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)

Scott Gettinger, MD
Yale Cancer Center, New Haven, CT, USA
## Presenter DISCLOSURES

<table>
<thead>
<tr>
<th>Ineligible Company (formerly: Commercial Interest)</th>
<th>Relationship(s)</th>
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<tbody>
<tr>
<td>Bristol Myers Squibb</td>
<td>Research Funding (to Institution), Trial Safety Board</td>
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<td>Genentech</td>
<td>Research Funding (to Institution)</td>
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<td>Iovance</td>
<td>Research Funding (to Institution), Trial Steering Committee</td>
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<tr>
<td>NextCure</td>
<td>Research Funding (to Institution)</td>
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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
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.

Manufacturing Method:
Delivers a cryopreserved TIL infusion product (lifileucel, LN-145, LN-145-S1) in 16–22 days
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

**Screening (≤28 days)**
- Ipilimumab + Nivolumab
  - Cohort 3C only

**Enrollment Surgical Resection**
- Pembrolizumab
  - Cohorts 1A, 2A, 3A
  - NMA-LD
    - Day -7 to Day -6: CY
    - Day -5 to Day -1: FLU
- Nivolumab
  - Cohort 3C only
- TIL Infusion
  - Day 0
- IL-2
  - Up to 6 Doses
- Pembrolizumab Q3W or Q6W
  - Cohorts 1A, 2A, 3A
- Nivolumab Q4W
  - Cohort 3C only

**Assessment Period: Day 0 to EOA**
- EOT
- Progression or New Therapy
- EOS

**GMP Manufacturing**

**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

#### 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 FEV1/forced vital capacity >0.7 or FEV1 >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

#### Table: Cohort Indication

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Indication</th>
<th>Count of prior lines of systemic therapy</th>
<th>Prior CPI required</th>
<th>Prior targeted therapy required</th>
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<tbody>
<tr>
<td>1A</td>
<td>Melanoma (Stage III or IV) Treatment naïve – 3 L*</td>
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<tr>
<td>1B</td>
<td>Melanoma (Stage III or IV) ≥1 L</td>
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<tr>
<td>1C</td>
<td>Melanoma (Stage III or IV) ≥1 L</td>
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</tr>
<tr>
<td>2A</td>
<td>HNSCC (advanced, recurrent, or metastatic) Treatment naïve – 3 L*</td>
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<tr>
<td>3A</td>
<td>NSCLC (Stage III or IV) Treatment naïve – 3 L*†</td>
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<tr>
<td>3B</td>
<td>NSCLC (Stage III or IV) 1 L – 3 L</td>
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<td>✓ #</td>
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<tr>
<td>3C</td>
<td>NSCLC (Stage III or IV) 1 L (CPI monotherapy)</td>
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</tbody>
</table>

*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. ¶Must have received BRAFi/MEKi if BRAF mutation positive. ||May 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; FEV1, 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.