



ADVANCING IMMUNO-ONCOLOGY

Investigating the Power of Tumor Infiltrating Lymphocytes for Treatment of Cancer

November 2020

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Forward Looking Statements

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These forward-looking statements include, but are not limited to, statements regarding the success, timing, projected enrollment, manufacturing and production capabilities, and cost of our ongoing clinical trials and anticipated clinical trials for our current product candidates (including both Company-sponsored and collaborator-sponsored trials in both the U.S. and Europe), such as statements regarding the timing of initiation and completion of these trials; the strength of the Company’s product pipeline; and the guidance provided for the Company’s future cash, cash equivalents, short-term investments, restricted cash balances and forecasted operating expenses, including our statements regarding the sufficiency of our cash reserves to execute commercial launch and pipeline programs, which assumes no material change in liabilities. 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our limited operating history in our current line of business, which makes it difficult to evaluate our prospects, our business plan or the likelihood of our successfully implementing such business plan; risks related to the timing of and our ability to successfully develop, submit, obtain and maintain FDA or other regulatory authority approval of, or other action with respect to, our product candidates (including with respect to lifileucel for the treatment of metastatic melanoma, for which we currently expect to submit a biologics licensing application (“BLA”) to the FDA during 2021), and our ability to successfully commercialize any product candidates for which we obtain FDA approval; our limited history in conducting clinical trials, on which our future profitability is substantially dependent, and our need to rely on third parties, including contract research organizations, contract manufacturing organizations and consultants, in connection with the conduct, supervision and monitoring of our clinical trials for our product candidates; preliminary and interim clinical results, which may include efficacy and safety results, from ongoing Phase 2 studies may not be reflected in the final analyses of our ongoing clinical trials or subgroups within these trials; the risk that a slower rate of enrollment may delay the Company’s clinical trial timelines or otherwise adversely impact our clinical development activities; the risk that enrollment may need to be adjusted for the Company’s 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 the Company’s cervical cancer trial may have an adverse effect on the results reported to date; the risk that the results obtained in our ongoing clinical trials may not be indicative of results obtained in future clinical trials or that data within these trials may not be supportive of product approval, including that later developments with the FDA may be inconsistent with already completed FDA meetings; the risk that the FDA may not agree with our approach to expand our cervical cancer trial to include Cohort 2 of the C-145-04 trial; the risk that changes in patient populations may result in changes in preliminary clinical results; the Company’s ability or inability to address FDA or other regulatory authority requirements relating to its clinical programs and registrational plans, such requirements including, but not limited to, clinical, safety, manufacturing and control requirements; the risk that regulatory authorities may potentially delay the timing of FDA or other regulatory approval of, or other action with respect to, our product candidates, or 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 the Company’s interpretation of the results of its clinical trials or communications with the FDA may differ from the interpretation of such results or communications by the FDA; our ability to obtain and maintain intellectual property rights related to our product pipeline; our ability to successfully implement our research and development programs and collaborations; the acceptance by the market of our product candidates and their potential reimbursement by payors, if approved; our ability to obtain tax incentives and credits and the risk that our existing net operating loss carryforwards and research tax credits may expire or otherwise be limited in use; the success of our manufacturing, license or development agreements; risks related to the Company’s ability to maintain and benefit from accelerated FDA review designations, including breakthrough therapy designation or regenerative medicine advanced therapy designation, which may not result in a faster development process or review of the Company’s product candidates (and which may later be rescinded by the FDA), and which does not assure approval of such product candidates by the FDA or the ability of the Company to obtain FDA approval in time to benefit from commercial opportunities; the ability or inability of the Company to manufacture its therapies using third party manufacturers or its own facility may adversely affect the Company’s potential commercial launch; the results of clinical trials with collaborators using different manufacturing processes may not be reflected in the Company’s sponsored trials; our dependence on additional financing to fund our operations and complete the development and commercialization of our product candidates, and the risks that raising such additional capital may restrict our operations or require us to relinquish rights to our technologies or product candidates; 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 the Company’s control.

2020 Recent Updates



Cervical: last patient dosed in the Cohort 1

HNSCC: Response in PD-1 naïve patients in combination with Keytruda at SITC 2020

IOV-LUN-202 in NSCLC initiated



> 90% manufacturing success rate in over 400 patients



FDA Type B Meeting held, Agreement on clinical follow up for Cohort 4 reached:

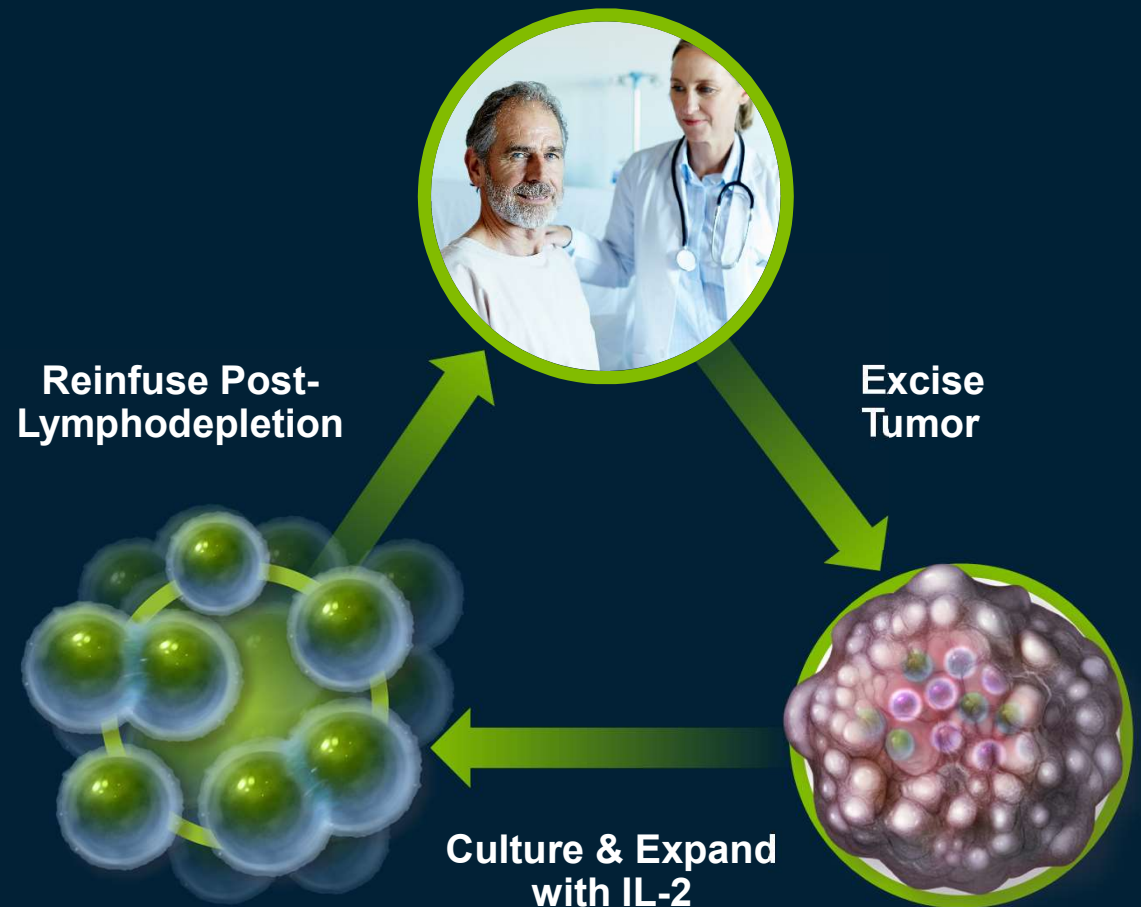
- 6 months from initial response by IRC
- Cohort 2 can be supportive

Additional work on potency assays underway. Communication with FDA will continue.

TIL: Leading Platform for Treatment of Solid Tumors

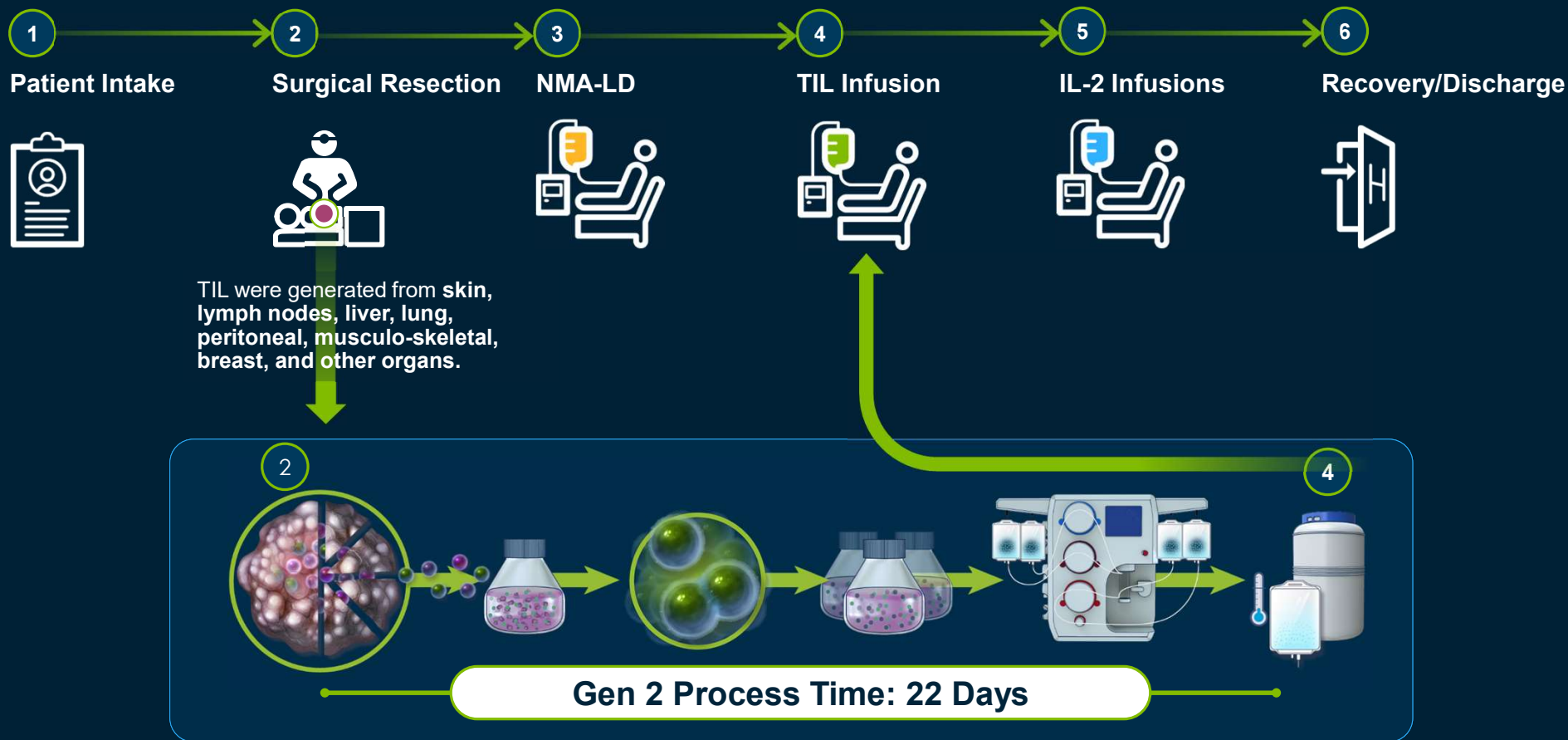
Tumor-Infiltrating Lymphocytes (TIL) – Unique Mechanism in Immuno-oncology

- Highly personalized therapy
- Our own immune system amplified and rejuvenated



¹Simpson-Abelson, *et. al*, Iovance Generation-2 Tumor-infiltrating Lymphocyte (TIL) Product Is Reinvigorated During the Manufacturing Process, ESMO 2020

Iovance Proprietary Centralized, Scalable, and Efficient GMP Manufacturing



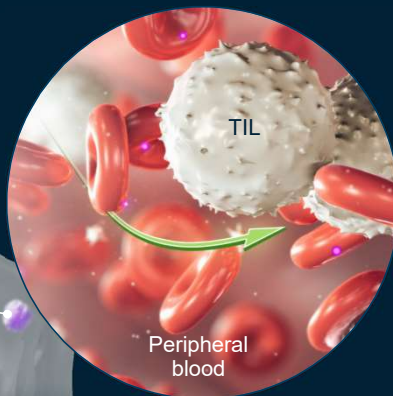
TIL Mechanism of Action

Infusion of
tumor-infiltrating
lymphocytes (TIL)

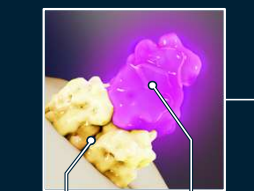
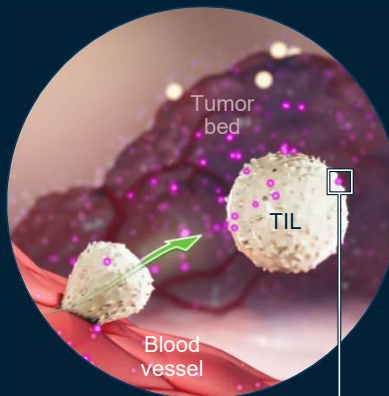


Tumor

Circulation

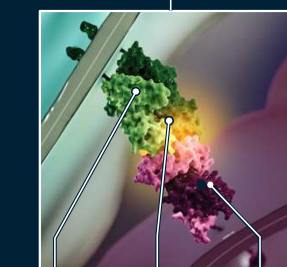
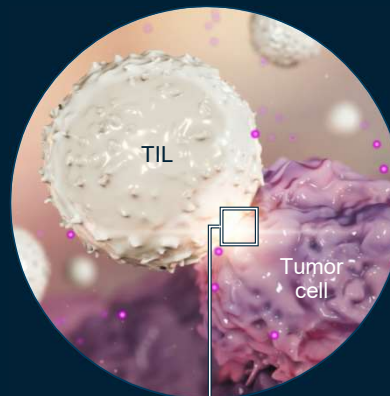


Migration



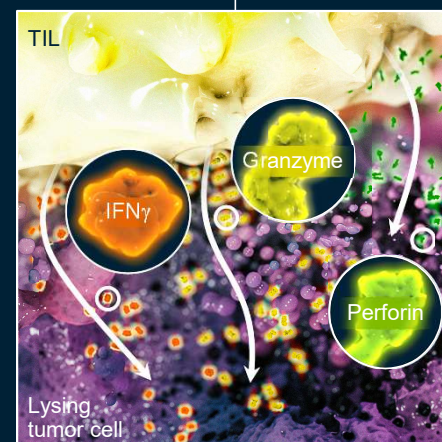
Chemokine receptor

Recognition



T-cell receptor
Tumor antigen peptide
MHC-I

Lysis



Leveraging Tumor Infiltrating Lymphocyte (TIL) to Address Unmet Need

Discovery

Manufacturing Development, Clinical Program Establishment

Pre-Commercialization

2011

TIL therapy conducted by Steven Rosenberg/NCI published results showing: **56% ORR⁽¹⁾** and **24% CR** rate in melanoma patients, with durable CRs as an early line therapy⁽²⁾

2015

FDA Orphan Drug Designation for lifileucel in malignant melanoma

2016

First patient dosed for Gen 1 lifileucel in melanoma

Gen 2 manufacturing developed and transferred to CMOs

2017

Head & Neck and Cervical studies began

FDA Fast Track designation for lifileucel in melanoma received

2018

FDA RMAT designation for lifileucel in advanced melanoma received

FDA EOP2 meeting for lifileucel held

Lifileucel Cohort 2 clinical data showed **38% ORR in 47 patients**, patients with average 3.3 prior lines of therapy

Two rounds of financing conducted: **over \$425 mil raised**

2019

First patient dosed for melanoma registrational trial

FDA Fast Track, BTD in cervical

FDA EOP 2 held for lifileucel for cervical

File IND for PBL in chronic lymphocytic leukemia (CLL), IND cleared and first patient dosed

Clinical IRC data from Cohort 2 of melanoma at SITC shows **35% ORR**

2020-2021

TIL manufactured by Moffitt shows **2 durable CRs** in post-PD1 NSCLC

Data presentation by investigator for: Cohort 2 at ASCO, early data in Cohort 4 pivotal melanoma

Last patient dosed in registrational program in cervical

HNSCC data in TIL plus Keytruda at SITC

Start a registration-directed NSCLC program, IOV-LUN-202

Hold pre-BLA meeting with FDA

Submit BLA for lifileucel

⁽¹⁾ Rosenberg, S. A., et al. *Clinical Cancer Research*, 2011, 17, 4550

⁽²⁾ Goff, S. L. et al. *Journal of Clinical Oncology*, 2016, 34(20), 2389-2397

Key Highlights for Melanoma Cohort 2 Data

**2019: Melanoma Data
update at SITC** (8 Nov 2019)⁽¹⁾

Melanoma Cohort 2 showed

36.4% ORR

by investigator and

34.8% ORR

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

2020: Updated Melanoma Data cut
ASCO20

**Median DOR not reached
at 18.7 months of median
study follow up**

(investigator assessed) ⁽²⁾

⁽¹⁾Sarnaik *et al.*, SITC 2019, P865.

⁽²⁾Sarnaik *et al.*, ASCO 2020, 10006.


Investment Highlights

Leading cell therapy company focused on treatment of solid tumors



Large market opportunity and 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, non-small cell lung cancer (NSCLC), and 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
- Last patient dosed in pivotal trial for melanoma and Cohort 1 in cervical
- BLA filings expected 2021
- Melanoma: RMAT, Orphan Drug, and Fast Track
- Cervical: BTM, Orphan Drug and Fast Track



Efficient and scalable proprietary manufacturing

- U.S. and E.U. capacity with contract manufacturers
- Building Iovance 136,000 sq. ft. manufacturing facility in Philadelphia
- Rapid 22-day Gen 2 manufacturing with 90%+ success rate
- **400+ patients treated with Iovance proprietary process**



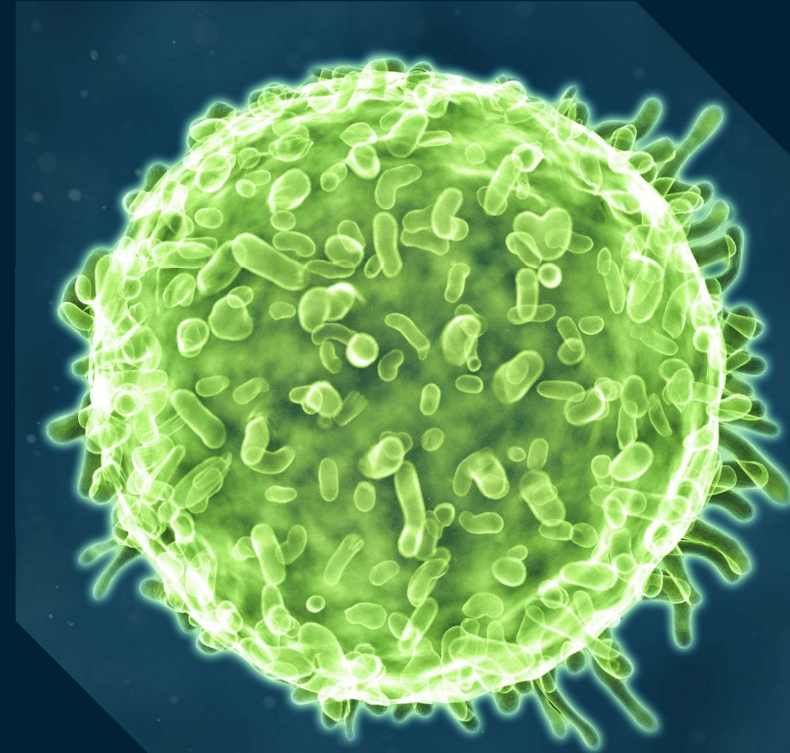
Broad platform and wide applications explored through partnerships

- Investigator-led programs to evaluate additional solid tumors or new combinations
- Data from Moffitt TIL in NSCLC as a new indication for Iovance
- Touch points with institutions including NIH/NCI, Moffitt Cancer Center, MD Anderson, Yale, and University of Montreal (CHUM)

Highly Individualized, Specific & Potent Attack Against Cancer

Leverages and enhances the body's natural defense against cancer using a patient's own Tumor Infiltrating Lymphocytes, or TIL

- **Polyclonal:** Can recognize multiple neoantigens
 - Effective in heterogeneous solid tumors
 - Data in melanoma, cervical, head & neck, and lung cancers
- **Individualized:** TIL of each patient is specific and private with little overlap of uCDR3 between patients⁽¹⁾
- **Persistence:** 100% of patients had TIL persisting at Day 42⁽¹⁾
- **Immunological memory:** No additional maintenance therapy after infusion
 - Responses in treatment naïve and refractory melanoma; including checkpoint refractory
 - Durable complete responses in cervical cancer patients, maintained at 53 and 67 months⁽²⁾
 - Durable CRs observed in NSCLC patients beyond one-year post-TIL⁽³⁾



⁽¹⁾ Gontcharova, et al., Persistence of cryopreserved tumor-infiltrating lymphocyte product lifileucel (LN-144) in C-144-01 study of advanced metastatic melanoma, AACR 2019, Abstract #LB-069. Gontcharova, et al., Add Viktoria's cervical poster here too from ESMO.

⁽²⁾ Stevanovic, et al., Treatment of Metastatic Human Papillomavirus-Associated Epithelial Cancers with Adoptive Transfer of Tumor-Infiltrating T Cells, ASCO 2018, Abstract #3004.

⁽³⁾ Creelan, et. al., Durable complete responses to adoptive cell transfer using tumor infiltrating lymphocytes (TIL) in non-small cell lung cancer (NSCLC): a phase I trial, AACR 2020, Abstract #20-LB-10617.

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-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, customized, and targeted immunotherapy**

Broad, Iovance-Owned IP Around TIL Therapy

Manufacturing

20 granted or allowed U.S. patents for compositions and methods of treatment in a broad range of cancers relating to Gen 2 manufacturing process including combinations with PD-1 antibodies

Advanced Technologies

Patent applications filed for a wide range of TIL technologies including:

- Marrow infiltrating (MIL) and peripheral blood lymphocyte therapies (PBL)
- Novel manufacturing processes including selected TIL process
- Use of costimulatory molecules in TIL therapy
- Stable and transient genetically-modified TIL therapies
- Patient subpopulations for TIL therapies

Iovance Cell Therapy Center (iCTC)



- Build-to-suit custom facility located in the Navy Yard, Philadelphia, PA
- ~136,000 sq. feet, \$85 mil investment
- First set of clean rooms ready by end 2020
- Commercial GMP production is expected to commence in 2022
- Significant reduction in COGS expected



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⁾

⁽¹⁾ <https://seer.cancer.gov>

IOVANCE

Move into earlier line of therapy →

Expand into other indications ↓	Solid Tumor Indication	Deaths ⁽¹⁾	New Cases ⁽¹⁾
	Melanoma	6,850	96,480
	Cervix Uteri	4,290	13,800
	Lung & Bronchus	136,000	229,000
	Oral Cavity, Pharynx & Larynx	15,000	65,000
	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

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 LN-145-S1 LN-145 + pembrolizumab LN-145 + pembrolizumab LN-145	IOV-COM-202	Melanoma Melanoma Head & neck Non-small cell lung Non-small cell lung	~75	—	<div></div>		
	LN-145	IOV-LUN-202	Non-small cell lung	95	—	<div></div>		
	IOV-2001	IOV-CLL-01	Chronic lymphocytic leukemia	~70	—	<div></div>		
Select investigator sponsored proof-of-concept studies	MDA TIL	NCT03610490	Ovarian, colorectal, pancreatic	~54	MD Anderson Cancer Network	<div></div>		
	LN-145	NCT03449108	Ovarian, sarcomas	~54	MD Anderson Cancer Network	<div></div>		
	Moffitt TIL + nivolumab	NCT03215810	Non-small cell lung	20	MOFFITT CANCER CENTER	<div></div>		

Metastatic Melanoma

Potential Market for Metastatic Melanoma

- Estimated 7,230⁽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⁾ in 2019, <https://seer.cancer.gov>.

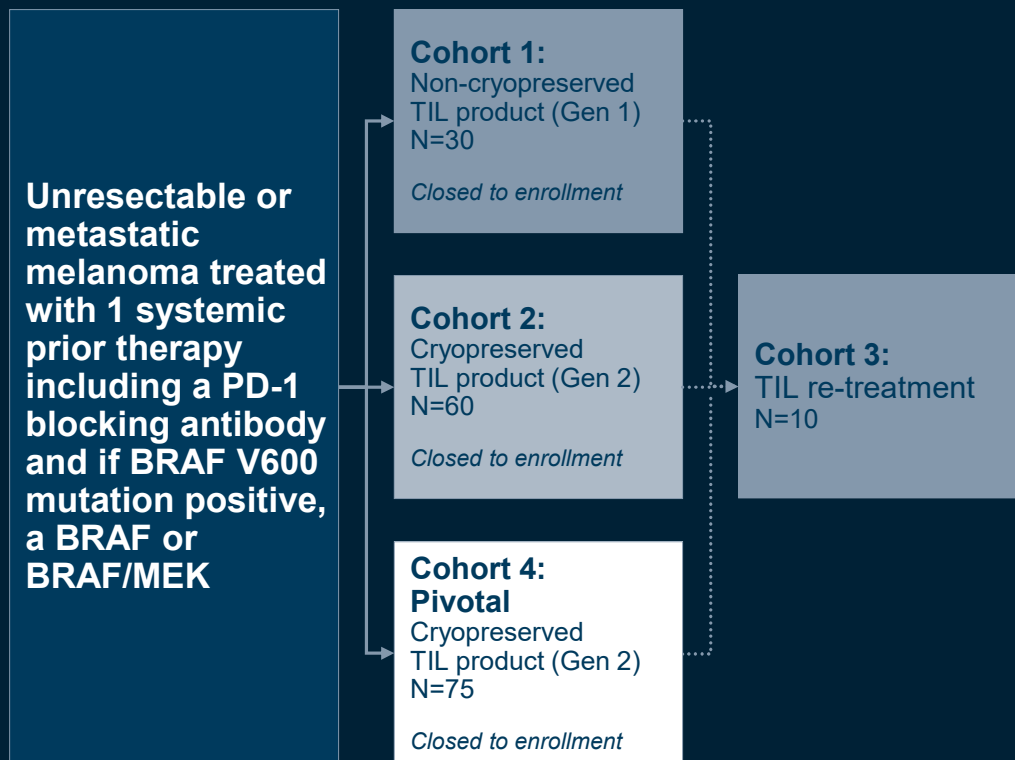
⁽²⁾ CheckMate-37 Trial Results (ICC 10%), Keytruda label (4%).

⁽³⁾ JAMA Oncol. 2019; 5(12):1749-1768. doi:10.1001/jamaoncol.2019.2996.

⁽⁴⁾ Eur J Cancer. 2016; 65:182-184. J Clin Oncol. 2018; 36 (suppl: abstr e21588).

C-144-01: Phase 2 Study Design

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



Endpoints

- Primary: Efficacy defined as IRC ORR

Study Updates

- Mar 2019: Cohort 4 (pivotal trial) FPI
- Jun 2019: Full Cohort 2 data on 66 patients presented at ASCO
- Nov 2019: IRC Cohort 2 data presented at SITC
- Nov 2019: Investigator read of Cohort 2 sub-analysis for primary refractory to PD-1 presented
- Jan 2020: last patient dosed
- May 2020: Cohort 4 early data show 32.4% ORR at 5.3 months of median study follow up
- May 2020 ASCO oral: Cohort 2 median DOR not reached at 18.7 months of median study follow up

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

CHARACTERISTIC	Cohort 2, N=66, (%)	CHARACTERISTIC	Cohort 2, N=66, (%)
Gender, n (%)		BRAF Status, n (%)	
Female	27 (41)	Mutated V600	17 (26)
Male	39 (59)	Wild Type	45 (68)
Age, years		Unknown	3 (5)
Median	55	Other	1 (2)
Min, Max	20, 79	Baseline LDH (U/L)	
Prior therapies, n (%)		Median	244
Mean # prior therapies	3.3	1-2 times ULN	19 (29)
Anti-PD-1	66 (100)	> 2 times ULN	8 (12)
Anti-CTLA-4	53 (80)	Target Lesions Sum of Diameter (mm)	
BRAF/MEK	15 (23)	Mean (SD)	106 (71)
Progressive Disease for at least 1 prior therapy		Min, Max	11, 343
Anti-PD-1	65 (99)	Number of Target and Non-Target Lesions (at Baseline)	
Anti-CTLA-4	41 (77 ⁽¹⁾)	>3	51 (77)
Baseline ECOG score, n (%)		Mean (SD)	6 (2.7)
0	37 (56)	Patients with Baseline Liver and/or	
1	29 (44)	Brain Lesions	28 (42)

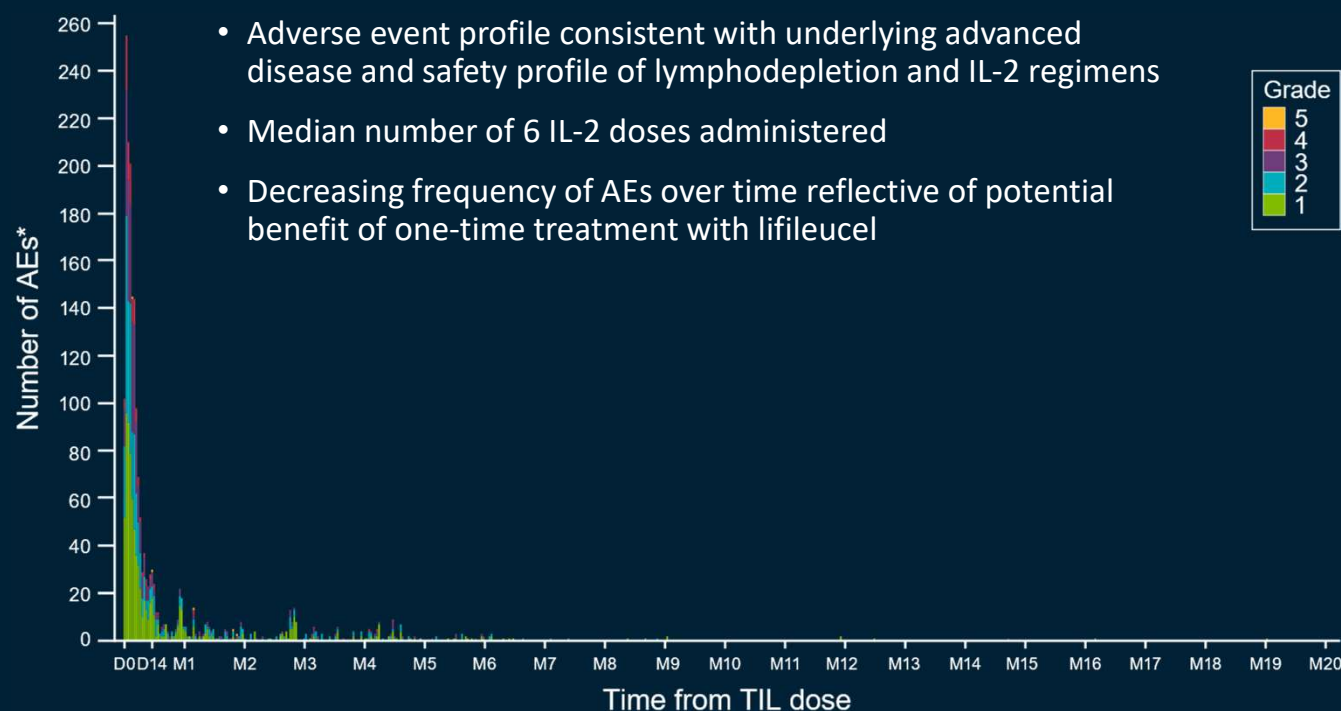
Cohort 2 patients have:

- 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 which describe the same medical condition were combined.

Potentially Efficacious Treatment for Patients with Limited Options

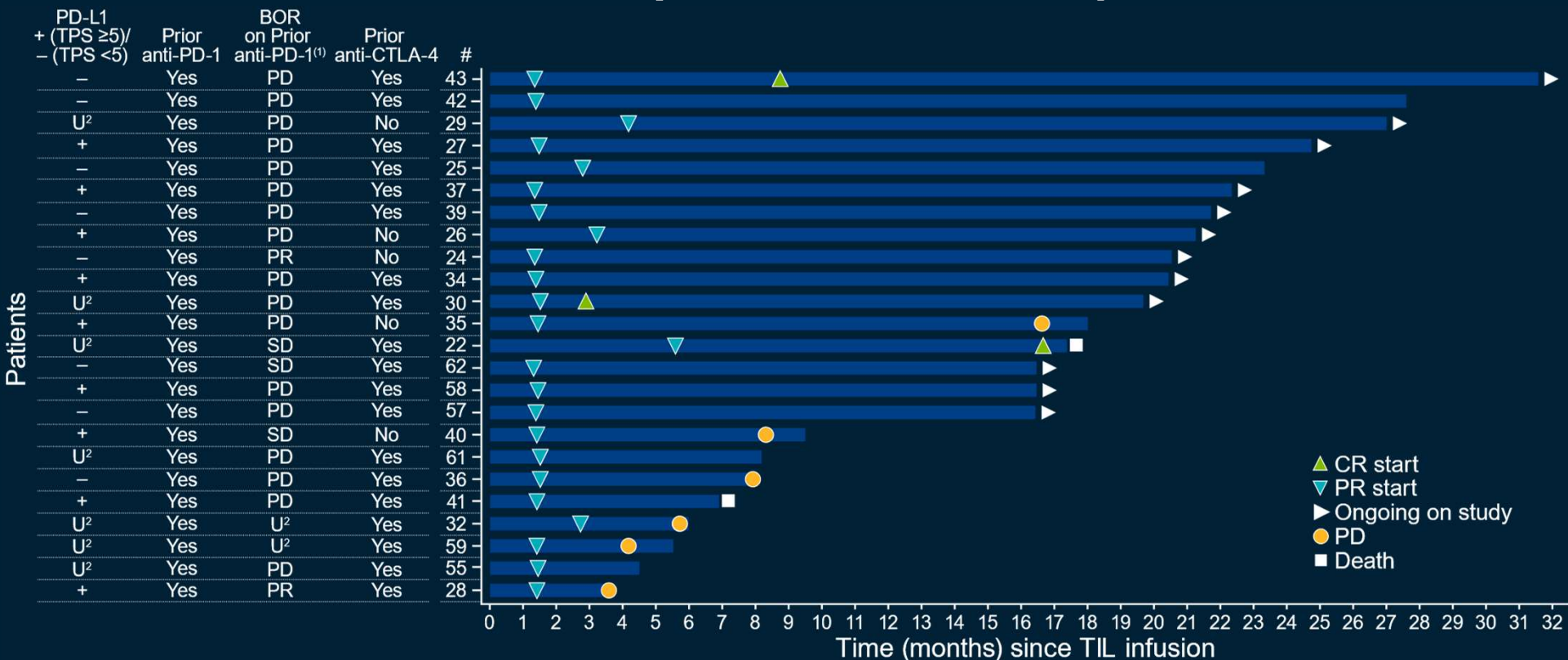
In heavily pretreated metastatic melanoma patients (3.3 mean prior therapies)

- **ORR 36%**
- **DCR 80%**
- ***Median DOR has not been reached at 18.7 mons of study follow up***
- Mean TIL cells infused: 27.3×10^9
- Median number of IL-2 doses: 5.5

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)
Median Duration of Response	Not Reached
Min, Max (months)	2.2, 26.9+

18% attrition in patients harvested (6% manufacturing failure).

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



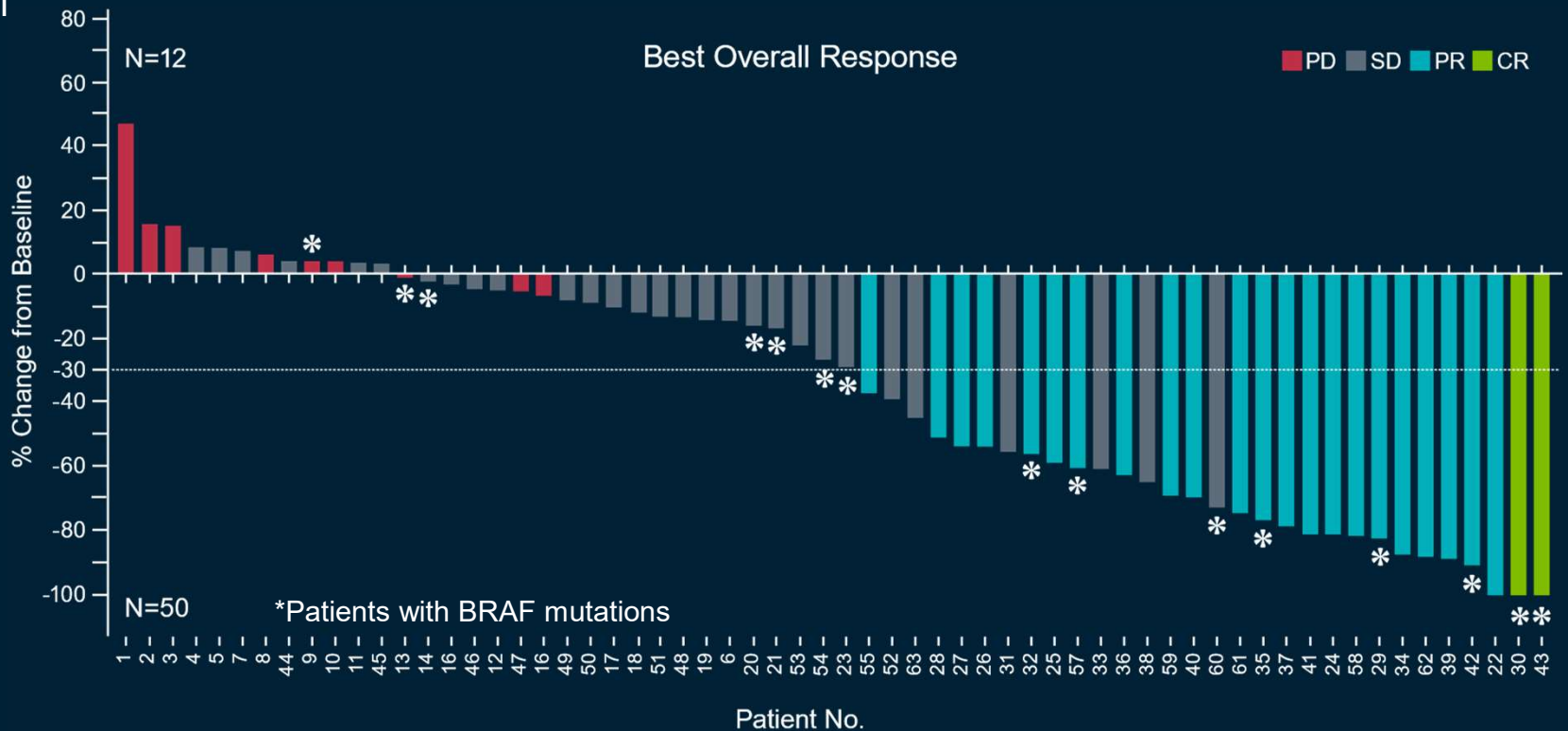
79% of responders had received prior ipilimumab. Responses deepen over time.

⁽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

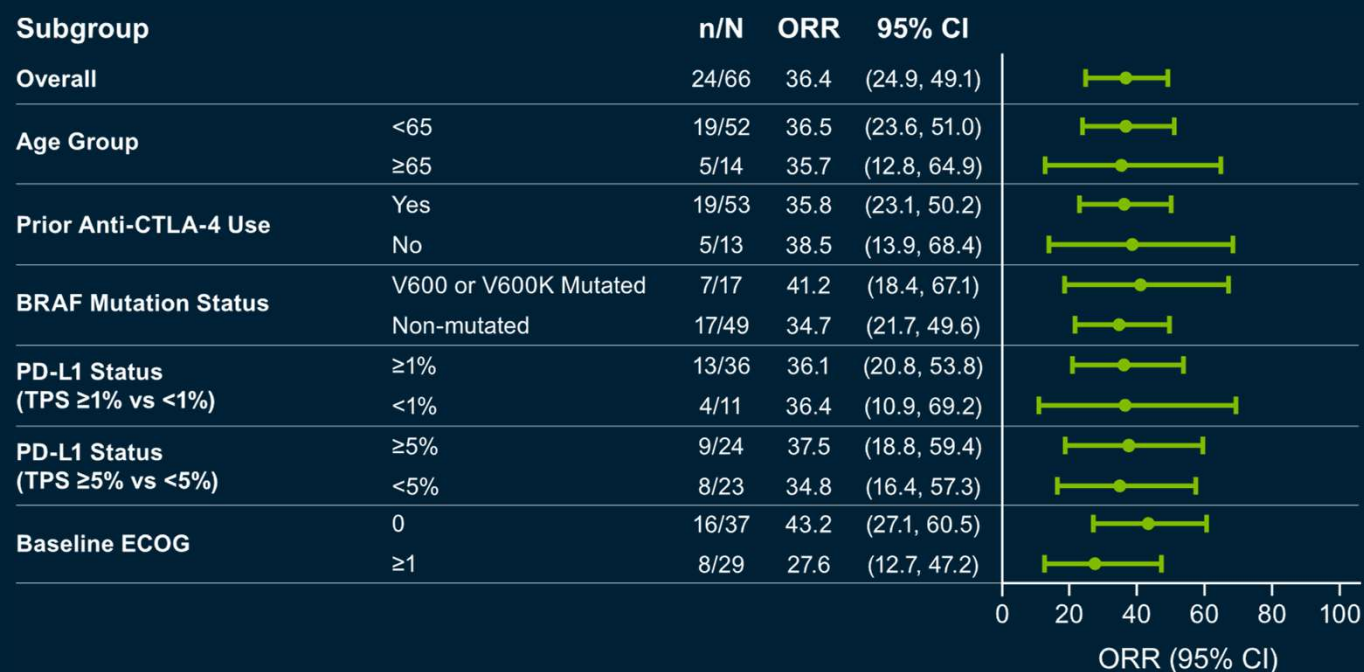
➤ 81% (50/62) of patients had a reduction in tumor burden

- Mean Time to response 1.9 months (range 1.3-5.6)
- Responses are deep – nearly all responders are >30%



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

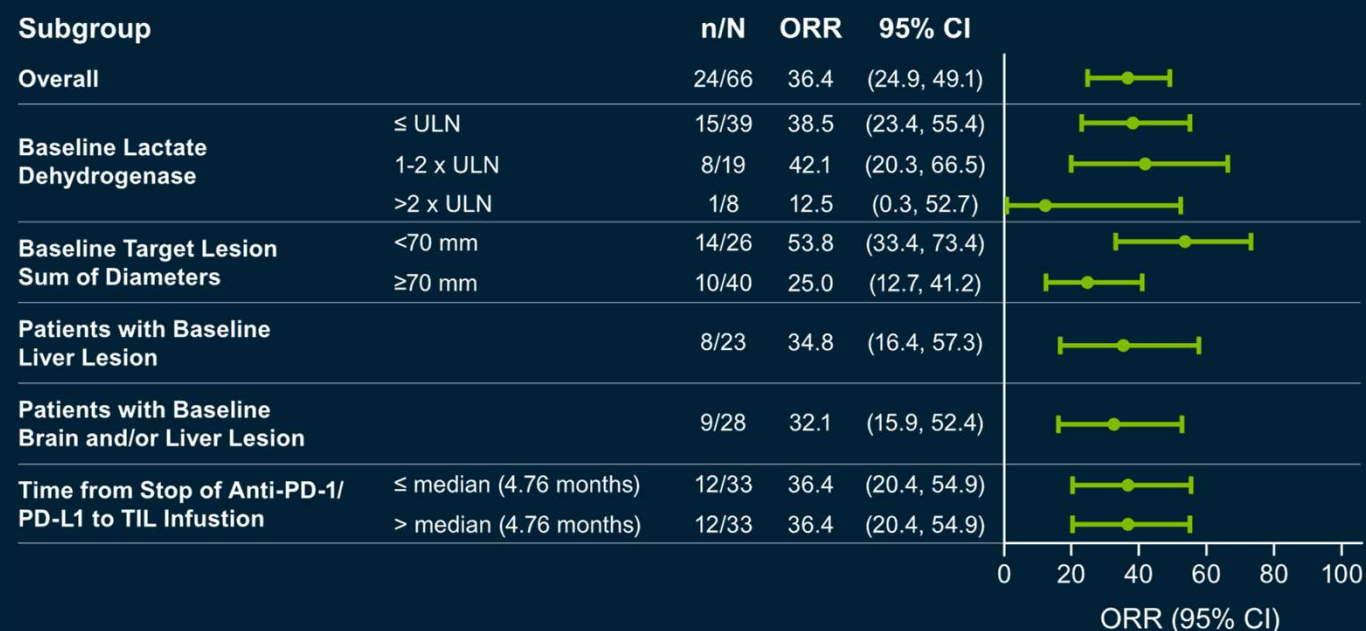


Responses were demonstrated:

- 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

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

ULN, Upper Limit 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 18.7 months of median study follow up
- 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, HDAC, kinase inh				
	IMO-2125 (Idera) + ipi	22% (N=62) ⁽²⁾	Phase 3, post-PD-1 melanoma ILLUMINATE 204	1-3	ECOG ≤1, intratumoral injection Median DOR was 11.4 months, mOS 10.1 months
	CMP-001 (CheckMate) + pembro	25% (N=82) ⁽³⁾	Phase 1b	1+	ECOG ≤1, intratumoral injection
	Lenvatinib + pembro	21.4% (N=103) ⁽⁴⁾	Phase 2	1+	Median DOR: 6.3 months mOS: 13.9 months
Single Agent	Entinostat (Syndax) + pembro	19% (N=53) ⁽⁵⁾	ENCORE 601	1+	ECOG ≤1
	Checkpoints				
	TIGIT, TIM-3	Unknown	Phase 1/2		
	Cytokines				
	HD IL-2	8% (N=9) ⁽⁶⁾		1+	HD IL-2 post anti-PD1
Single Agent	Other				
	TIL	36.4% (N=66)⁽⁷⁾	Phase 2, Cohort 2	3.3	All post anti-PD1

⁽¹⁾ Ascierto P et al., ESMO 2017; ⁽²⁾ Diab, et al., ESMO 2020; ⁽³⁾ Milhem M et al., SITC 2019; ⁽⁴⁾ Fernandez et al., ESMO 2020, LBA44;
⁽⁵⁾ Ramalingam et al., AACR 2019; ⁽⁶⁾ Buchbinder EI et al., JCO 2017; ⁽⁷⁾ Sarnaik et al., SITC 2019

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%

Available Care
for chemotherapy
in 2L metastatic
cervical patients
4.5-13%⁽⁴⁾⁽⁵⁾

⁽¹⁾ JAMA Oncol. 2019;5(12):1749-1768. doi:10.1001/jamaoncol.2019.2996.

⁽²⁾ <https://seer.cancer.gov>

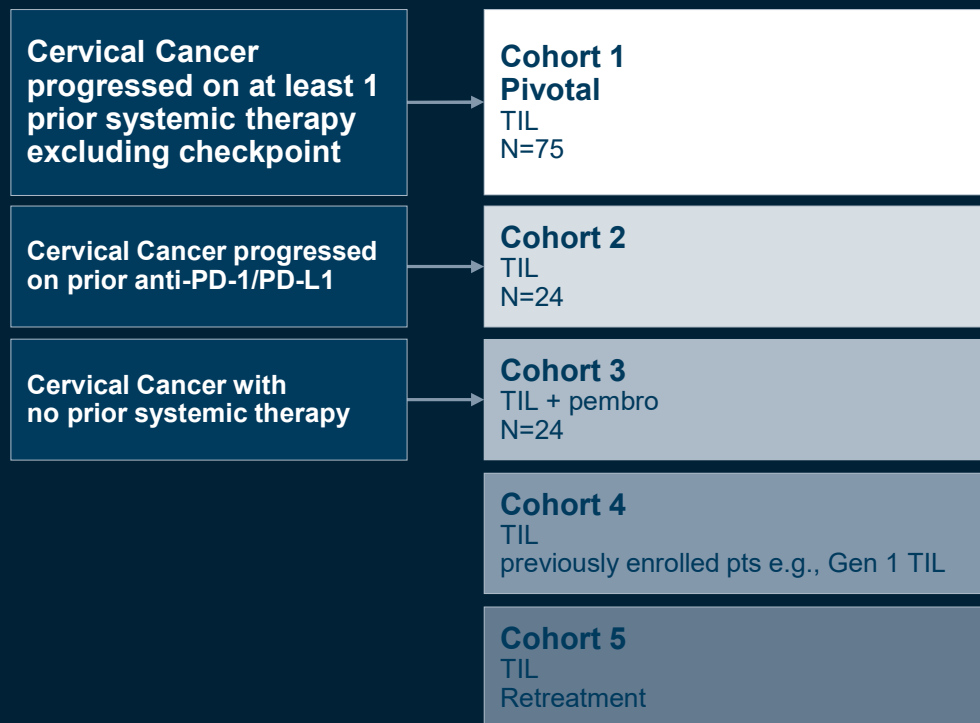
⁽³⁾ https://www.merck.com/product/usa/pi_circulars/k/keytruda/keytruda_pi.pdf

⁽⁴⁾ Schilder et al., Gynecologic Oncology, 2005.

⁽⁵⁾ Weiss, et al., A phase II trial of carboplatin for recurrent or metastatic squamous carcinoma of the uterine cervix: A Southwest Oncology Group Study.

C-145-04: Pivotal Phase 2 Trial in Cervical Cancer

Phase 2, multicenter study to evaluate the efficacy and safety of autologous TIL (lifileucel, formerly LN-145) in patients with recurrent, metastatic or persistent cervical carcinoma (NCT03108495)



Endpoints

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

Study Updates

- March 2019: Fast Track designation
- May 2019: Breakthrough Therapy Designation
- June 2019: ASCO data presentation
- June 2019: FDA EOP2 held-existing study may be sufficient to support registration of lifileucel
- July 2019: Study expanded to enroll a total of 75 patients
- November 2019: Additional cohorts added (Cohorts 2-5)
- 3Q 2020: Last patient dosed in Cohort 1

Lifileucel in Cervical Cancer Interim Update at ASCO 2019

Key Inclusion Criteria

- Recurrent, metastatic or persistent cervical carcinoma with at least 1 prior therapy
- Age ≥ 18

Endpoints

- Primary: efficacy defined as ORR by IRC per RECIST 1.1
- Secondary: safety and efficacy

Study Updates

- Fast Track and BTD received
- EOP2 meeting held with FDA

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-L1	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)

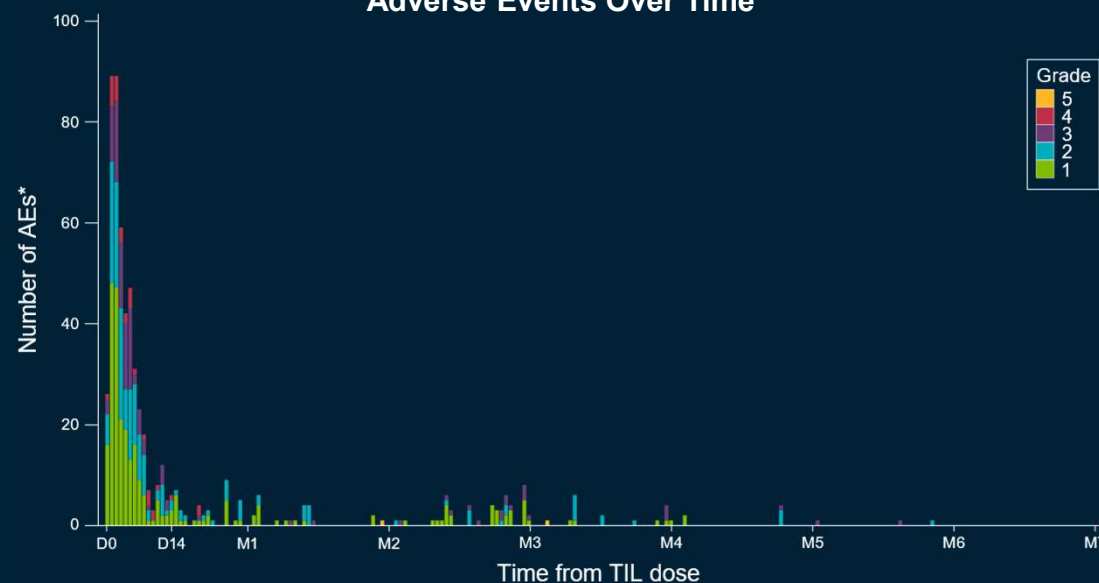
Adverse Events Tend to be Early and Transient

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

N=27

Preferred Term	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

Adverse Events Over Time



*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 Patients with Limited Options

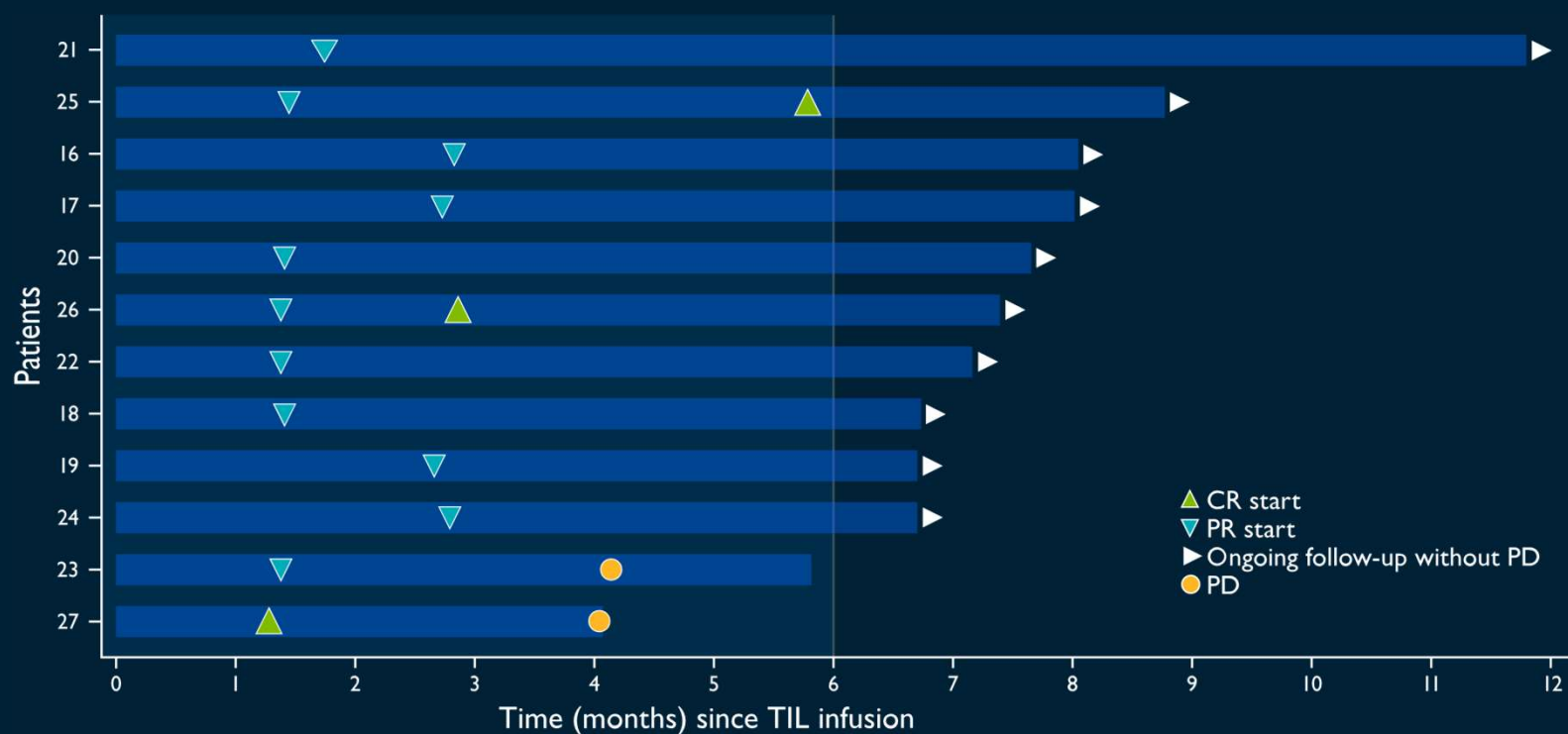
In heavily pretreated cervical cancer patients (2.4 mean prior therapies)

- **CR 11%**
- **ORR 44%**
- **DCR 85%**
- **Median DOR has not been reached**
 - Median follow-up 7.4 months
- Mean TIL cells infused: **28 x 10⁹**
- Median number of IL-2 doses: 6.0

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%)

Responses Observed Early On and Consistent with Melanoma

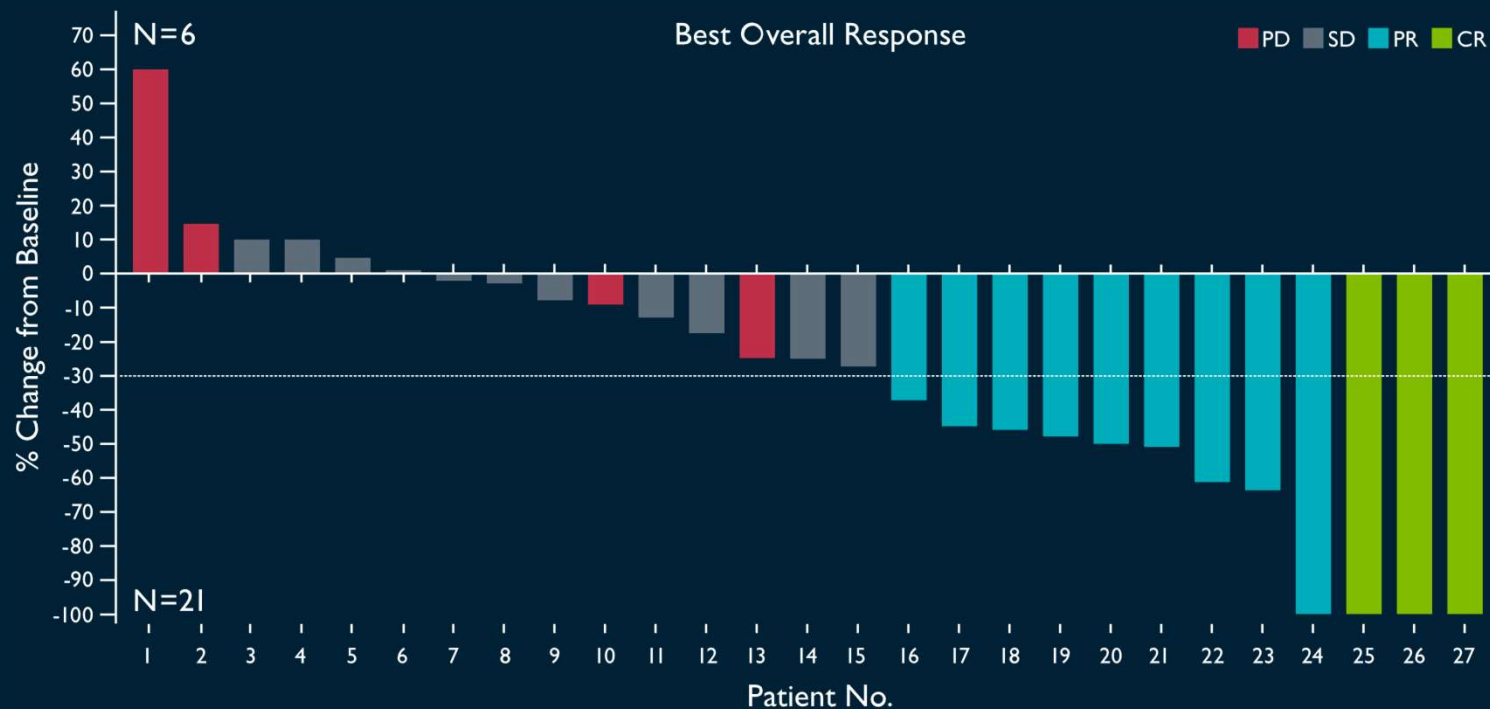
Lifileucel time to response and current duration for evaluable patients (partial response or better)



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

Three Complete Responses Observed with Lifleucel

Lifleucel 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 with majority of responders are over 30%

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 (most had received at least two prior therapies), median DOR=8.3 months, median OS=12.1 months
Anti-PD-1				
AGEN2034 (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
cemiplimab (Regeneron)	10% (N=10) ⁽³⁾	Phase 3	2+	Recurrent or metastatic cervical cancer resistant to, or intolerant of, platinum therapy
TKI				
neratinib (Puma Biotechnology)	27% (N=11) ⁽⁴⁾	Phase 2	2	Metastatic HER2-positive cervical cancer (percentage of HER2+ in cervical cancer is ~3.9%) ⁽⁵⁾
Cell therapies				
TIL (Iifileucel)	44% (N=27)	Phase 2	2.4 (mean)	All patients progressed on or after chemo; median DOR not reached (median follow-up 7.4 months)

⁽¹⁾ Coleman, et al., ESMO 2020; ⁽²⁾ O'Malley, et al. ESMO 2020; ⁽³⁾ Rischin, et al. ESMO 2018; ⁽⁴⁾ D'Souza et al. SGO 2019; ⁽⁵⁾ Yan, et al. *Cancer Metastasis Rev.* 2015.

HNSCC

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

“The use of TIL markers, such as CD3 and CD8, to predict recurrence and cancer-related death is of particular clinical interest in advanced stage HNSCC, as high-risk patients may potentially benefit from the implementation of novel immunotherapy to stimulate T cells in combination with chemoradiotherapy.”

— P. Balermipas, M.D.⁽⁵⁾
Department of Radiation Therapy and Oncology,
Johann Wolfgang Goethe University

HNSCC Facts

890k	New Cases WW each year ⁽¹⁾	507k	Deaths WW each year ⁽¹⁾
65k	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 ⁽⁶⁾	16%	8 months

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

(1) JAMA Oncol. 2019;5(12):1749-1768. doi:10.1001/jamaoncol.2019.2996

(2) <https://seer.cancer.gov/statfacts/html/oralcav.html> and <https://seer.cancer.gov/statfacts/html/larynx.html>

(3) Keytruda USPI and Szturz, P. et al., Ann Transl Med, 2020, 8 (15), 975.

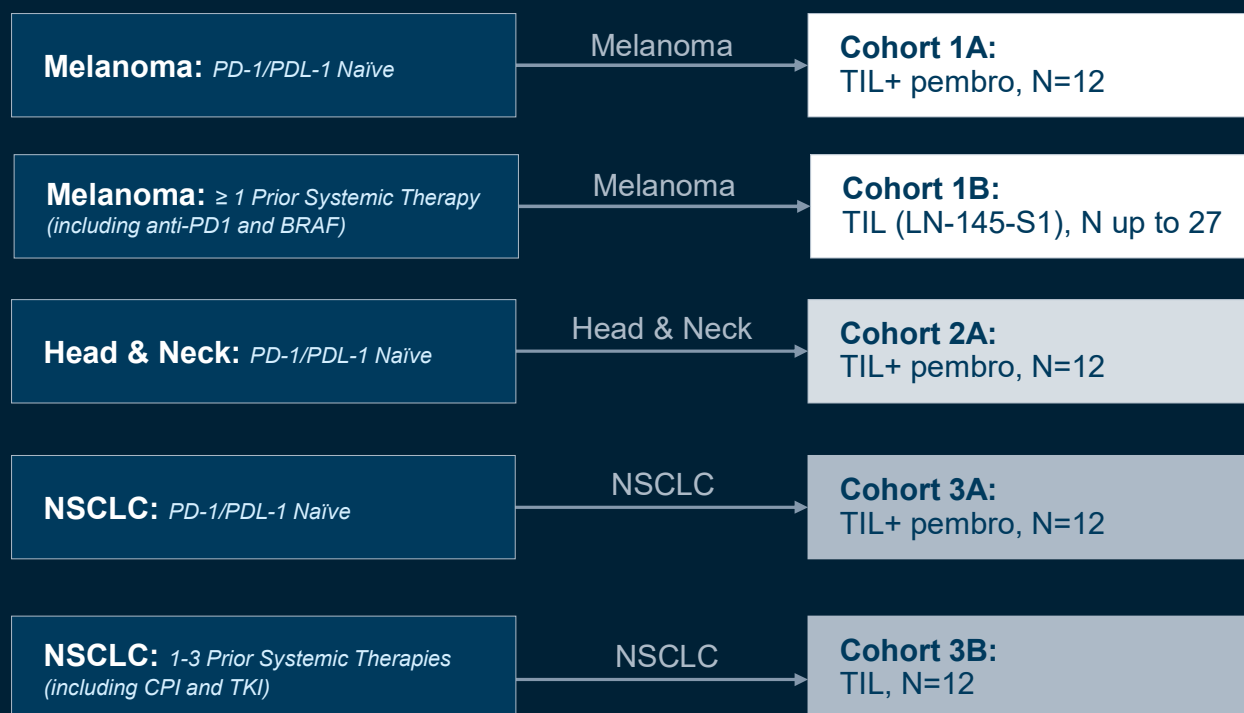
(4) Vermorken, J. B. et al., NEJM, 2008, 359, 1116.

(5) British Journal of Cancer (2014) 110, 501–509 | doi: 10.1038/bjc.2013.640

(6) Baum, et al., J Clin Oncol. 2017, 10;35(14):1542-1549.

TIL in Earlier Lines of Therapy in Combination with SOC

A prospective, open-label, multi-cohort, non-randomized, multicenter Phase 2 study evaluating adoptive cell therapy (ACT) with TIL LN-144 (Lifileucel)/LN-145 in combination with pembrolizumab or TIL LN-145/LN-145-S1 as a single therapy (NCT03645928)



Endpoints

- Primary: ORR and safety
- Secondary: CR rate

Study Updates

- 28 sites are activated globally
- Sites in the U.S., Canada and Europe

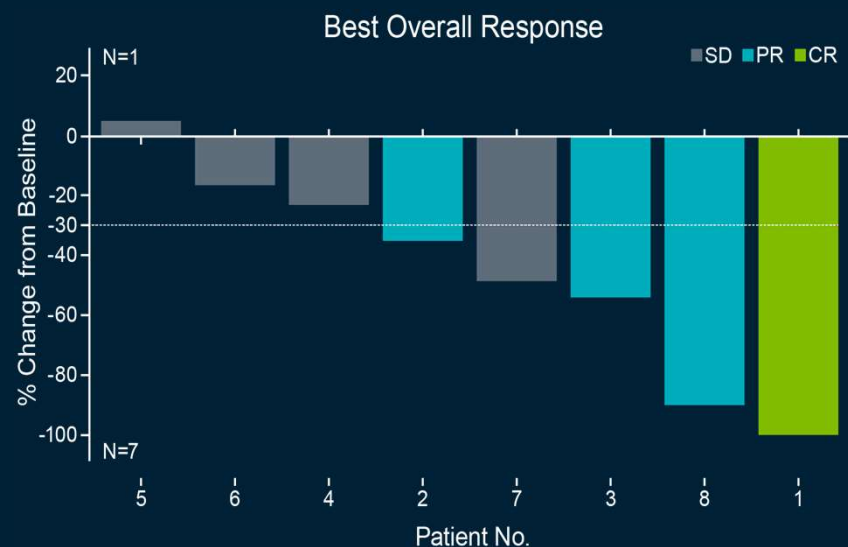
LN-145 in Anti-PD-1 Naïve HNSCC- Cohort 2A

TEAE consistent with other indications

Efficacy

ORR=44%

DCR=89%



PD-L1 Status

CPS ≥ 20

CPS ≥ 20

CPS $< 20^*$

CPS ≥ 20

* CPS > 1



⁽¹⁾ Jimeno, et. al., Safety and efficacy of tumor infiltrating lymphocyte (TIL; LN-145) in combination with pembrolizumab for advanced, recurrent or metastatic HNSCC, SITC 2020, Abstract #353

Non-Small Cell Lung Cancer (NSCLC)

Efficacy Data Post Moffitt TIL Infusion

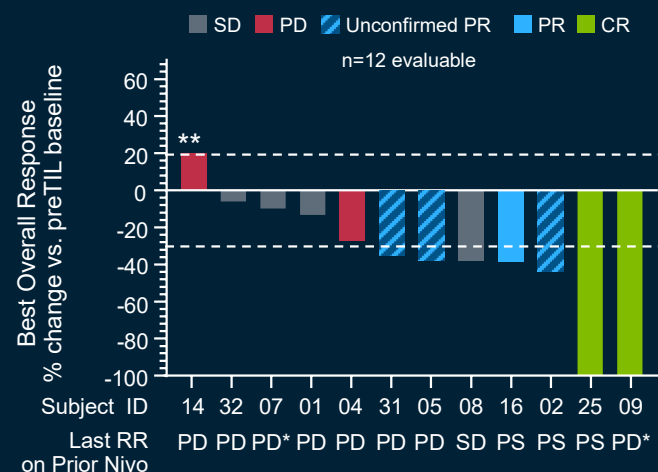
Responses	N=12 (%)
Objective Response Rate	3 (25%)
Complete Response	2 (17%)
Partial Response	1 (8%)

- **ORR 25%;**
 - 1 CR is noted in EGFR^{ΔEx19} post afatinib, osimertinib, nivolumab
 - 1 additional uPR may confirm to increase the ORR to 33%
- **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%)

Moffitt TIL in Post-Nivolumab NSCLC

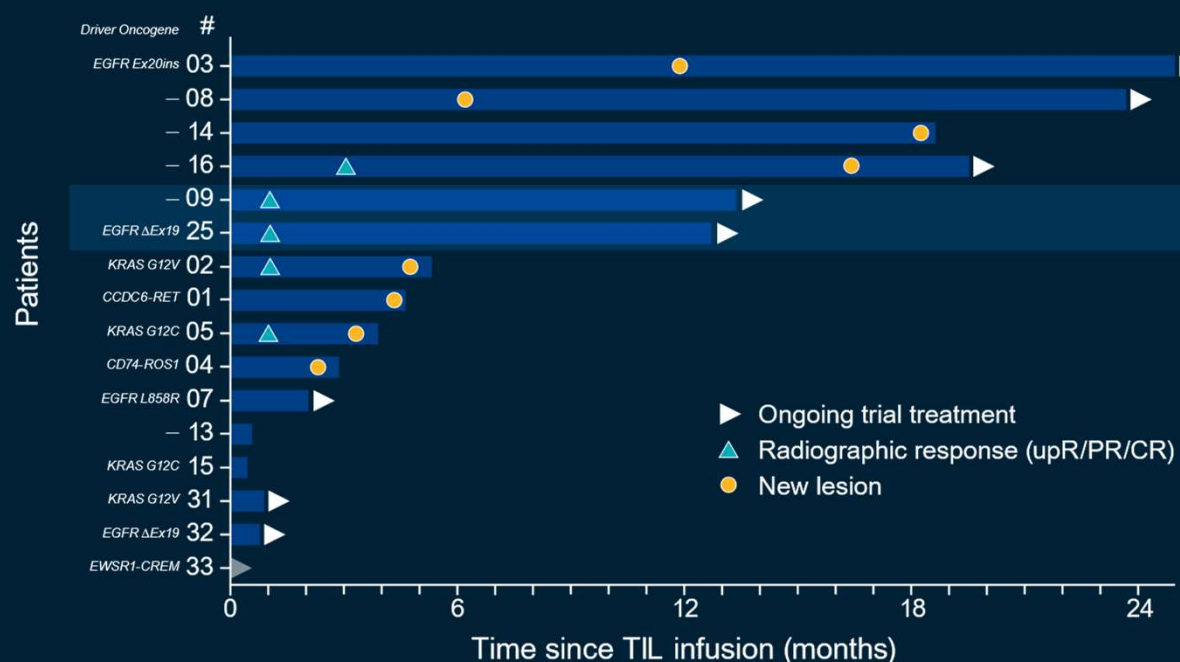
Nivolumab and Tumor Infiltrating Lymphocytes (TIL) in Advanced Non-Small Cell Lung Cancer (NCT03215810)

Post-TIL



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

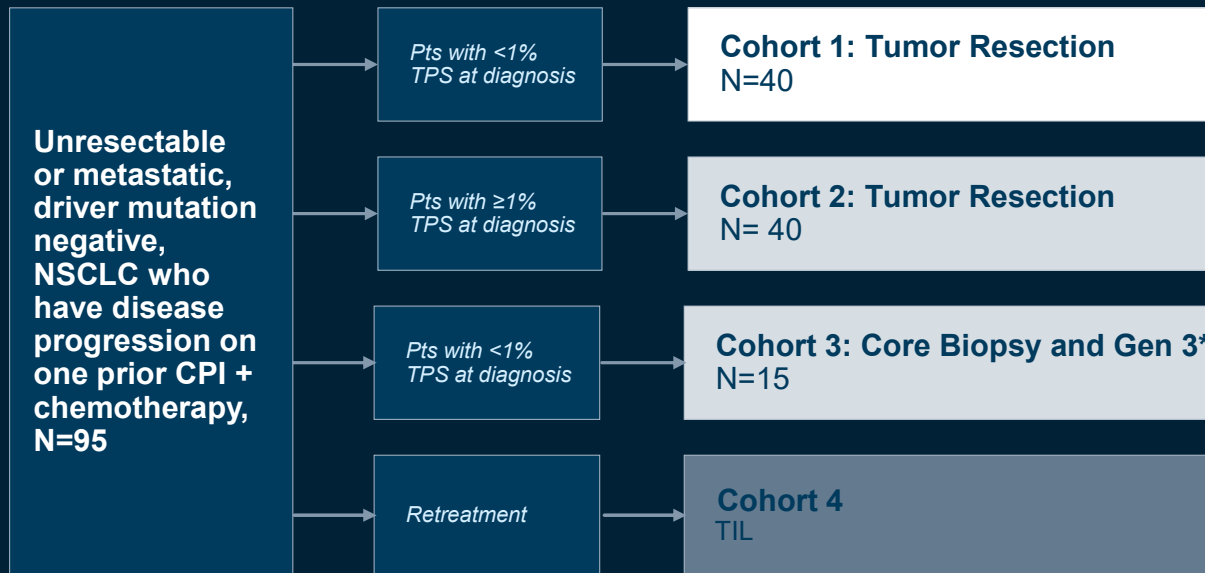
- Two CRs out to one year
 - (PD-L1 low=1, EGFR mutation=1)
- ORR 25% (or 33% if a uPR confirms)



(1) Creelan, et. al., Durable complete responses to adoptive cell transfer using tumor infiltrating lymphocytes (TIL) in non-small cell lung cancer (NSCLC): a phase I trial, AACR 2020, Abstract #20-LB-10617

IOV-LUN-202

Phase 2, multicenter study of Autologous Tumor Infiltrating Lymphocytes (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

*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



Select more potent TIL

- PD-1 positive selected TIL by Iovance
- 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 (ESMO 2020)



Process optimization

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

Iovance Biotherapeutics Global Reach and Scale



Iovance Biotherapeutics has >200 employees

- Headquartered in San Carlos, CA
- 3 additional offices
- Iovance commercial manufacturing facility in Philadelphia, PA (*under construction*)

Well Capitalized in Pursuit of TIL Commercialization

September 30, 2020	In millions (unaudited)
Common shares outstanding	146.6 ⁽¹⁾
Preferred shares outstanding	3.6 ⁽²⁾
Options	12.8
Cash, cash equivalents, short-term investments, restricted cash	\$719.7 ⁽³⁾
Anticipated year-end cash balance	>\$630 ⁽³⁾
Debt	\$0

⁽¹⁾ Includes May 2020 offering of 19,475,806 shares of common stock.

⁽²⁾ Preferred shares are shown on an as-converted basis.

⁽³⁾ Includes Restricted Cash of \$5.5 million.

Milestones 2020-2021

- ☒ Last patient dosed in Cohort 4 for lifileucel in support of registration in melanoma
- ☒ Data presentation at ASCO for long term follow up of melanoma Cohort 2
- ☒ Early cohort 4 data from melanoma
- ☒ Last patient dosed in pivotal program of lifileucel for cervical cancer
- ☒ Data presentation for combination of TIL plus Keytruda in various indications
- ☐ Hold a pre-BLA meeting with FDA
- ☐ Initiate NSCLC registration-supporting study
- ☐ Submit BLA for lifileucel



ADVANCING IMMUNO-ONCOLOGY

Thank You

