Trial in progress: A Phase 2, multicenter study of autologous tumor-infiltrating lymphocytes (TIL, lifileucel [LN-144], LN-145, LN-145-S1) in patients with solid tumors (IOV-COM-202)

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Presenter DISCLOSURES

Ineligible Company (formerly: Commercial Interest)	**Relationship(s)**
Bristol Myers Squibb	Research Funding (to Institution), Trial Safety Board
Genentech	Research Funding (to Institution)
Iovance	Research Funding (to Institution), Trial Steering Committee
NextCure	Research Funding (to Institution)

Background

- Adoptive cell transfer (ACT) using autologous tumor-infiltrating lymphocytes (TIL) has been shown to be effective for the treatment of advanced metastatic melanoma, and other solid tumors with high tumor mutational burden[1,2]
- TIL cell therapy (lifileucel [LN-144], LN-145) has demonstrated efficacy and safety in clinical trials for several high unmet medical need patient populations; specifically unresectable and metastatic melanoma; relapsed, refractory or persistent cervical cancer; and head and neck squamous cell carcinoma (HNSCC)[3-5]
- Further, TIL cell therapy has shown evidence of efficacy in metastatic non-small cell lung cancer (mNSCLC) in a Phase 1 study in combination with nivolumab[6]

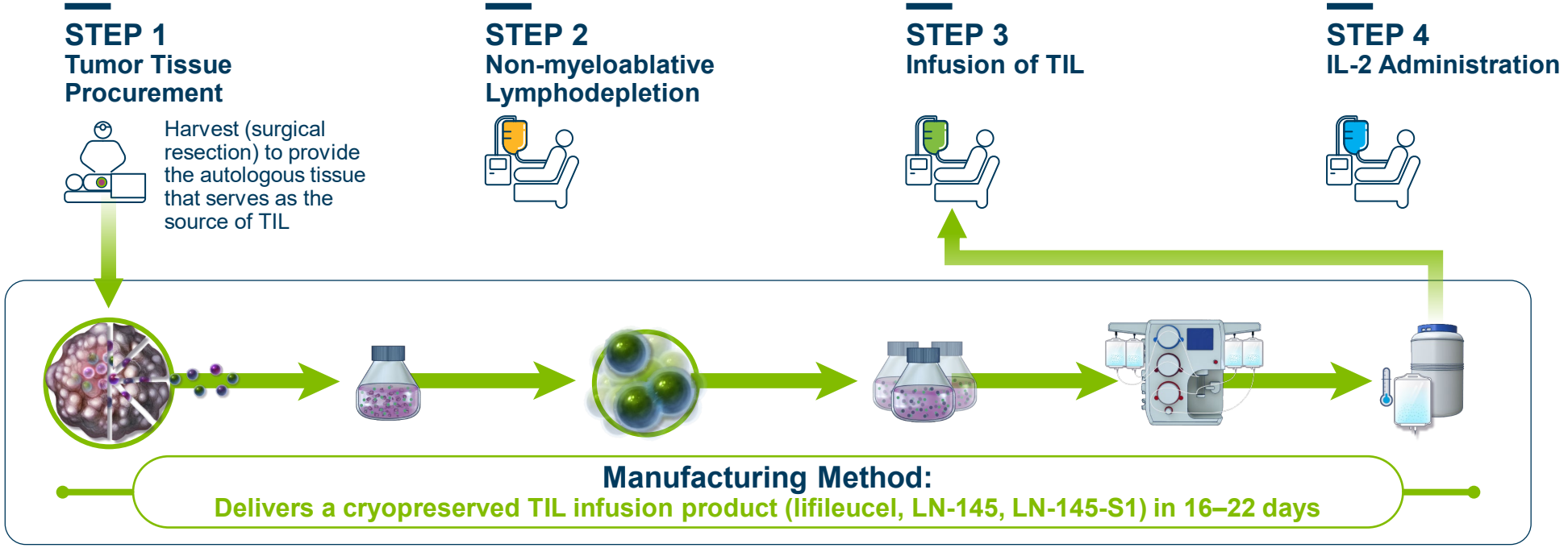
IOV-COM-202

- **IOV-COM-202 (NCT03645928)** is a prospective, open-label, multi-cohort, non-randomized, multicenter Phase 2 study evaluating TIL cell therapy (lifileucel, LN-145, LN-145-S1) in combination with immune checkpoint inhibitors (ICI) and as a single therapy

1. Goff SL, et al. JCO. 2016;34(20):2389-97.
2. Stevanović S, et al. Clin Can Res. 2019;25(5):1486-1493.
3. Sarnaik A, et al. JCO. 2020;38 (suppl; abstr 10006).
4. Jazaeri A, et al. JCO. 2019;37 (suppl; abstract 2538).
5. Jimeno A, et al. JITC. 2020;8 (suppl; abstract A378).
6. Creelan, B et al. Can Res. 2020;80:16 (suppl; abstract CT056).

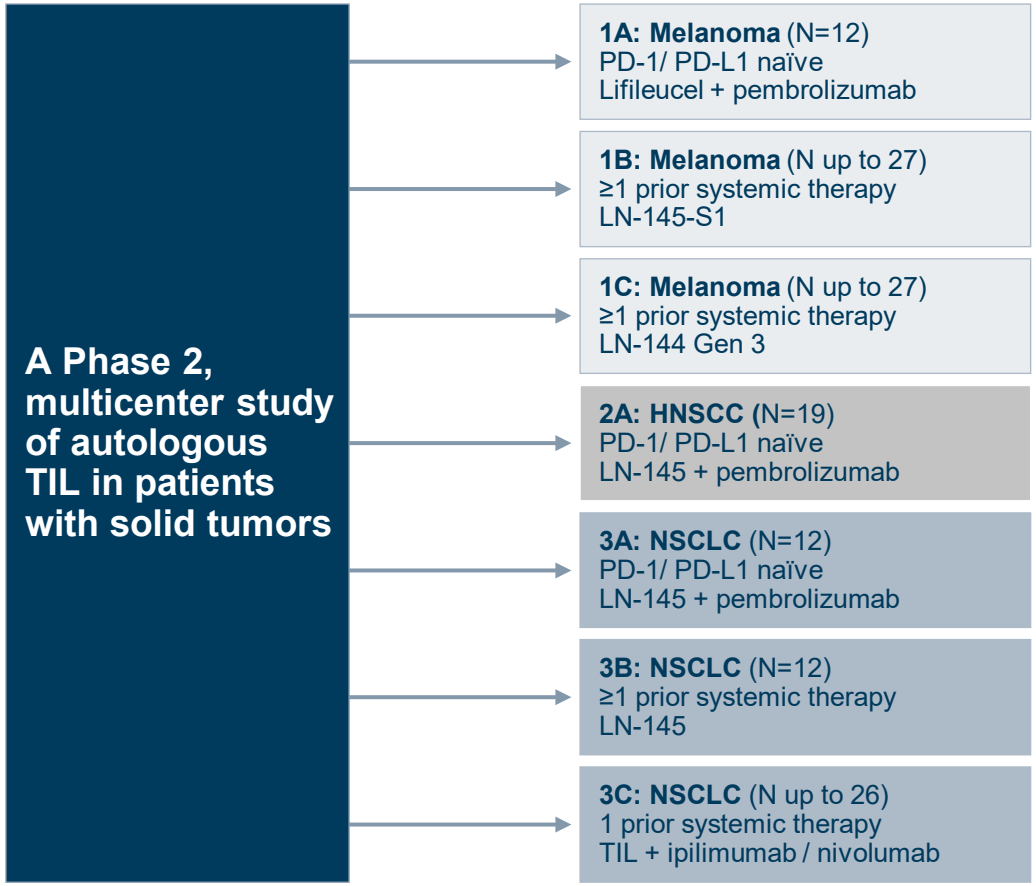
TIL Manufacturing and Patient Journey

- The one-time TIL cell therapy requires procurement of an ~1.5-cm sample of tumor tissue, which is shipped to a central GMP facility; outside of the suppressive tumor microenvironment, the TIL are reinvigorated and expanded to ~10^9–10^{11} cells
- TIL manufacturing is a 16–22-day process



Abbreviations: GMP, good manufacturing practice; IL-2, interleukin-2; TIL, tumor-infiltrating lymphocytes.

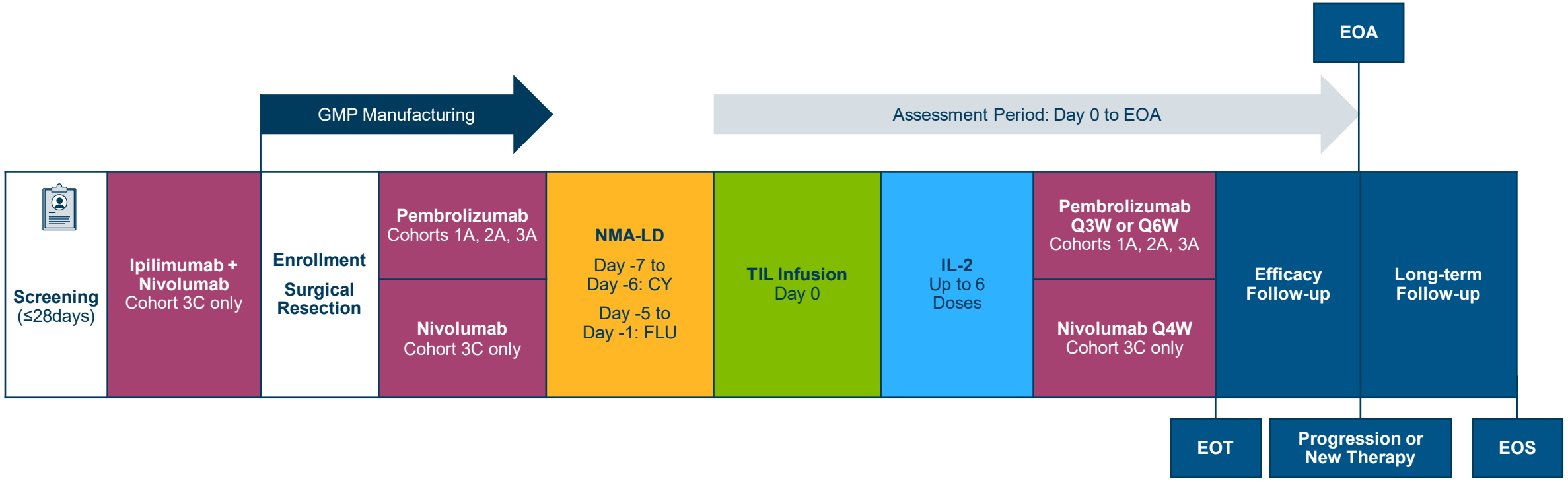
Study Overview, Design, and Endpoints



- Up to ~135 patients to be enrolled at ~50 clinical sites in the US, Canada, and Europe
- Co-primary endpoints
  - Efficacy: ORR per RECIST 1.1 (investigator-assessed)
  - Safety: incidence of Grade ≥3 TEAEs
- Secondary endpoints
  - Additional efficacy parameters
- Exploratory endpoints
  - Predictive and pharmacodynamic biomarkers of clinical response to TIL products
- TIL specifications
  - Lifileucel, LN-145: 22-day manufacturing
  - LN144 Gen 3: 16-day manufacturing
  - LN-145-S1: PD-1–selected TIL

Abbreviations: HNSCC, head and neck squamous cell carcinoma; NSCLC, non-small cell lung cancer; ORR, objective response rate; PD-1, programmed cell death protein-1; PD-L1, programmed death ligand-1; RECIST, response evaluation criteria in solid tumors; TEAEs, treatment-emergent adverse events; TIL, tumor-infiltrating lymphocytes.

IOV-COM-202 Patient Treatment Schema



Abbreviations: CY, cyclophosphamide; EOA, end of assessment; EOS, end of study; EOT, end of treatment; FLU, fludarabine; GMP, good manufacturing practice; IL-2, interleukin-2; NMA-LD, non-myeloablative lymphodepletion; Q3W, every 3 weeks; Q4W, every 4 weeks; Q6W, every 6 weeks; TIL, tumor-infiltrating lymphocytes.

Key Inclusion and Exclusion Criteria

Inclusion Criteria – All Patients

- ≥1 resectable lesion with remaining measurable disease (per RECIST 1.1) following tumor resection
- ≥18 years of age at the time of consent; enrollment of patients >70 years of age may be permitted after consultation with the Medical Monitor
- ECOG performance status of 0 or 1, and an estimated life expectancy of ≥6 months

Cohort	Indication	Count of prior lines of systemic therapy	Prior CPI required	Prior targeted therapy required
1A	Melanoma (Stage IIIC or IV)	Treatment naïve – 3 L*		‖
1B	Melanoma (Stage IIIC or IV)	≥1 L	✓ ‡	✓ ¶
1C	Melanoma (Stage IIIC or IV)	≥1 L	✓ ‡	✓ ¶
2A	HNSCC (advanced, recurrent, or metastatic)	Treatment naïve – 3 L*		
3A	NSCLC (Stage III or IV)	Treatment naïve – 3 L*†		✓ #
3B	NSCLC (Stage III or IV)	1 L – 3 L	✓ §	✓ #
3C	NSCLC (Stage III or IV)	1 L (CPI monotherapy)	✓	

Exclusion Criteria – All Patients

- Received an organ allograft or prior cell transfer therapy that included a nonmyeloablative or myeloablative chemotherapy regimen within the past 20 years
- Symptomatic and/or untreated brain metastases
- Receiving systemic steroid therapy of prednisone ≥10 mg/day or another steroid equivalent
- Receiving steroids as replacement therapy for adrenocortical insufficiency at ≤10 mg/day of prednisone or another steroid equivalent may be eligible
- Active medical illness(es), which in the opinion of the Investigator, would pose increased risks for study participation
- Any form of primary immunodeficiency
- History of hypersensitivity to any component of the study drugs
- Left ventricular ejection fraction >45% or New York Heart Association Class II or higher
- Patients with respiratory dysfunction or history of smoking require pulmonary function testing and are excluded if not meeting either of FEV_1/forced vital capacity >0.7 or FEV_1 >50%

Cohort-Specific

- Patients in cohorts 1A, 2A, 3A, and 3C may not have a medical history of autoimmune disorders requiring treatment or active management

*Must be ICI naïve. †Or ≤4 lines if ≥2 TKIs. ‡Must include PD-1 blocking antibody. §Except for those patients with known oncogene drivers that are sensitive to targeted therapies. ‖May have received BRAFi/MEKi if BRAF mutation positive. ¶Must have received BRAFi/MEKi if BRAF mutation positive. #Must have received targeted therapy if known oncogene driver mutations.
Abbreviations: BRAFi, BRAF inhibitor; CPI, checkpoint inhibitor; ECOG, Eastern Cooperative Oncology Group; FEV_1, forced expiratory volume in 1 second; HNSCC, head and neck squamous cell carcinoma; ICI, immune checkpoint inhibitor; MEKi, MEK inhibitor; NSCLC, non-small cell lung cancer; PD-1, programmed cell death protein-1; RECIST, response evaluation criteria in solid tumors; TIL, tumor-infiltrating lymphocytes; TKI, tyrosine kinase inhibitor.

Disclosures:
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