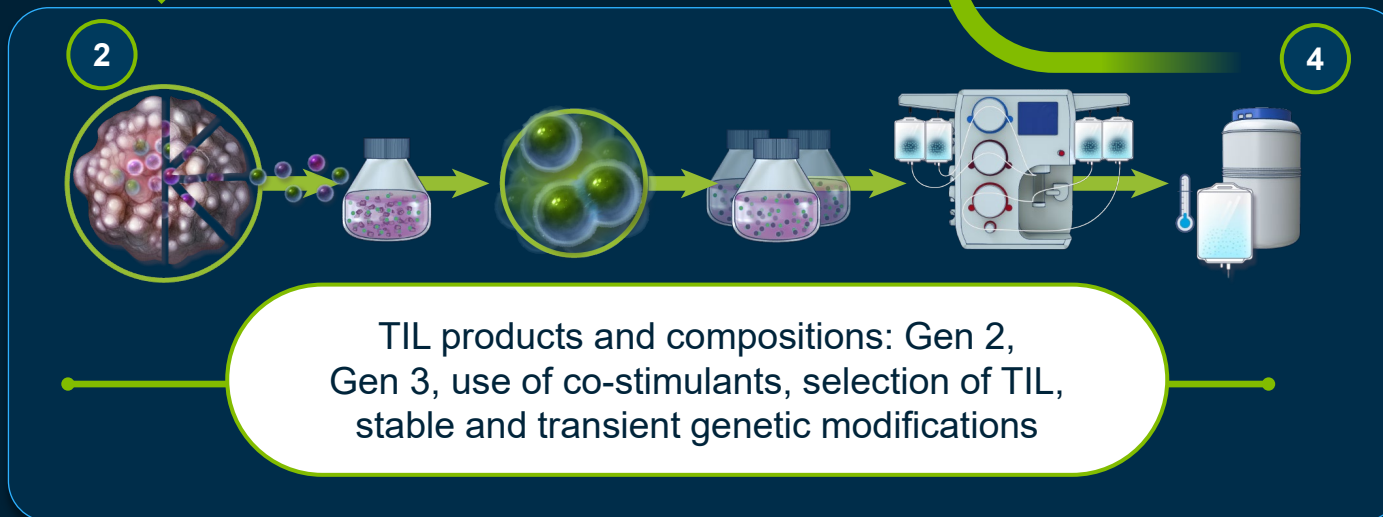
⁽¹⁾ Rosenberg et al., Clin Cancer Res 2011

⁽²⁾ Goff et al., J Clin Oncol 2016

Broad, Iovance-Owned IP Around TIL Therapy



- ✓ >20 granted or allowed US and international patents
- ✓ Compositions of matter for TIL products
- ✓ Methods of treatment in a broad range of cancers
- ✓ Manufacturing processes



Significant Market Potential in Solid Tumors

90%

of all cancer cases
are solid tumors

1.6M

New cases of solid
tumors in the U.S.⁽¹⁾

Move into earlier line of therapy →

Expand into other indications ↓

Solid Tumor Indication	Deaths ⁽¹⁾	New Cases ⁽¹⁾
Melanoma	6,850	100,350
Cervix Uteri	4,290	13,800
Lung & Bronchus	135,720	228,820
Oral Cavity, Pharynx & Larynx	14,500	65,630
Breast	42,170	276,480
Pancreatic	47,050	57,600
Brain & Other Nervous System	18,020	23,890
	Potential to address unmet need in late lines of treatment	Potential market for early lines in combo with standard of care

⁽¹⁾ <https://seer.cancer.gov> accessed March 2021

Current Clinical Pipeline and Select Collaboration Studies

	Regimen	Trial	Indication	N	Partner	Phase 1	Phase 2	Pivotal
Company sponsored studies	Lifileucel	C-144-01	Melanoma	178	—	<div></div>		
	Lifileucel	C-145-04	Cervical cancer	138	—	<div></div>		
	LN-145/ LN-145-S1	C-145-03	Head & neck cancer	55	—	<div></div>		
	Lifileucel + pembrolizumab	IOV-COM-202	Melanoma	~135	—	<div></div>		
	LN-145-S1		Melanoma					
	LN-144 (Gen 3)		Melanoma					
	LN-145 + pembrolizumab		Head & neck cancer					
	LN-145 + pembrolizumab		Non-small cell lung					
Select investigator sponsored proof-of-concept studies	LN-145	IOV-LUN-202	Non-small cell lung	95	—	<div></div>		
	IOV-2001	IOV-CLL-01	Chronic lymphocytic leukemia	~70	—	<div></div>		
	MDA TIL	NCT03610490	Ovarian, colorectal, pancreatic	~54	MD Anderson Cancer Network	<div></div>		
	LN-145	NCT03449108	Ovarian, sarcomas, thyroid	~54	MD Anderson Cancer Network	<div></div>		
	Moffitt TIL + nivolumab	NCT03215810	Non-small cell lung	20	MOFFITT CANCER CENTER	<div></div>		

For the studies listed in our collaboration pipeline table, the partner listed above is the sponsor of the clinical trial. Such partner may not use our Gen 2 manufacturing process and/or the therapeutic dosing may differ from our clinical trials. As a result, such partner data may not be representative of our data.

Metastatic Melanoma

Potential Market for Metastatic Melanoma

- Estimated 7,000⁽¹⁾ U.S. patient deaths due to melanoma
- Limited options after progression on checkpoint and BRAF/MEK inhibitors

“Nature has selected TIL to recognize features unique to the tumor not present on normal tissues, which helps make a TIL therapy approach effective compared to other cell therapy strategies for solid tumors. Iovance TIL treatment has a novel mechanism of action, completely separate from those of other treatment options, and has resulted in highly durable responses in patients that have progressed on prior FDA-approved treatment for their metastatic melanoma.”

— Dr. Amod Sarnaik
Department of Cutaneous Oncology,
the Immunology Program and the Melanoma
Center of Excellence at Moffitt Cancer Center

Metastatic Melanoma Facts

309k

New Cases WW
each year⁽³⁾

62k

Deaths WW
each year⁽³⁾

100k

Diagnoses in U.S.
each year⁽¹⁾

7k

Deaths in U.S.
each year⁽¹⁾

1st line:
Immuno
-therapy

BRAF/MEK
inhibitors for
BRAF
positive

Chemotherapy
ORR 4-10%⁽²⁾
OS ~7-8 mons⁽⁴⁾

⁽¹⁾ <https://seer.cancer.gov> accessed March 2021

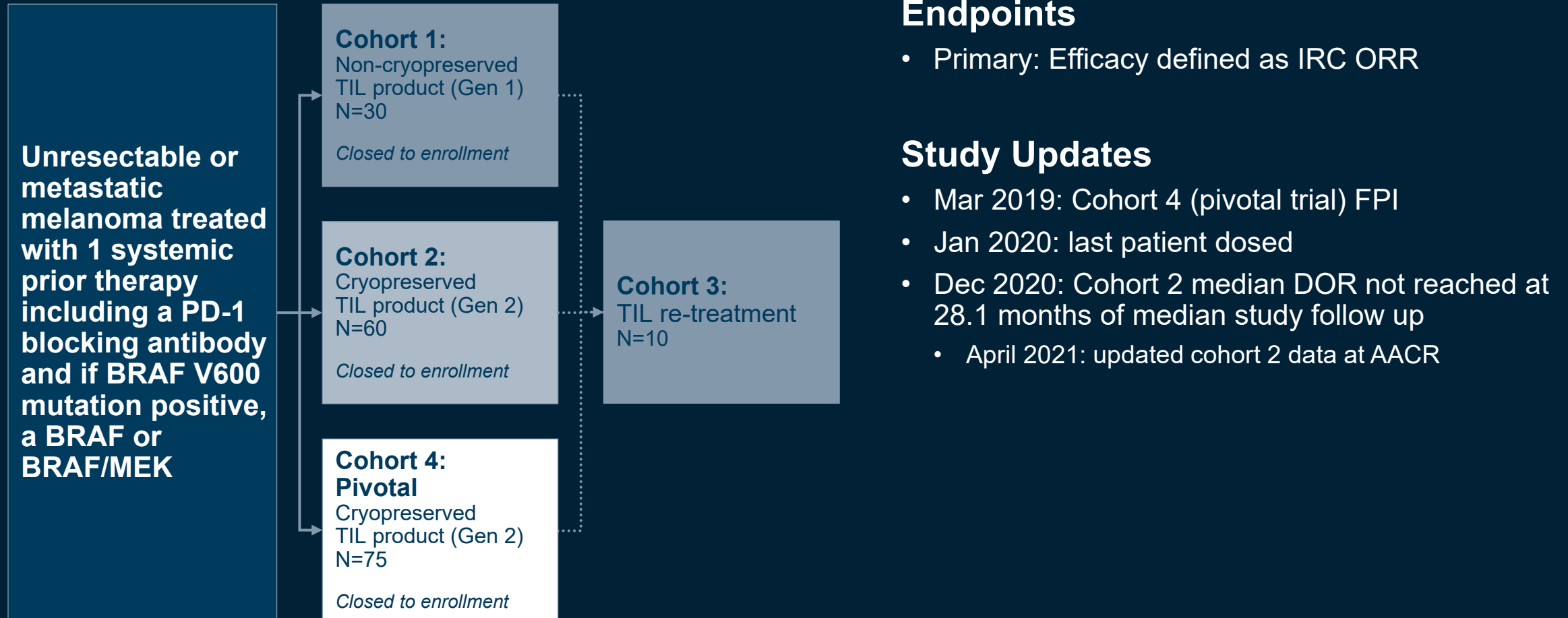
⁽²⁾ Keytruda USPI accessed Mar 2021 (4%) and Weber et al., Lancet Oncol 2015 (ICC 10%)

⁽³⁾ Global Burden of Disease Cancer Collaboration, JAMA Oncol 2019

⁽⁴⁾ Kirchburger et al., Eur J Cancer 2016 and Goldinger et al., J Clin Oncol 2018

C-144-01: Phase 2 Study Design

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



C-144-01: Cohort 2 Patient Characteristics at ASCO 2020

CHARACTERISTIC	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	66 (100)
Anti-CTLA-4	53 (80)
BRAF/MEK	15 (23)
Progressive Disease for at least 1 prior therapy	
Anti-PD-1	65 (99)
Anti-CTLA-4	41 (77 ⁽¹⁾)
Baseline ECOG score, n (%)	
0	37 (56)
1	29 (44)

CHARACTERISTIC	Cohort 2, N=66, (%)
BRAF Status, n (%)	
Mutated V600	17 (26)
Wild Type	45 (68)
Unknown	3 (5)
Other	1 (2)
Baseline LDH (U/L)	
Median	244
1-2 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 (at Baseline)	
>3	51 (77)
Mean (SD)	6 (2.7)
Patients with Baseline Liver and/or Brain Lesions	28 (42)

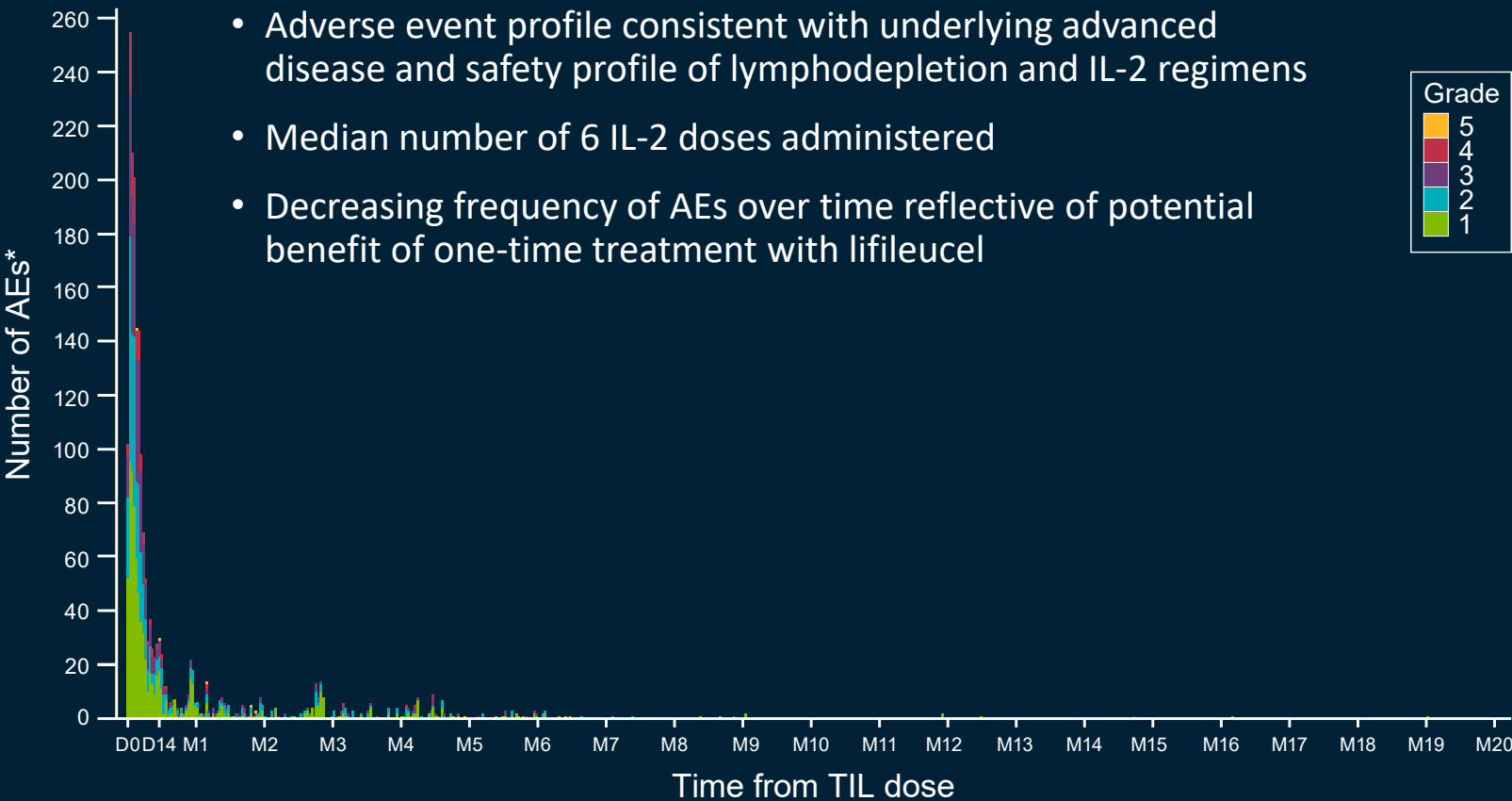
Cohort 2 patients have:

- 3.3 mean prior therapies, ranging from 1-9
- High tumor burden at baseline: 106 mm mean sum of diameters of the target lesions

⁽¹⁾ The denominator is the 53 patients who received prior anti-CTLA-4.

Adverse Events Tend to be Expected, Early and Transient

Frequency of AEs over time is reflective of potential benefit of one-time treatment with lifileucel



- Adverse event profile consistent with underlying advanced disease and safety profile of lymphodepletion and IL-2 regimens
- Median number of 6 IL-2 doses administered
- Decreasing frequency of AEs over time reflective of potential benefit of one-time treatment with lifileucel

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

*The number of AEs is cumulative and represent the total number of patients dosed. Treatment-Emergent Adverse Events refer to all AEs starting on or after the first dose date of TIL up to 30 days. Patients with multiple events for a given Preferred Term are counted only once using the maximum grade under each Preferred Term. Safety terms that describe the same medical condition were combined.

Potentially Efficacious Treatment for Patients with Limited Options

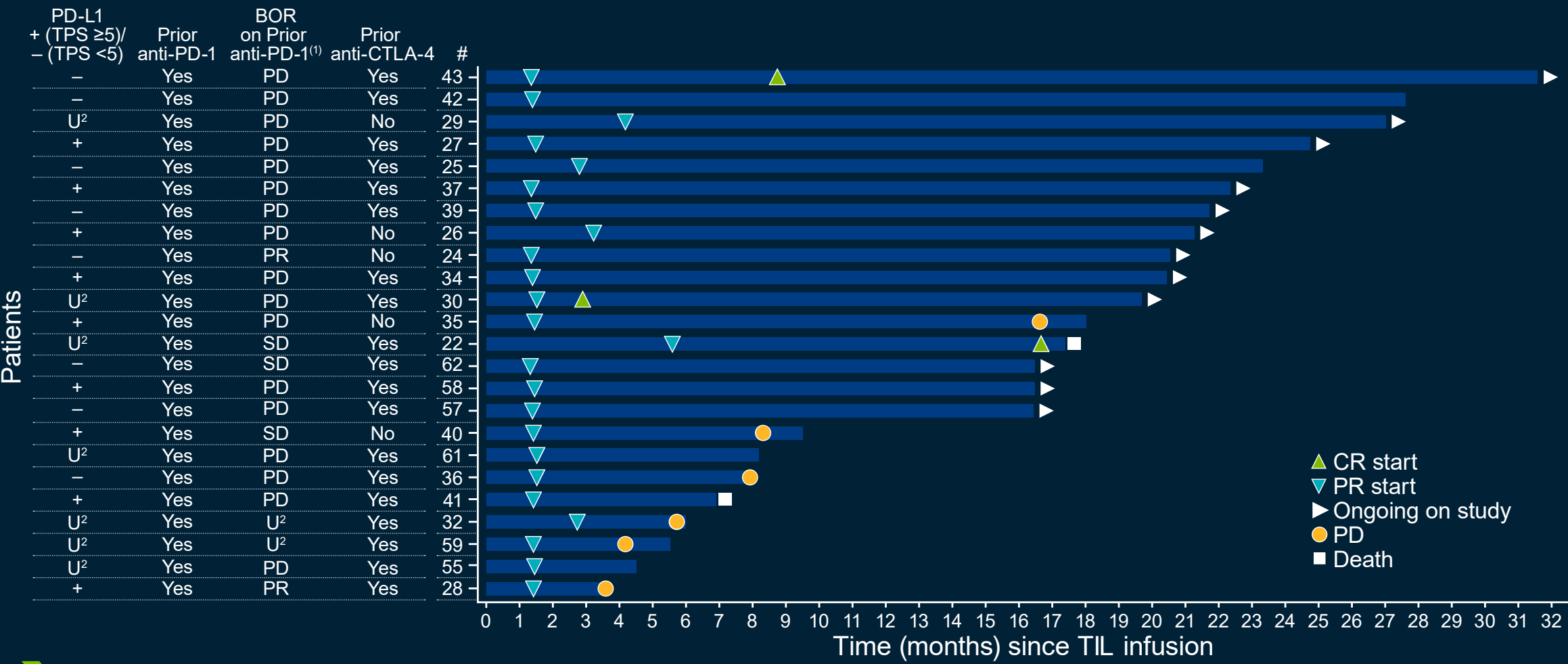
In heavily pretreated metastatic melanoma patients (3.3 mean prior therapies)

- **ORR 36%**
- **DCR 80%**
- Mean TIL cells infused: 27.3×10^9
- ***Median DOR has not been reached at 28.1 months of study follow up (14 Dec 2020 data extract)***

Response	Patients, N=66 n (%)
Objective Response Rate	24 (36.4)
Complete Response	2 (3.0)
Partial Response	22 (33.3)
Stable Disease	29 (43.9)
Progressive Disease	9 (13.6)
Non-Evaluable ⁽¹⁾	4 (6.1)
Disease Control Rate	53 (80.3)

⁽¹⁾ Non-evaluable due to not reaching first assessment

C-144-01 Cohort 2 Efficacy: Time to Response



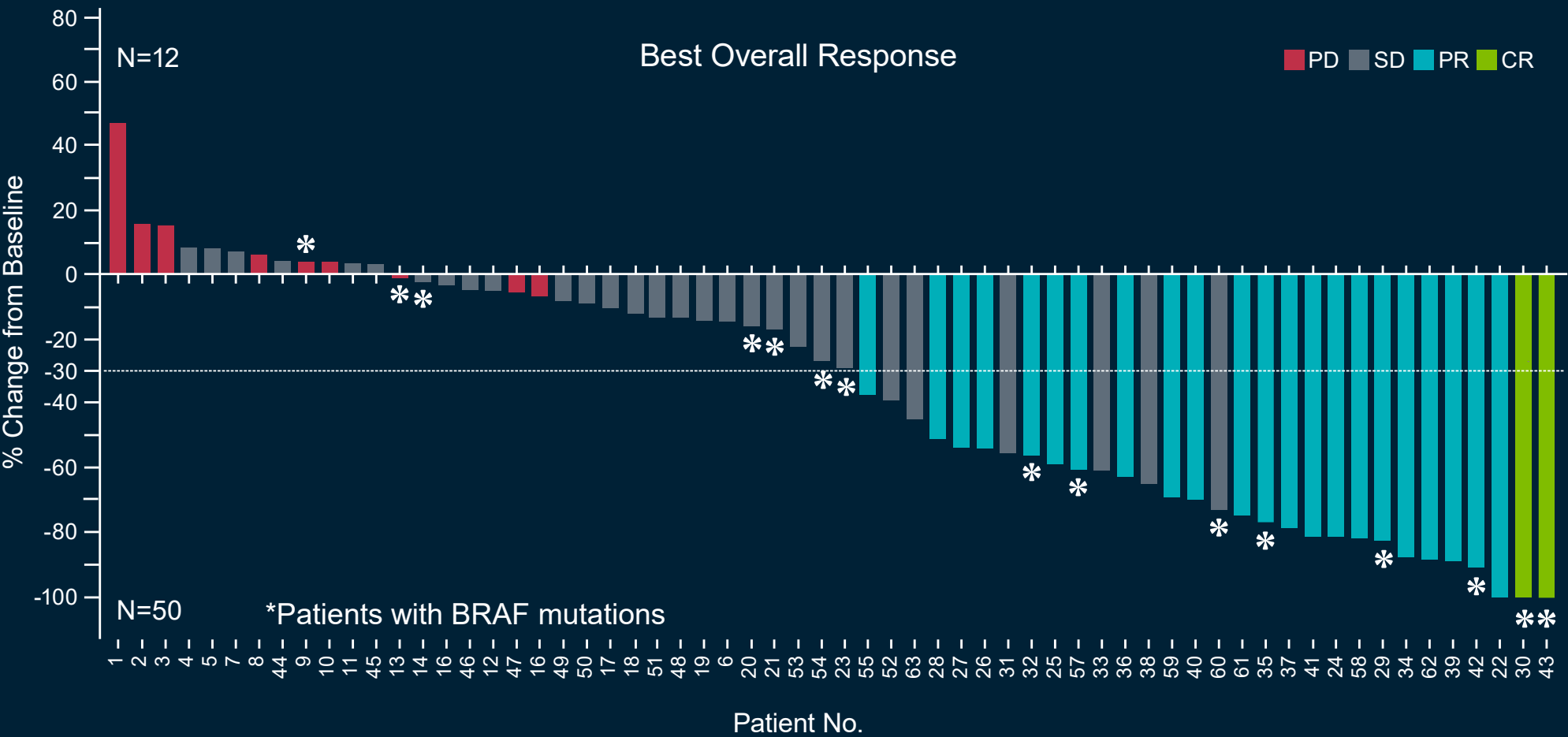
➤ 79% of responders had received prior ipilimumab. Responses deepen over time.

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

C-144-01 Cohort 2 Efficacy: Best Overall Response

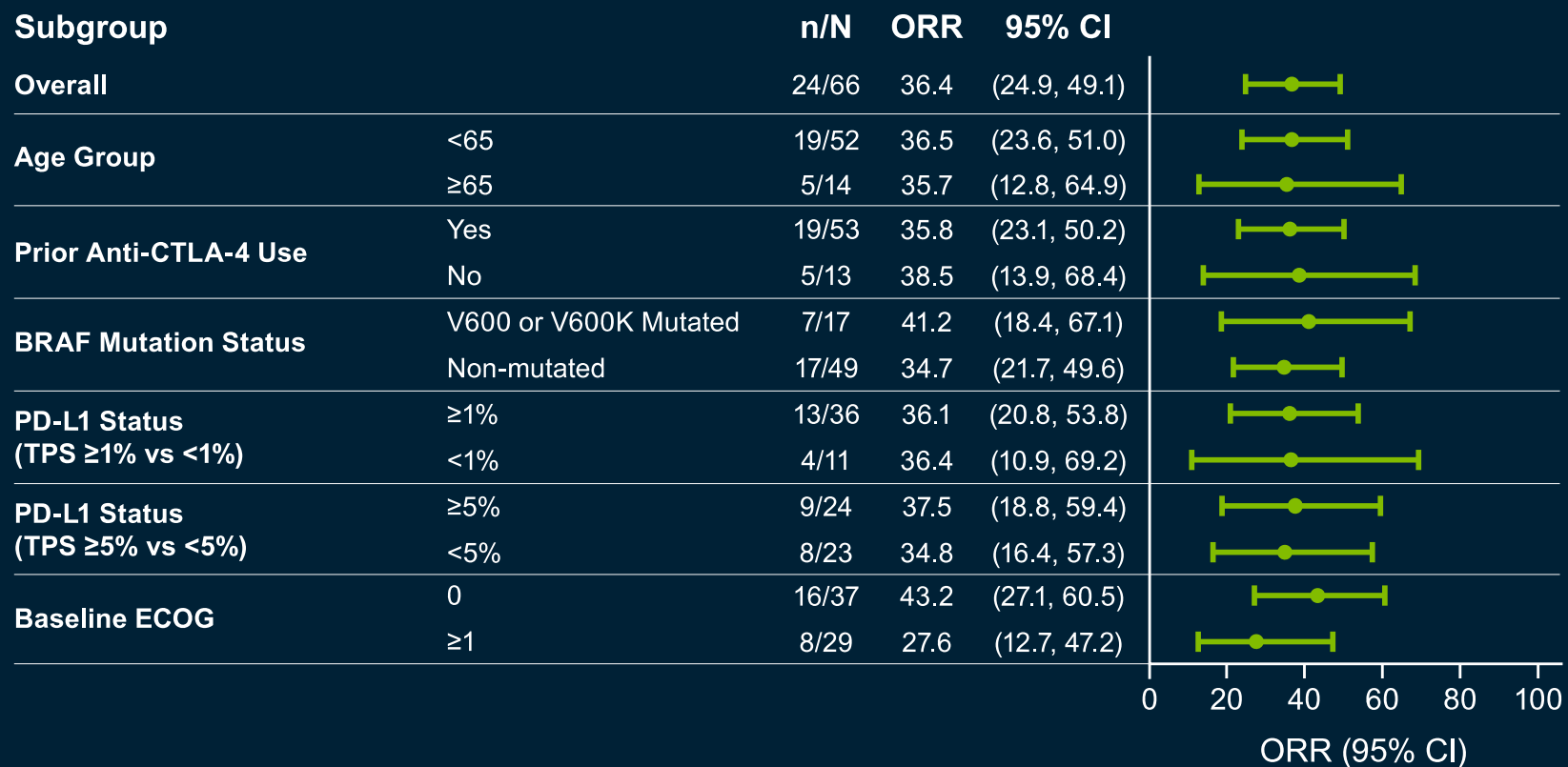
➤ 81% (50/62) of patients had a reduction in tumor burden

- Mean Time to response 1.9 months (range 1.3-5.6)
- Responses are deep



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

C-144-01 Cohort 2 ORR By Subgroup

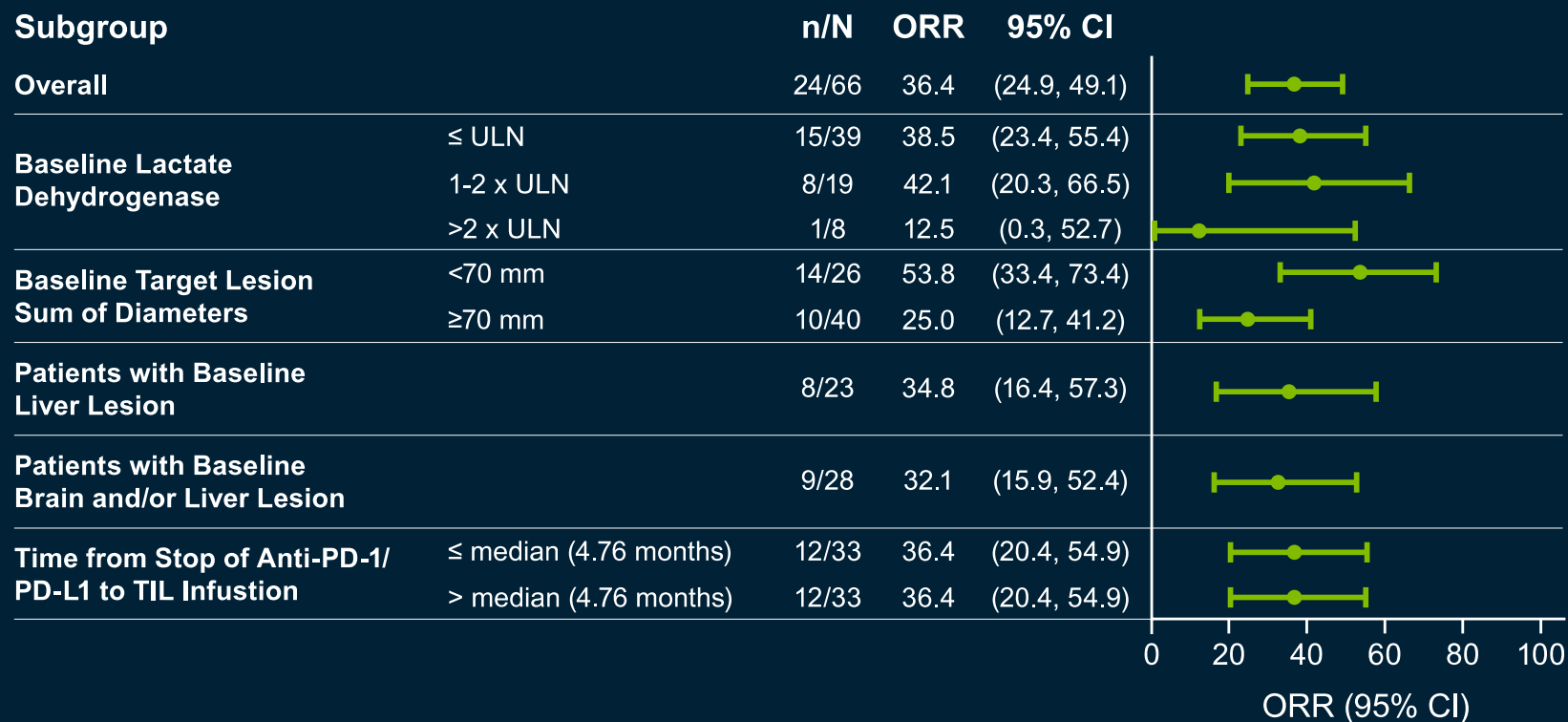


Responses were demonstrated:

- Across a wide age range
- Even in patients who have progressed on prior anti-CTLA-4 or prior BRAF
- Regardless of the BRAF mutational status
- Equally in patients with PD-L1 low or high levels

Abbreviation: CI, Confidence interval.
95% CI is calculated using the Clopper-Pearson Exact test.

C-144-01 Cohort 2 ORR By Subgroup



Responses were demonstrated:

- In patients with elevated LDH (1-2x)
- In patients with bulky disease at baseline
- Patients with lesions in liver and/or brain
- Patients post anti-PD-1 regardless of duration of time from the patient's last anti-PD-1/L1

Abbreviations: ULN, upper limit of normal; CI, confidence interval
95% CI is calculated using the Clopper-Pearson Exact test.

C-144-01 Cohort 2: Conclusions

- In heavily pretreated metastatic melanoma patients with high baseline disease burden who progressed on multiple prior therapies, including anti-PD-1 and BRAF/MEK inhibitors, if BRAFV600 mutant, lifileucel treatment results in:
 - 36.4% ORR
 - 80.3% DCR
 - Median DOR was still not reached at 28.1 months of median study follow up (Dec 2020 update)
 - Responses deepen over time
- Lifileucel has demonstrated potential efficacy and durability of response for patients with metastatic melanoma regardless of prior therapy with immune checkpoint therapies, or BRAF status.

Late Stage (2L/3L) Melanoma Treatment Development Efforts

2L/3L melanoma treatment has no current standard of care

	Agent	ORR % (N)	Current Development Status	Prior Lines of Tx	Patient Characteristics
Combination with Anti-PD-1	Checkpoints				
	LAG-3 + nivo (BMS)	12% (N=61) ⁽¹⁾	Multiple 1L studies	1+	All comers, ECOG ≤2 • LAG-3 expression ≥1% (N=33) ORR=18%; • LAG-3 expression <1% (N=22) ORR=5%
	TLR9 agonists, TKI, oncolytic virus				
	IMO-2125 (Idera) + ipi	8.8% (combination) 8.6% (ipilimumab alone) (N=481) ⁽²⁾	Phase 3, post-PD-1 Primary endpoint (ORR) was not met		ECOG ≤1, intratumoral injection DCR (combination): 34.5%
	CMP-001 (CheckMate) + pembro	23.5% (N=98) ⁽³⁾	Phase 1b	1+	PD or SD (>12 wks) on prior anti-PD-1 Monotherapy CMP-001: ORR: 11.5%-17.5% mDOR: 5.6 mons
	Lenvatinib + pembro	21.4% (N=103) ⁽⁴⁾	Phase 2	1+	mDOR: 6.3 mons mOS: 13.9 months
Single Agent	RP1 (Replimune) + nivolumab	31% (N=16) ⁽⁵⁾	Phase 2	1+	
	Cytokines				
	HD IL-2	8% (N=9) ⁽⁶⁾		1+	HD IL-2 post anti-PD1
	Cell therapy				
	TIL	36.4% (N=66)⁽⁷⁾	Phase 2, Cohort 2	3.3	All post anti-PD1, 80% post anti-CTLA-4

⁽¹⁾ Ascierto et al., ESMO 2017 ⁽²⁾ Idera Press Release, 18 March 2021 ⁽³⁾ Milhem et al., SITC 2020 ⁽⁴⁾ Fernandez et al., ESMO 2020

⁽⁵⁾ Replimune Corp Deck, Mar 2021 ⁽⁶⁾ Buchbinder et al., J Clin Oncol 2016 ⁽⁷⁾ Sarnaik et al., ASCO 2020

Cervical Cancer

Potential Market for Cervical Cancer

“TIL immunotherapy with lifileucel is literally redefining what is treatable and potentially curable in advanced metastatic chemo-refractory cervical cancer. Patients who only two years ago would be facing hospice as their only alternative now have access to this potentially life extending new treatment. This is the most exciting news in this field in decades.”

— Amir Jazaeri, M.D.
Director of the Gynecologic Cancer
Immunotherapy Program in the
Department of Gynecologic Oncology and
Reproductive Medicine at MD Anderson

Cervical Cancer Facts

601k New Cases WW
each year⁽¹⁾

260k Deaths WW
each year⁽¹⁾

14k Diagnoses in U.S.
each year⁽²⁾

4k Deaths in U.S.
each year⁽²⁾

Available care:
**Chemo
-therapy**
as first line option

For PD-L1+
patients, post-
chemo receiving
Keytruda⁽³⁾
ORR 14.3%
Third line patients:
ORR 3.4%⁽⁶⁾

Available Care
for chemotherapy
in 2L or 3L metastatic
cervical patients
3.4 - 13%⁽⁴⁻⁶⁾

⁽¹⁾ Global Burden of Disease Cancer Collaboration, JAMA Oncol 2019

⁽²⁾ <https://seer.cancer.gov> accessed Mar 2020

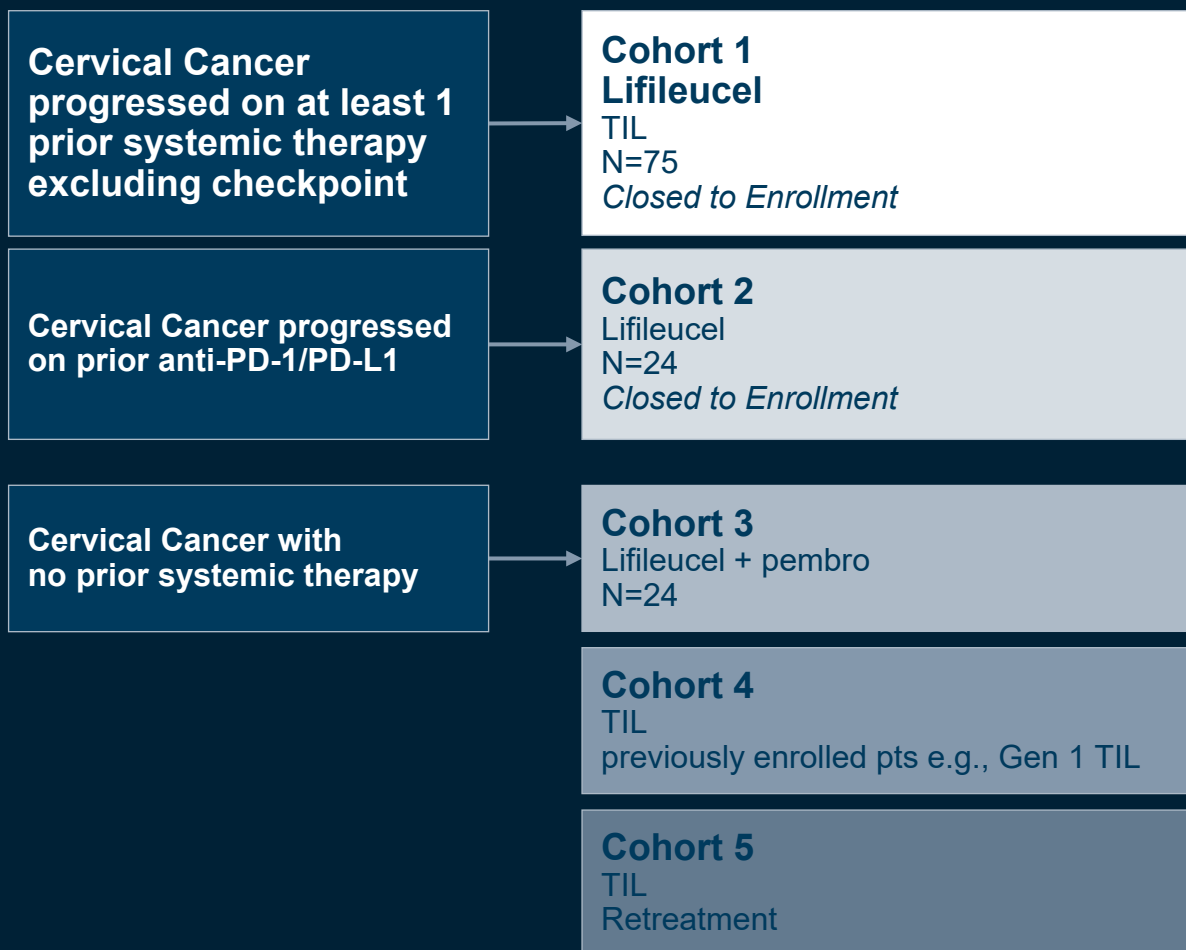
⁽³⁾ Keytruda USPI accessed Mar 2021

⁽⁴⁾ Schilder et al., Gynecol Oncol 2005

⁽⁵⁾ Weiss et al., Gynecol Oncol 1990

⁽⁶⁾ McLachlan et al., Clin Oncol 2017

Pivotal Phase 2 Study of TIL Therapy Lifileucel (Formerly LN-145) in Recurrent, Metastatic or Persistent Cervical Carcinoma (NCT03108495)



Endpoints

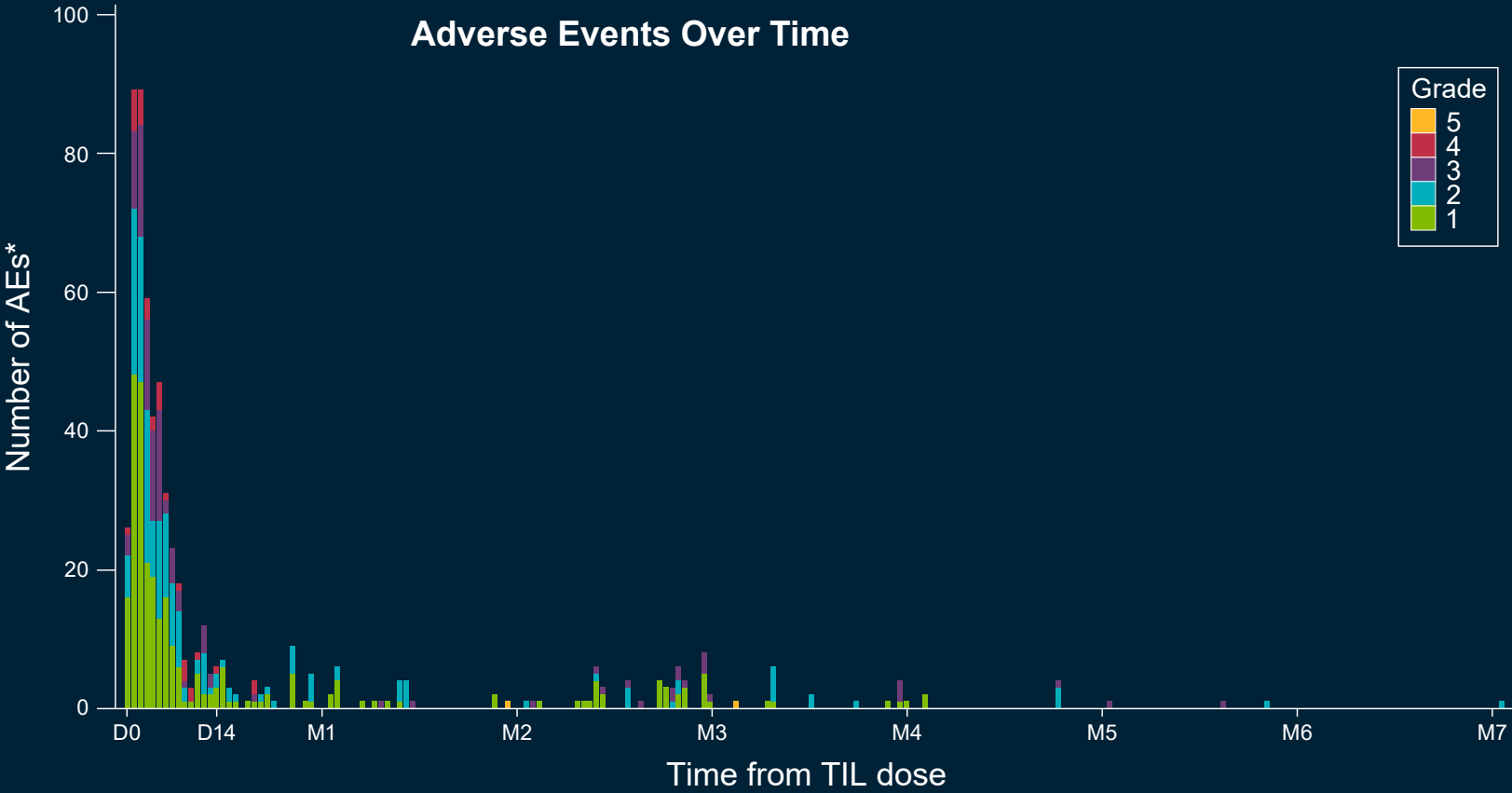
- Primary: ORR as determined by IRC
- Secondary: safety and efficacy

Study Updates

- 3Q 2020: Last patient dosed in Cohort 1
- 1Q 2021: Enrollment closed and last patient dosed in Cohort 2 - may be supportive of registration due to changing landscape of care

Adverse Events Tend to be Early and Transient

Frequency of AEs over time is reflective of potential benefit of one-time treatment with TIL (lifileucel)



Preferred Term	(N=27)		
	Any Grade, n (%)	Grade 3/4, n (%)	Grade 5, n (%)
Number of patients reporting at least one Treatment-Emergent AE**	27 (100)	26 (96.3)	0
Chills	21 (77.8)	0	0
Anemia	15 (55.6)	15 (55.6)	0
Diarrhea	14 (51.9)	2 (7.4)	0
Pyrexia	14 (51.9)	1 (3.7)	0
Thrombocytopenia	14 (51.9)	12 (44.4)	0
Neutropenia	11 (40.7)	8 (29.6)	0
Vomiting	11 (40.7)	1 (3.7)	0
Hypotension	10 (37.0)	4 (14.8)	0
Dyspnea	9 (33.3)	1 (3.7)	0
Febrile neutropenia	9 (33.3)	8 (29.6)	0
Hypoxia	9 (33.3)	3 (11.1)	0
Leukopenia	9 (33.3)	6 (22.2)	0
Hypomagnesemia	8 (29.6)	0	0
Sinus tachycardia	8 (29.6)	0	0

*The number of AEs is cumulative and represent the total number of patients dosed. Treatment-Emergent Adverse Events refer to all AEs starting on or after the first dose date of TIL up to 30 days. Patients with multiple events for a given preferred term are counted only once using the maximum grade under each preferred term. Safety terms which describe the same medical condition were combined;

Significant Response Observed in Heavily Pretreated Patients

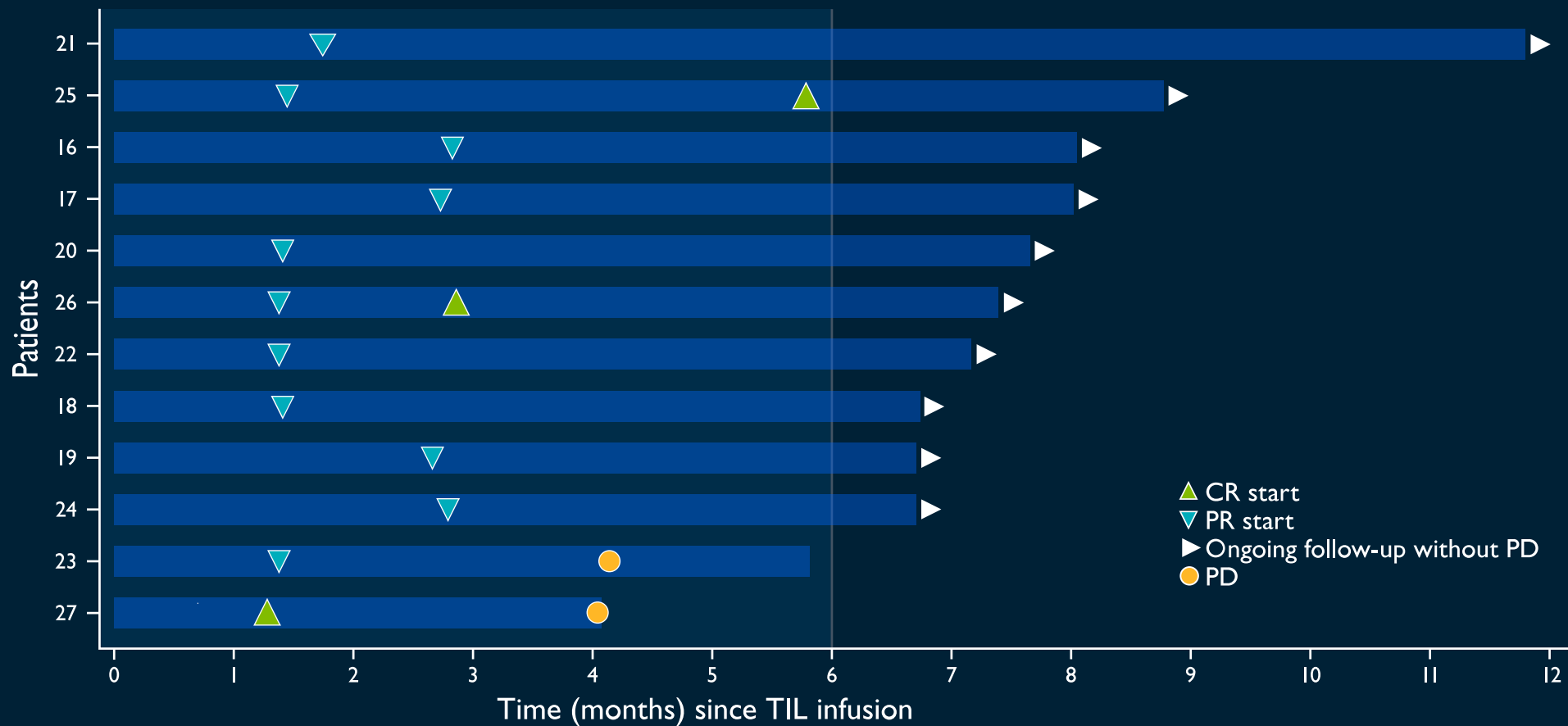
Baseline Demographics	N=27 (%)
Prior therapies	
Mean # prior therapies	2.4
Platinum-based	27 (100)
Taxane	26 (96)
Anti-VEGF	22 (82)
PD-1/PD-L-1	4 (15%)
Target lesions sum of diameter (mm)	
Mean (SD)	61 (38)
Min, Max	10, 165
Histologic Cell Type, n (%)	
Squamous Cell Carcinoma	12 (44)
Adenocarcinoma	12 (44)
Adenosquamous Carcinoma	3 (11)
Number of target & non-target lesions (at baseline)	
>3	17 (63)
Mean (min,max)	4 (1,9)

Responses	N=27 (%)
Objective Response Rate	12 (44%)
Complete Response	3 (11%)
Partial Response	9 (33%)
Stable Disease	11 (41%)
Progressive Disease	4 (15%)
Non-Evaluable	0
Disease Control Rate	23 (85%)

- **Median DOR not reached at 7.4 months median follow up**
- Adverse event profile consistent with underlying advanced disease and safety profile of lymphodepletion and IL-2
- Mean TIL cells infused: **28 x 10⁹**
- Median number of IL-2 doses: 6.0

Responses Observed Early On and Consistent with Melanoma

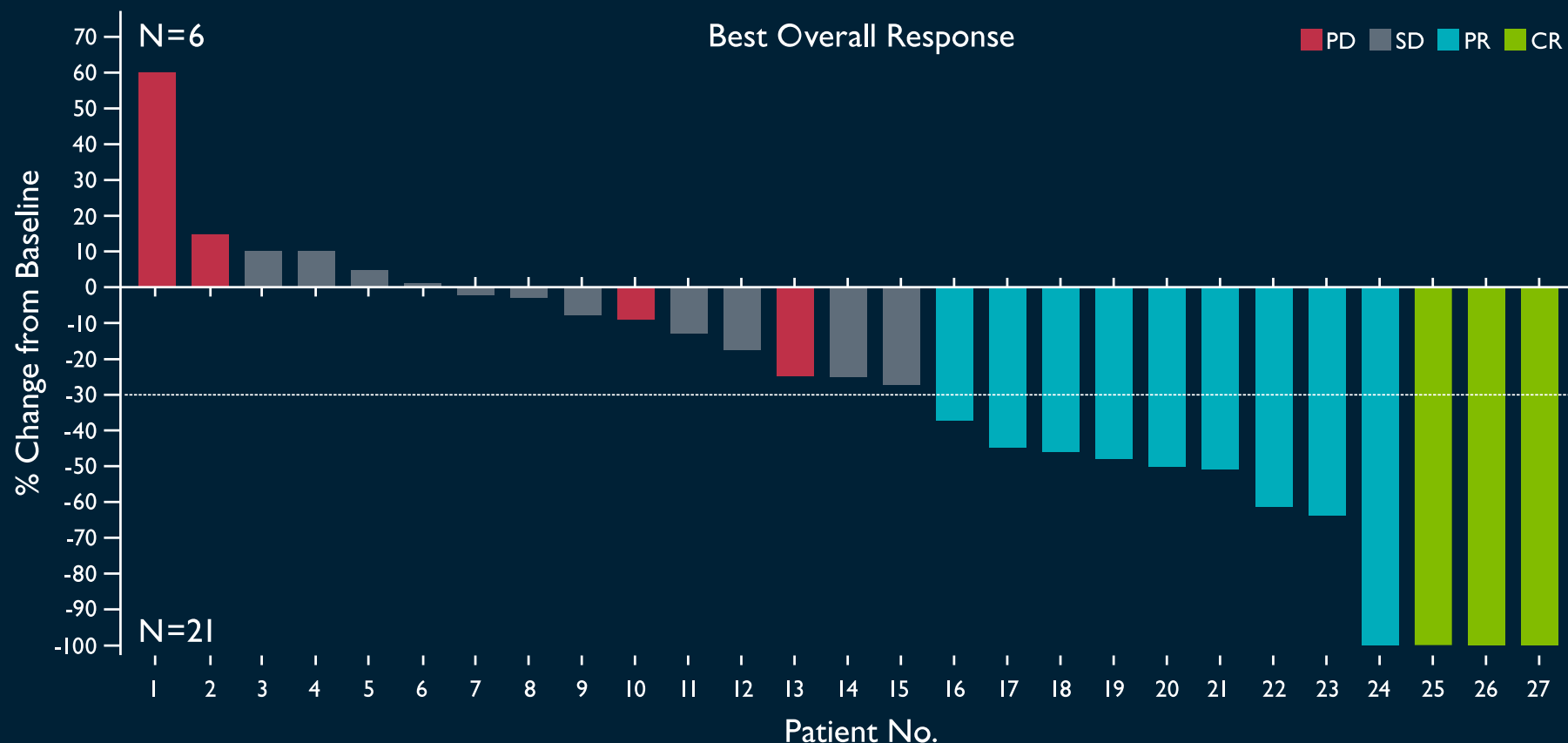
Lifileucel time to response and current duration for evaluable patients (partial response or better)



- Mean time to first response 1.9 months
- Mean time to best response 2.4 months

Three Complete Responses Observed with Lifileucel

Lifileucel best overall response rate



- 78% of patients had a reduction in tumor burden
- Mean time to response 1.9 months
- All assessments are by RECIST 1.1
- Responses are deep

Development Efforts in Recurrent, Metastatic or Persistent Cervical Carcinoma

Recurrent, metastatic, or persistent cervical carcinoma has no current standard of care

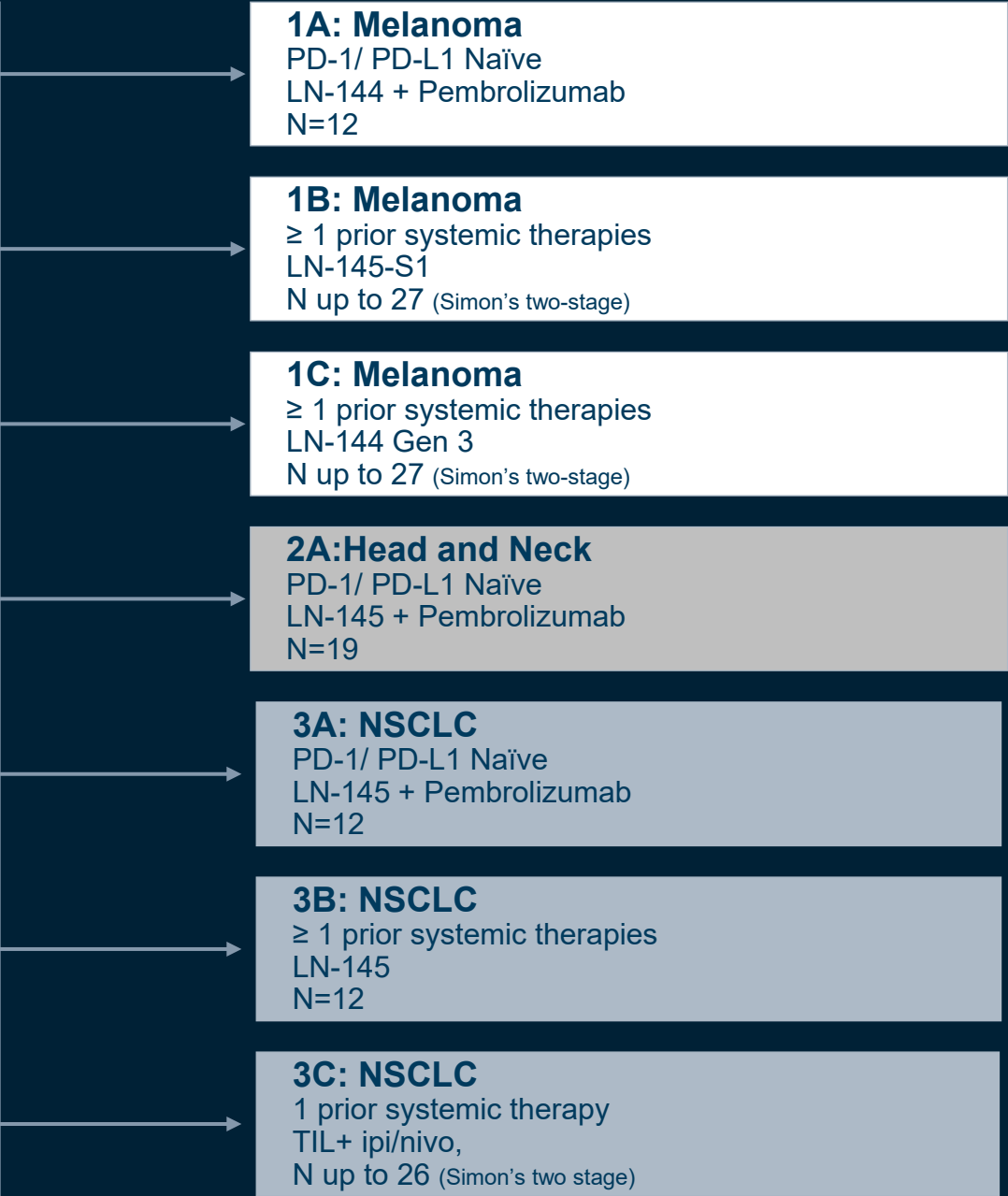
Agent	ORR % (N)	Current Dev Status	Prior Line of Tx	Patient Characteristics
Antibody-drug conjugate				
tisotumab vedotin (TV) (Genmab/Seagen)	24% (N=101) ⁽¹⁾	Phase 2	1+	Recurrent or metastatic cervical cancer that progressed on standard therapy ≤2 prior systemic regimens mDOR= 8.3 mons, mOS= 12.1 mons
Anti-PD-1 alone or combination with anti-CTLA4				
Balstilimab (Agenus)	14% (N=160) ⁽²⁾	Phase 2	1+	Patients must have relapsed after a platinum-containing doublet administered for treatment of advanced disease, median DOR=15.4 months
Balstilimab + Zalifrelimab	22% (N=143) ⁽²⁾	Phase 2	1+	
cemiplimab (Regeneron)	10% (N=10) ⁽³⁾	Phase 1 Phase 3 read out	2+	Recurrent or metastatic cervical cancer resistant to, or intolerant of, platinum therapy. Ph 3 mOS 12.0 mons
Cell therapies				
TIL (Ilficleucel)	44% (N=27)⁽⁴⁾	Phase 2	2.4 (mean)	mDOR not reached at median study follow up of 7.4 mons

⁽¹⁾ Coleman et al., ESMO 2020 ⁽²⁾ O'Malley et al., ESMO 2020

⁽³⁾ Rischin et al., ESMO 2018 ⁽⁴⁾ Jazaeri et al., ASCO 2019

HNSCC & NSCLC

A Phase 2, multicenter study of autologous Tumor Infiltrating Lymphocytes in patients with solid tumors



Endpoints

- Primary: Efficacy and safety: ORR (RECIST 1.1) assessed by investigator
- Secondary: Additional efficacy

Study Updates

- Additional cohorts 1C and 3C were added in 1Q21
- Sample size for cohort 2A was increased

Head and Neck Squamous Cell Carcinoma (HNSCC)

Potential Market for Head and Neck Squamous Cell Carcinoma (HNSCC)

“The majority of patients did experience a tumor shrinkage that in some cases met the criteria for an objective response. It is hard to generalize from such a small cohort, but with that caveat complete responses are relatively rare with PD-1 inhibition alone based on what has been reported in PD-1 inhibitor first-line trials in PD-1 naïve patients with head and neck carcinoma.”

— Antonio Jimeno M.D., Ph.D.
Professor of Medicine/Oncology and
Otolaryngology University of Colorado
School of Medicine

HNSCC Facts

890k New Cases WW
each year⁽¹⁾

507k Deaths WW
each year⁽¹⁾

66k Diagnoses in U.S.
each year⁽²⁾

15k Deaths in U.S.
each year⁽²⁾

Available Care (NCCN)

ORR

DOR

First Line

Anti PD-1 antibody⁽³⁾

16%

22.6 months

Anti PD-1 antibody + Chemo⁽³⁾

36%

6.7 months

Chemotherapy (EXTREME)⁽⁴⁾

36%

5.6 months

Second Line

Anti PD-1 antibody⁽⁵⁾

16%

8 months

Abbreviations: ORR, objective response rate; TIL, tumor infiltrating lymphocytes.

⁽¹⁾ Global Burden of Disease Cancer Collaboration, JAMA Oncol 2019 ⁽²⁾ <https://seer.cancer.gov> accessed Mar 2021

⁽³⁾ Keytruda USPI accessed Mar 2021 and Szturcz et al., Ann Transl Med 2020 ⁽⁴⁾ Vermorken et al., NEJM 2008 ⁽⁵⁾ Bauml et al., J Clin Oncol 2017

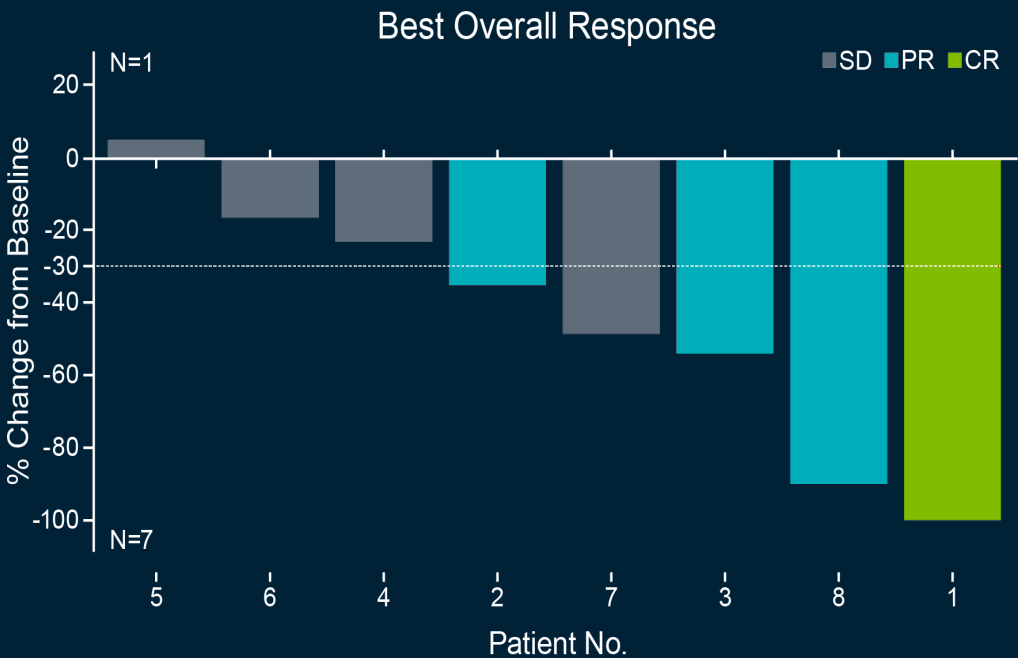
LN-145 in Anti-PD-1 Naive HNSCC: Cohort 2A

TEAE consistent with other indications

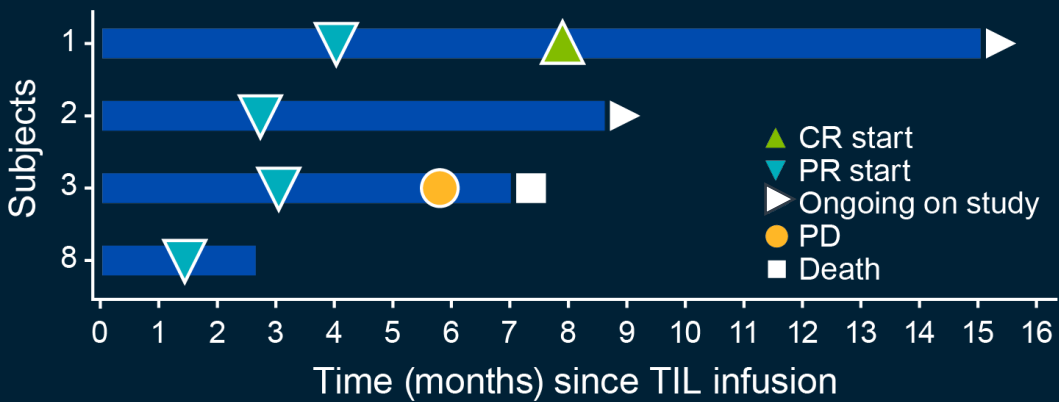
Efficacy (N=9)

ORR=44% (11% CR and 33% PR)

DCR=89%



PD-L1 Status	
CPS ≥ 20	
CPS ≥ 20	
CPS < 20*	
CPS ≥ 20	
* CPS > 1	



Non-Small Cell Lung Cancer (NSCLC)

Potential Market for Non-Small Cell Lung Cancer (NSCLC)

Addressing a Defined Unmet Need in Second Line NSCLC

“We’re excited about carrying TILs further in lung cancer.”

“Despite progression on nivolumab, we did see a decrease in tumor size for many patients, and the ORR was in around one-quarter of patients, and perhaps in a one-third of patients if our unconfirmed PR is confirmed...Clonotype and phenotype analyses suggested good persistence of the transferred TILs—going out to several months.”

— Ben Creelan, M.D.*
Thoracic Oncology Program at Moffitt Cancer Center

* OncLive, AACR 2020, “TIL Therapy Elicits Encouraging Activity in Advanced NSCLC”

Lung Cancer Facts

2.1M New Cases WW
each year⁽¹⁾

1.8M Deaths WW
each year⁽¹⁾

229k Diagnoses in U.S.
each year⁽²⁾

136k Deaths in U.S.
each year⁽²⁾

Available NSCLC
care:
**Checkpoint
Inhibitor +
Chemo**
as first line option

9% ORR for
docetaxel
in 2L NSCLC following
progression on chemo⁽³⁾

⁽¹⁾ Global Burden of Disease Cancer Collaboration, JAMA Oncol 2019

⁽²⁾ <https://seer.cancer.gov> accessed Mar 2021

⁽³⁾ Brahmer et al., NEJM 2015

Efficacy Data Post Moffitt TIL Infusion

Responses	N=12 (%)
Objective Response Rate	3 (25%)
Complete Response	2 (17%)
Partial Response	1 (8%)

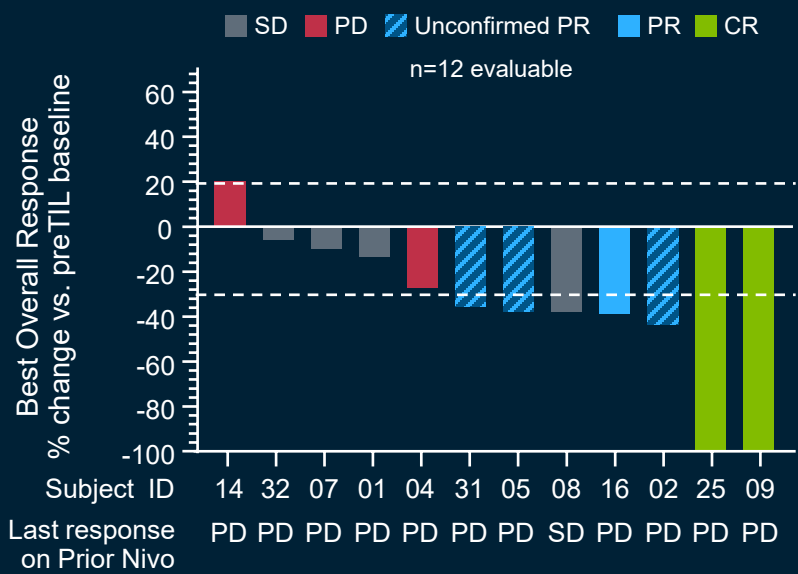
- **ORR 25%;**
 - 1 CR is noted in EGFR^{ΔEx19} post afatinib, osimertinib, nivolumab
- **Median DOR not reached;**
 - All 3 responders on TIL were relapsed or refractory to monotherapy Nivo
 - The TIL CR responses were ongoing
 - 2/3 responders were PD-L1 low (TPS<5%)

⁽¹⁾ Creelan et al., AACR 2020

Moffitt TIL in Post-Nivolumab NSCLC

Nivolumab and Tumor Infiltrating Lymphocytes (TIL) in Advanced Non-Small Cell Lung Cancer (NCT03215810)

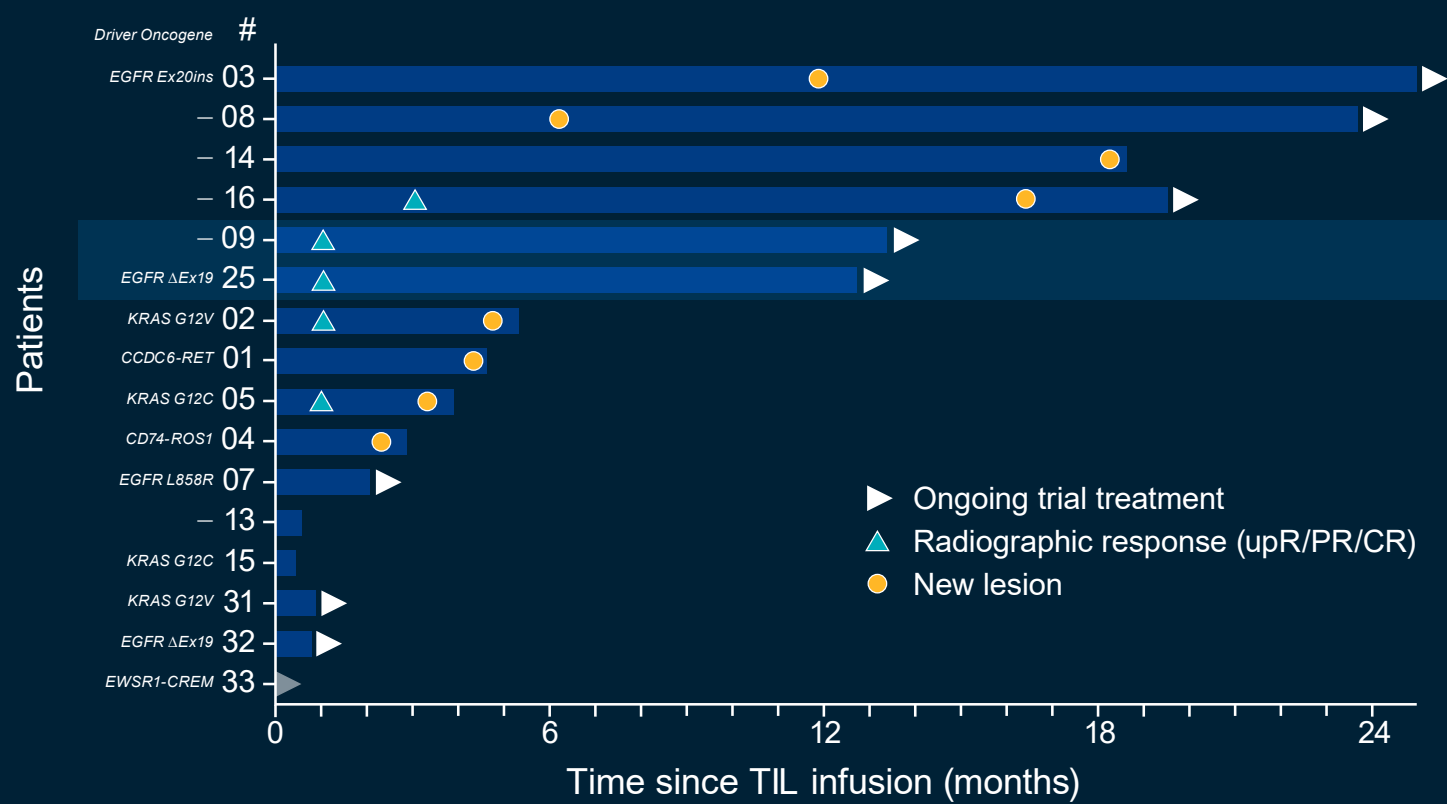
Post-TIL



In 12 evaluable patients with advanced NSCLC who received nivolumab and TIL:

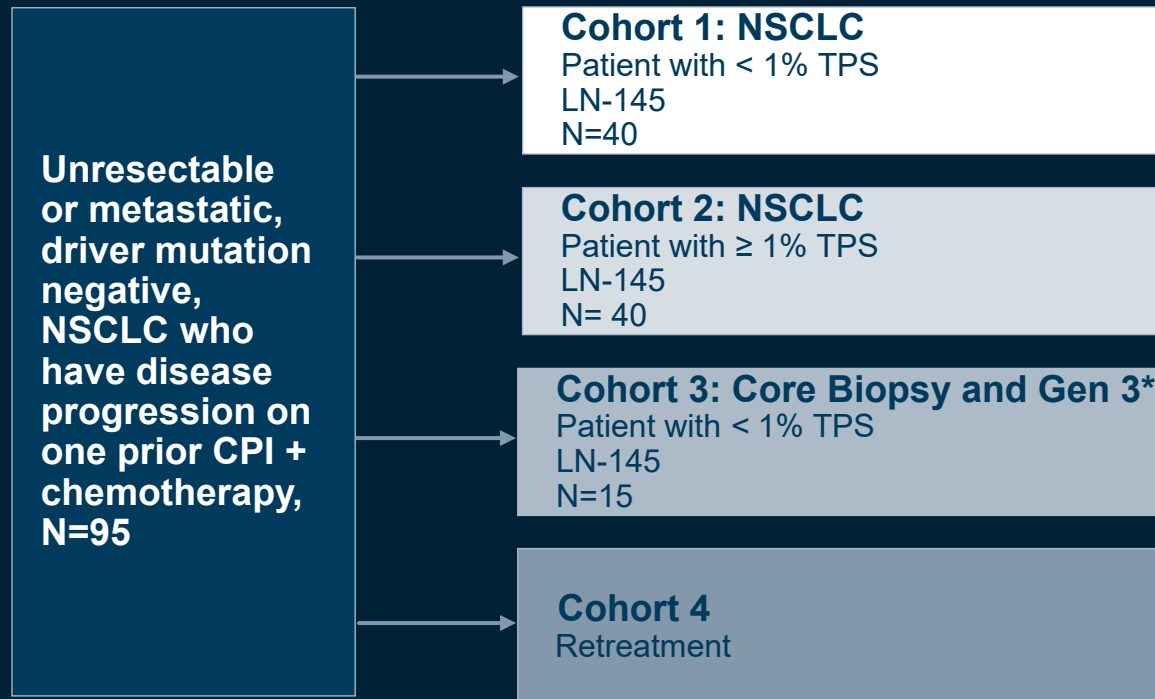
- Two CRs out to one year
 - (PD-L1 low=1, EGFR mutation=1)
- ORR 25%

⁽¹⁾ Creelan et al., AACR 2020



IOV-LUN-202

Phase 2, multicenter study of LN-145 in Patients with Metastatic Non-Small-Cell Lung Cancer, IOV-LUN-202 (NCT04614103)



Endpoints:

- Primary: Efficacy defined as ORR by IRC
- Secondary: Safety and efficacy

Study Updates

- Two sites are active

*Cohort 3 patients unable to undergo surgical harvest, TIL grown from core biopsy

Research Focus into Next Generation TIL



Expand the TIL platform into new indications/regimens

- IOV-3001 IL-2 analog licensed from Novartis: IND enabling studies in 2021



Select more potent TIL

- Iovance PD-1 positive selected TIL
- PD-1 positive selected TIL also through collaboration with CHUM



Genetically modify to make a more tumor-reactive TIL

- Cellectis TALEN® collaboration agreement in place to support a clinical program ⁽¹⁾



Process optimization

- Gen 3 (16-day) process (COM-202)
- Core biopsy (LUN-202 study)

⁽¹⁾ Ritthipichai et al., ESMO 2020

Iovance Global Reach and Scale



Iovance Biotherapeutics has ~250 employees

- >76% of employees have over 1 year of cell therapy experience
- Headquartered in San Carlos, CA
- 4 additional offices
- Iovance commercial manufacturing facility in Philadelphia, PA

Well Capitalized in Pursuit of TIL Commercialization

December 31, 2020	In millions (unaudited)
Common shares outstanding	146.9
Preferred shares outstanding	3.6 ⁽¹⁾
Options	12.6
Cash, cash equivalents, short-term investments, restricted cash	\$635.0 ⁽²⁾
Anticipated cash runway sufficient into 2023	
Debt	\$0

⁽¹⁾ Preferred shares are shown on an as-converted basis.

⁽²⁾ Includes Restricted Cash of \$5.5 million.



ADVANCING IMMUNO-ONCOLOGY

Thank You