IOVANCE BIOTHERAPEUTICS

ADVANCING IMMUNO-ONCOLOGY

Request for New ICD-10-PCS Code for the Inpatient Administration of Lifileucel

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ICD-10 Coordination & Maintenance Committee Meeting

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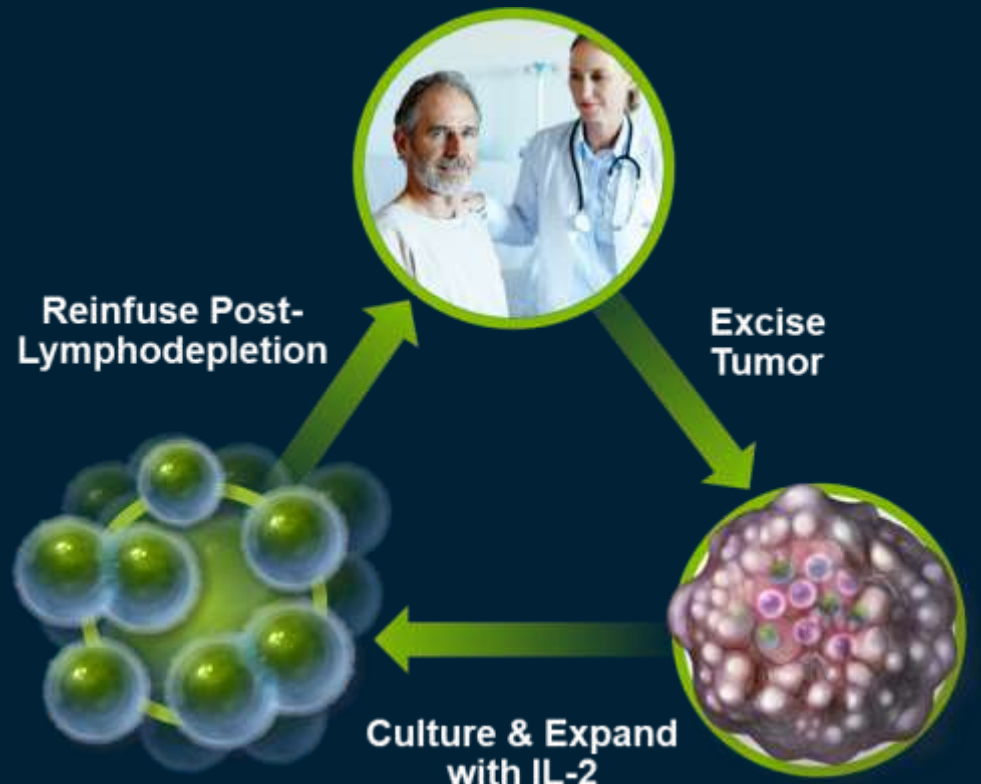
Lifileucel, Tumor-Infiltrating Lymphocytes (TIL) for Treatment of Cancer

TIL-therapy offers a highly personalized new treatment option for patients with solid tumors

- Lifileucel is anticipated to be the first FDA-approved therapy indicated for:
  - Patients with unresectable or metastatic melanoma who have been previously treated with at least one systemic therapy, including a PD-1 blocking antibody and, if BRAF V600 mutation positive, a BRAF inhibitor or BRAF inhibitor with MEK inhibitor
- Regulatory status for melanoma:
  - Orphan Drug designation; Fast Track designation; Regenerative Medicine Advanced Therapy (RMAT) designation
  - On track to submit a biologics license application (BLA) in late 2020
- Plan to submit FY 2022 New Technology Add-on Payment (NTAP) application
- Lifileucel is also being studied in metastatic cervical cancer, expected to be the second regulatory filing

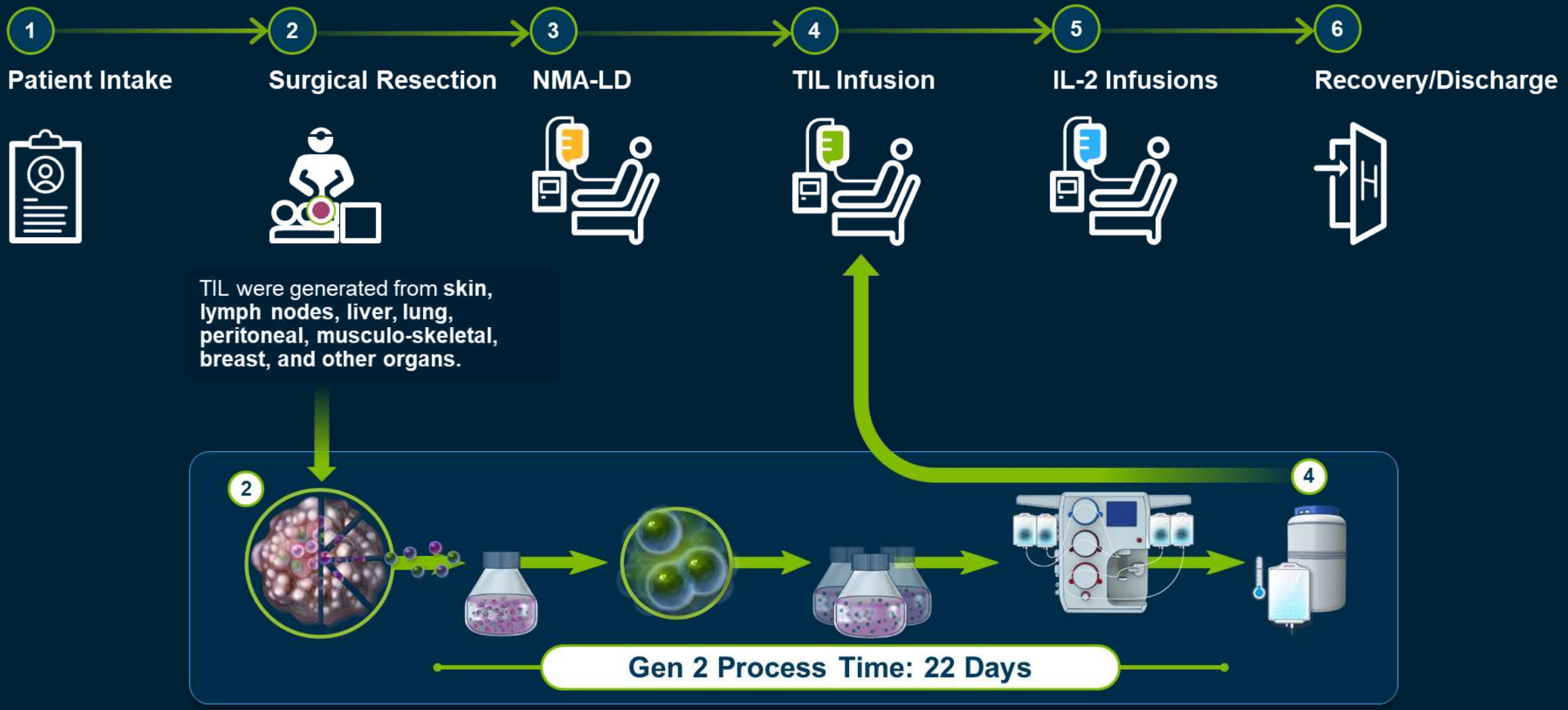


Significant Unmet Need for Metastatic Melanoma Patients

- Melanoma is the most aggressive form of skin cancer; tends to metastasize beyond its primary site[1]
  - **96K diagnoses** in U.S. each year[2]
  - **7K deaths** in U.S. each year[2]
- Most patients will not achieve long-lasting remission[3]
- Retreatment with anti-PD1 or chemotherapy post progression on anti-PD1 and BRAF/MEK has limited efficacy
  - **Objective Response Rate (ORR) 4-10%**[4]
  - **Overall Survival (OS) ~7-8 months**[5]
- The 5-year survival rate for metastatic disease is < 25%[6,7]
- There are currently no approved agents for patients with metastatic melanoma whose disease progressed after immune checkpoint inhibitors (ICIs) and BRAF/MEK inhibitors

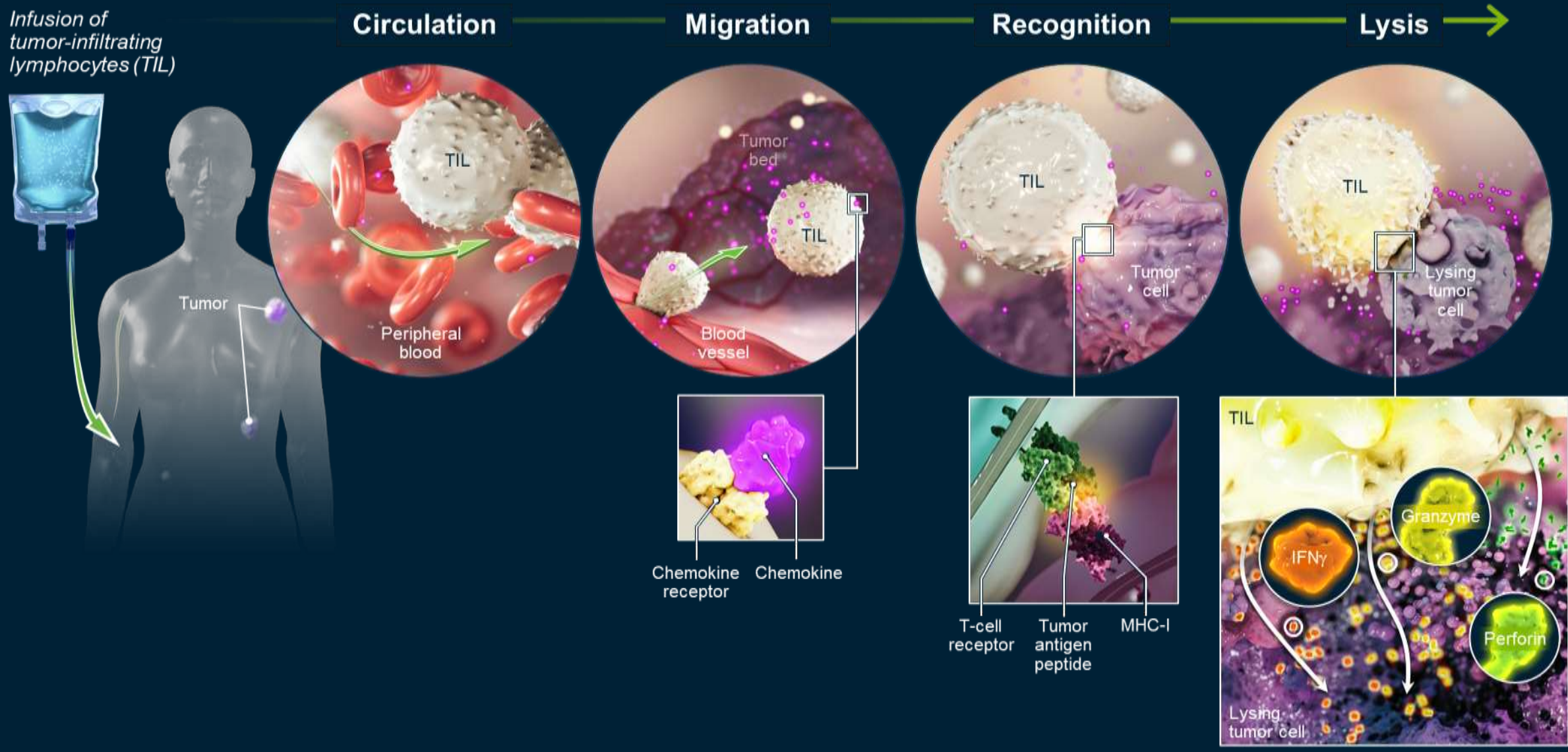
1. *Cutaneous Melanoma: Etiology and Therapy.* Chapter 1: Epidemiology of melanoma. doi:10.15586/codon.cuttaneousmelanoma.2017.ch1; 2. in 2019, https://seer.cancer.gov'; 3. *Nat Rev Clin Oncol.* 2017;14:463-82; 4. CheckMate-37 Trial Results (ICC 10%), Keytruda label (4%); 5. *Eur J Cancer.* 2016; 65:182-184. *J Clin Oncol.* 2018; 36 (suppl: abstr e21588); 6. Melanoma Research Alliance: https://www.curemelanoma.org/about-melanoma/melanoma-staging/melanoma-survival-rates/ Accessed February 10, 2020. 7. NCI – Melanoma Treatment (PDQ®)-Health Professional Version. https://www.ancer gov/types/skin/hp/melanoma-treatment-pdq. Accessed February 10, 2020.

Patient Journey and TIL Manufacturing Process



Abbreviation: NMA-LD, nonmyeloablative lymphodepletion

TIL, A Novel Mechanism of Action for Treatment of Solid Tumors



Advantages of TIL in Solid Tumors

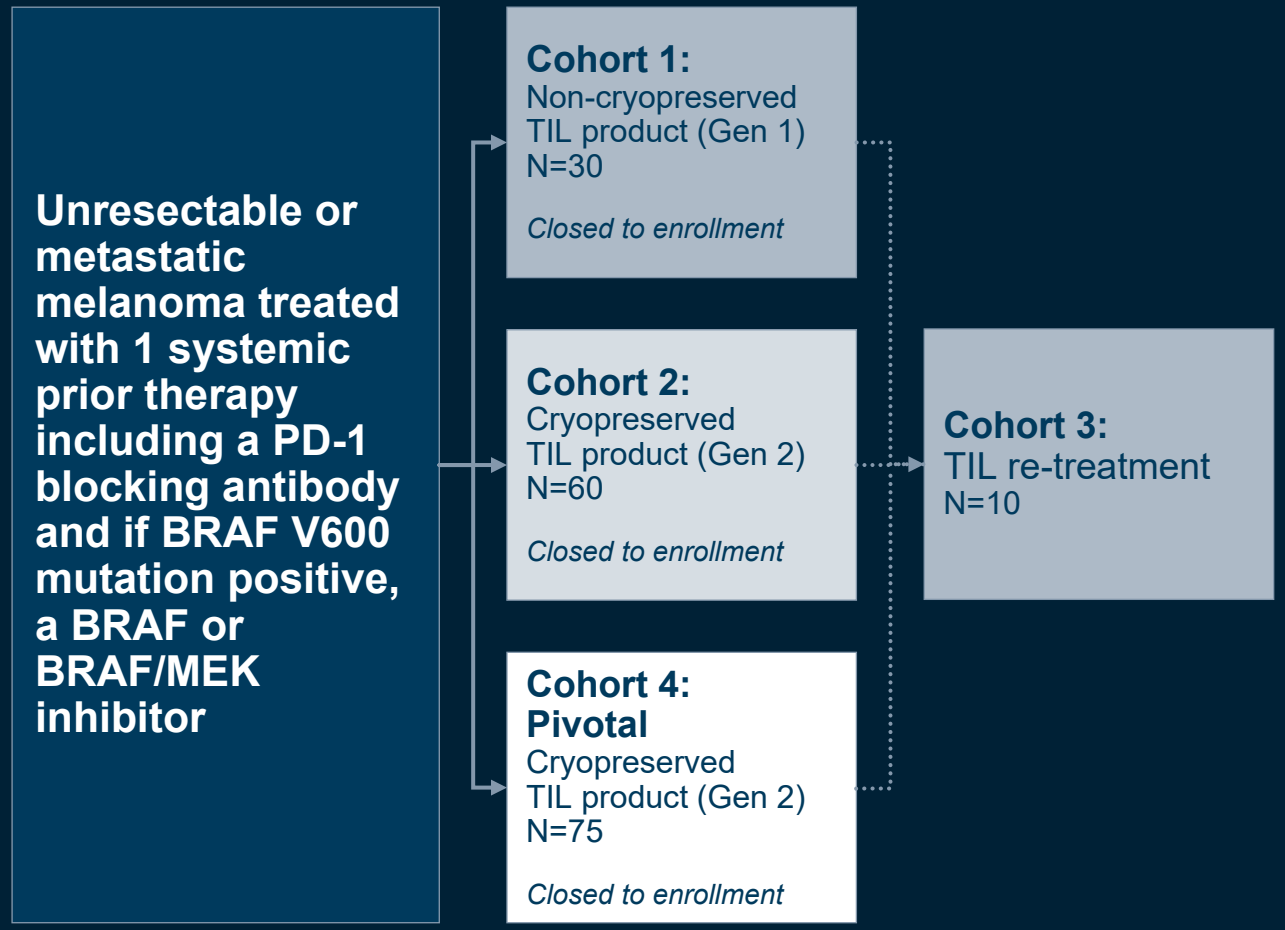
Checkpoint Inhibitors	TCR	CAR-T (Liquid tumors)	TIL (Solid tumors)
Target multiple tumor antigens	Target only single tumor antigen	Mainly target only single/ surface tumor antigen	**Target multiple tumor antigens**
Long maintenance period	One-time treatment	One-time treatment	**One-time treatment**
Utility 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**

TCR therapies are still several years from commercial readiness

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

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)



Endpoints

- Primary: Efficacy defined as IRC ORR

Study Updates

- Cohort 2: June 2019: Full Cohort 2 data on 66 patients presented at ASCO
  - Median age: 55 (20,79)
  - Median # prior therapies: 3.3
- Cohort 2: November 2019: IRC-assessed data presented at SITC
- Cohort 4: Jan 2020: Last patient dosed
- Cohort 4: May 2020: Early data released

Abbreviations: DOR, duration of response; GMP, Good Manufacturing Practice; IRC, independent review committee; TIL, tumor infiltrating lymphocytes

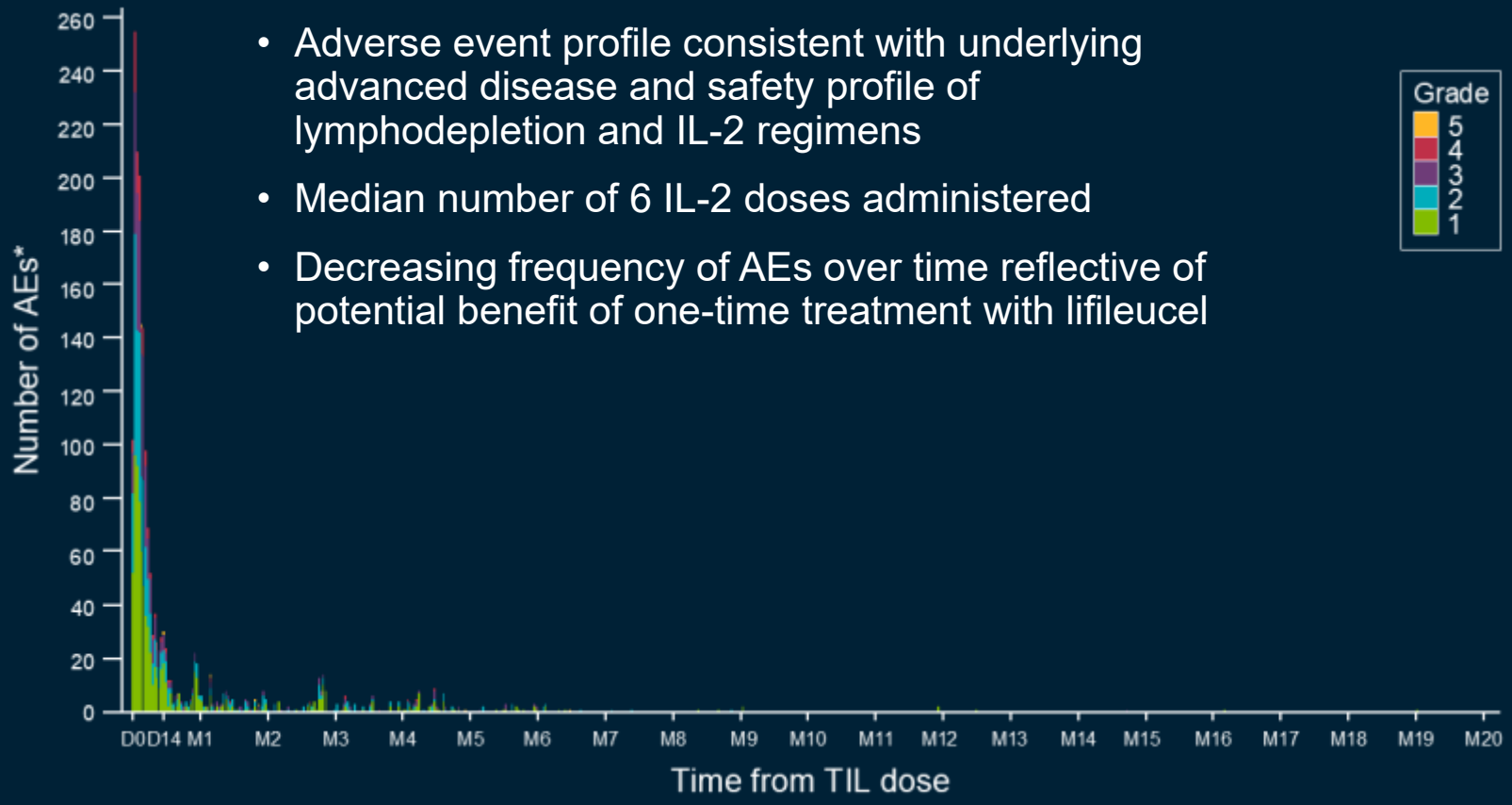
C-144-01 Cohort 2, Lifileucel Efficacy

Response	Patients, N=66 n (%)
Objective Response Rate (ORR)	**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	4 (6.1)
Disease Control Rate	53 (80.3)
Median Duration of Response (DOR)	**Not Reached**
Min, Max (months)	2.2, 26.9+

- After a median study follow-up of 18.7 months, mDOR was still not reached (range 2.2, 26.9+)
- ORR was demonstrated:
  - Regardless of location of tumor resected
  - Across a wide age range
    - ≥ 65 yrs: ORR: 35.7%
    - < 65 yrs: ORR: 36.5%
  - 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

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%)

	Cohort 2 (N=66)		
Preferred term	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.

Data Support the Potential Benefit of the One-time Administration of Lifileucel TIL Therapy in Advanced Melanoma Patients

Cohort 2 – Investigator Assessment

- **Median DOR not reached at 18.7 months of median study follow up[1]**
- **36.4% ORR[2]**

Cohort 4 Early Data – Investigator Assessment

- **32.4% ORR at 5.3 months of median study follow up[3]**

Retreatment with anti-PD1 or chemotherapy post progression on anti-PD1 and BRAF/MEK has limited efficacy

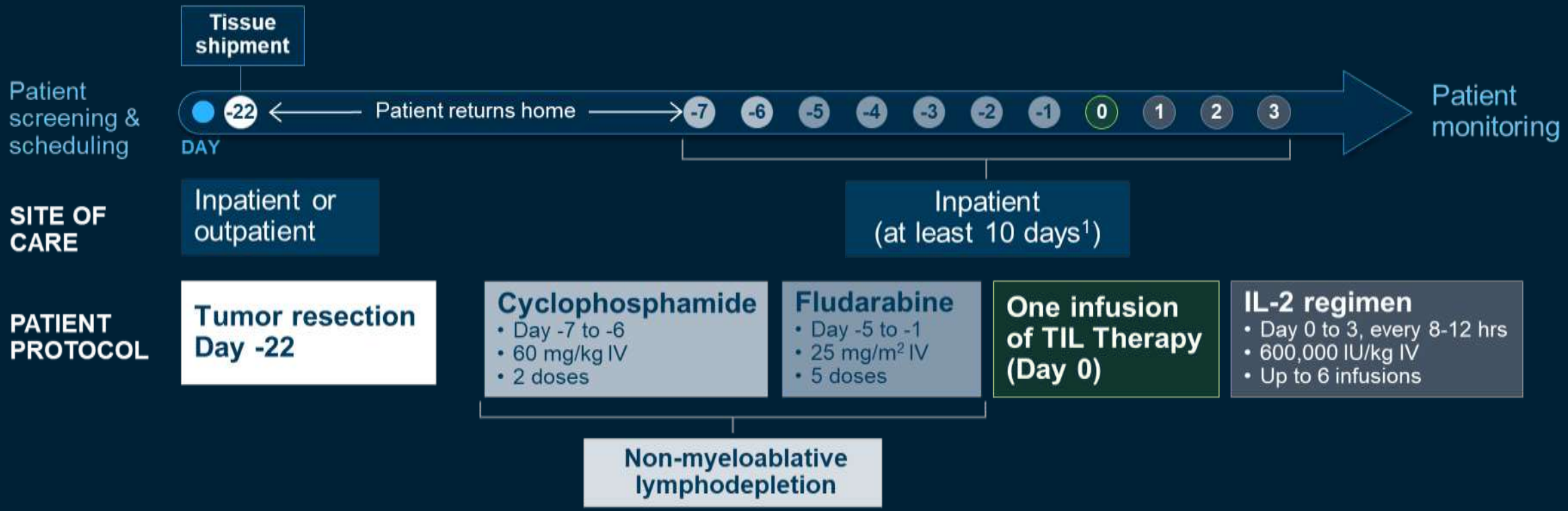
ORR 4-10%[4]

OS ~7-8 months[5]

1. Sarnaik *et al*., ASCO 2020, 10006; 2. Sarnaik *et al*., SITC 2019, P865; 3. Iovance press release, May 27, 2020; 4. CheckMate-37 Trial Results (ICC 10%), Keytruda label (4%); 5. *Eur J Cancer*. 2016; 65:182-184. *J Clin Oncol*. 2018; 36 (suppl: abstr e21588)

One-Time Treatment with Lifileucel Requiring Significant Hospitalization

Intravenous infusion administered peripherally or centrally (primarily inpatient setting))



(1)Inpatient stays estimated based upon Iovance clinical protocols.