133a: Phase 2, multicenter study of the lifileucel regimen and pembrolizumab after frontline platinum-doublet chemotherapy and pembrolizumab in advanced non-small cell lung cancer

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Background

- Resistance to frontline immune checkpoint inhibitor (ICI) therapy ± chemotherapy presents a challenge in the treatment of metastatic non-small cell lung cancer (NSCLC)[1]
- In cohort 3A of the IOV-COM-202 phase 2 study, tumor-infiltrating lymphocyte (TIL) therapy with lifileucel plus pembrolizumab demonstrated durable and deepening responses in patients with anti–PD-(L)1–naive, *EGFR*–wild-type, locally advanced or metastatic NSCLC[2]
  - Objective response rate (ORR) was 64.3%, with an ORR of 54.5% in patients with PD-L1–negative disease
  - Four of 5 ongoing responses lasted >20 months from start of therapy
  - No new safety signals were observed
- Optimal timing for TIL therapy may be during the minimal residual disease phase when the effector:target ratio is lowest[3] and before prolonged immune checkpoint exposure[4]
- Adding lifileucel to the maintenance period of frontline platinum-doublet chemotherapy and pembrolizumab in metastatic NSCLC may extend benefit beyond the historical median progression-free survival (PFS) of 6.4 to 8.8 months seen with pembrolizumab and chemotherapy alone[5,6]

Study Endpoints

- Primary endpoint
  - Percentage of patients for whom lifileucel is successfully manufactured and meets release specification
- Secondary endpoints
  - Investigator-assessed ORR, CR rate, DOR, DCR, and PFS per RECIST v1.1
  - OS
  - Incidence of grade ≥3 TEAEs
- Exploratory endpoints
  - In vivo T-cell persistence
  - Correlative biomarkers
  - Circulating tumor DNA
  - Health-related quality of life (European Organization for Research and Treatment of Cancer Core quality of life questionnaire [EORTC QLQ-C30] and the EORTC QLQ specific to lung cancer [LC13])
- Approximately 20 patients will be enrolled per cohort at sites in Europe and North America

IOV-COM-202 Cohorts 3D and 3E: Objective and Overview

- IOV-COM-202 (NCT03645928) is a prospective, open-label, multicohort, nonrandomized, international, phase 2 study evaluating lifileucel in combination with ICIs and as a single therapy
- Two new cohorts were added to this study to evaluate the feasibility of producing lifileucel using tumor samples obtained before or during frontline platinum-doublet chemotherapy and pembrolizumab and the efficacy and safety profile of the lifileucel regimen in combination with pembrolizumab (± pemetrexed) incorporated with frontline platinum-doublet chemotherapy and pembrolizumab in patients with stage IV NSCLC (**Table 1** and **Figure 1**)
  - Cohort 3D: lifileucel produced from tumors procured from patients with treatment-naive advanced NSCLC before standard-of-care (SOC) therapy
  - Cohort 3E: lifileucel produced from tumors procured from patients with treatment-naive advanced NSCLC who have been given 1, 2, or 3 cycles of SOC therapy prior to TIL harvest followed by completion of the SOC regimen
    - TIL harvest occurs when the investigator determines it is oncologically safe to do so

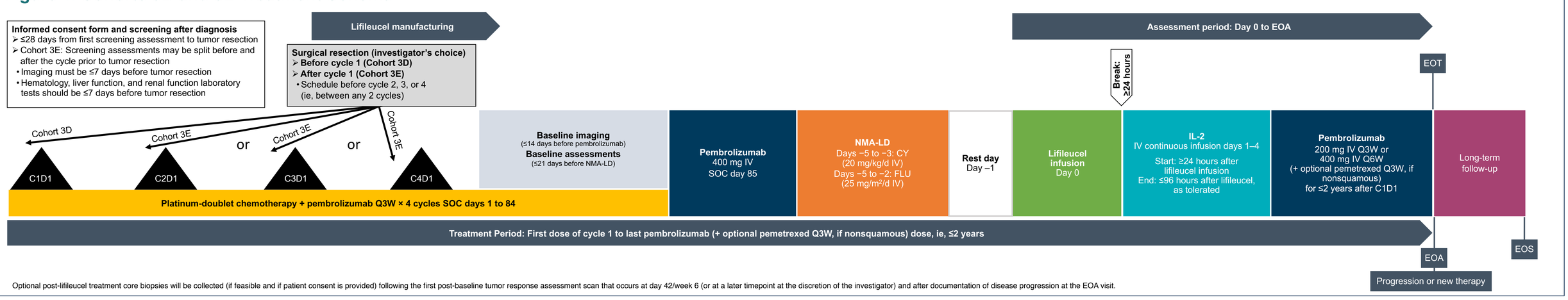
Key Eligibility Criteria

- Inclusion criteria
  - Age ≥18 years; age >70 years permitted after discussion with the medical monitor
  - Stage IV NSCLC with no *EGFR*, *ALK*, or *ROS1* mutations
  - No prior systemic therapy for stage IV metastatic disease, aside from ongoing frontline platinum-doublet chemotherapy plus pembrolizumab
  - Eastern Cooperative Oncology Group performance status 0–1
  - Estimated life expectancy ≥6 months
  - ≥1 resectable lesion (or aggregate lesions) with an expected minimum 1.5 cm short axis diameter for lifileucel production
  - Adequate organ function
- Exclusion criteria
  - Prior organ allograft or cell transfer therapy
  - Symptomatic brain metastases
  - Current systemic steroid therapy >10 mg/day of prednisone or other steroid equivalent
  - Active illnesses or autoimmune disorders
  - Any form of primary or acquired immunodeficiency (eg, severe combined immunodeficiency or AIDS)
  - Other primary malignancy in the past 3 years

Table 1. Treatment in Cohorts 3D and 3E

Platinum-doublet chemotherapy and pembrolizumab: Up to 4 cycles (Q3W) based on tumor histology and institutional SOC	Lifileucel regimen	Continued therapy in the maintenance setting
• Nonsquamous histology: – Carboplatin OR cisplatin – Pemetrexed – Pembrolizumab • Squamous histology: – Carboplatin – Paclitaxel OR nab-paclitaxel – Pembrolizumab	• NMA-LD – Cyclophosphamide/mesna – Fludarabine • Lifileucel • IL-2	• Nonsquamous histology: – Pembrolizumab – Pemetrexed (optional) • Squamous histology: – Pembrolizumab

Figure 1. Cohorts 3D and 3E Treatment Schema



Optional post-lifileucel treatment core biopsies will be collected (if feasible and if patient consent is provided) following the first post-baseline tumor response assessment scan that occurs at day 42/week 6 (or at a later timepoint at the discretion of the investigator) and after documentation of disease progression at the EOA visit.

References, Disclosures, Abbreviations, and Acknowledgments

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Disclosures

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Abbreviations

AIDS, acquired immunodeficiency syndrome; ALK, anaplastic lymphoma kinase; C1D1, cycle 1 day 1; CR, complete response; CY, cyclophosphamide; DCR, disease control rate; DOR, duration of response; EGFR, endothelial growth factor receptor gene; EORTC QLQ, European Organization for Research and Treatment of Cancer quality of life questionnaire; FLU, fludarabine; ICI, immune checkpoint inhibitor; IL-2, interleukin-2; IV, intravenously; NMA-LD, nonmyeloablative lymphodepletion; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PD-(L)1, programmed cell death protein-1/programmed death-ligand 1; PFS, progression-free survival; Q3W, every 3 weeks; Q6W, every 6 weeks; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1; ROS1, ROS proto-oncogene 1; SCID, severe combined immunodeficiency; SOC, standard-of-care; TEAE, treatment-emergent adverse event; TIL, tumor-infiltrating lymphocytes

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The study record for IOV-COM-202 at ClinicalTrials.gov can be accessed through this Quick Response (QR) code