



# Multicenter Phase II Trial Of LN-145 TIL Cell Therapy Plus Pembrolizumab in Patients With ICI-Naïve Metastatic NSCLC



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# IOV-COM-202 3A: LN-145 + anti-PD-1 in ICI-naïve mNSCLC

## Merging Potent Immunotherapy Modalities

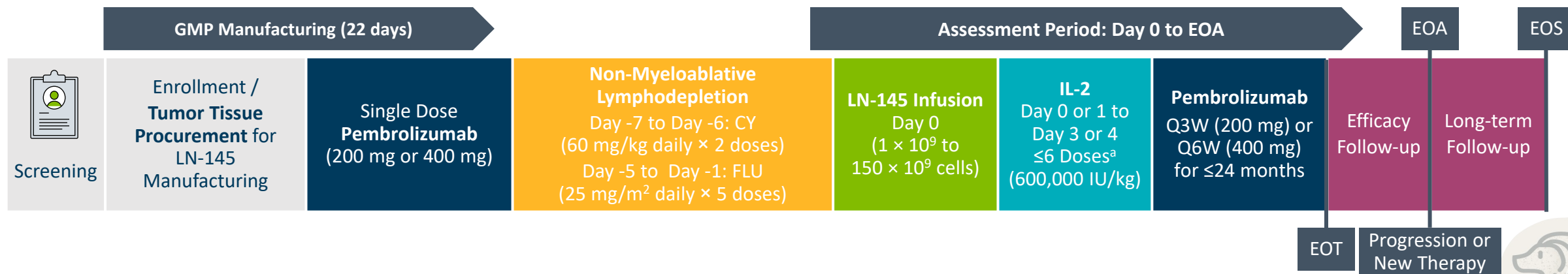
### Introduction

- Benefit from front-line ICI ± chemotherapy in patients with mNSCLC is limited by primary and secondary resistance
- TIL cell therapy has produced durable objective responses in patients with extensively pretreated mNSCLC<sup>1,2</sup>
- Integration of TIL cell therapy in front-line regimens may improve long-term benefit

### Methods and Objective

- IOV-COM-202 (NCT03645928) is a global, phase 2, multicenter, multicohort open-label study of autologous TIL cell therapy in patients with solid tumors
- Cohort 3A includes patients with anti-PD-1/PD-L1 naïve locally advanced or metastatic NSCLC with disease progression
- We report data for patients in Cohort 3A treated with LN-145 plus pembrolizumab (**Figure 1**)

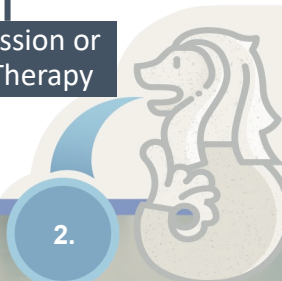
**Figure 1. Treatment Schema**



1. Schoenfeld A, et al. *J Immunother Cancer* 2021;9(Suppl 2):A458. 2. Creelan BC, et al. *Nat Med* 2021;27(8):1410–1418.

<sup>a</sup>Every 8–12 hours (3–24 hours after completion of LN-145 infusion).

CY, cyclophosphamide; EOA, end of assessment; EOS, end of study; EOT, end of treatment; FLU, fludarabine; GMP, Good Manufacturing Practice; ICI, immune checkpoint inhibitor; IL-2, interleukin-2; IU, international units; mNSCLC, metastatic non-small cell lung cancer; PD-1, programmed cell death protein 1; PD-L1, programmed death ligand-1; TIL, tumor-infiltrating lymphocyte.



# Results: Baseline Demographics and Safety Data

## Majority of Patients Were PD-L1–Negative With High Disease Burden

**Table 1. Baseline Patient and Disease Characteristics**

Characteristics	Cohort 3A (N=19)
Median age, y (min, max)	55.4 (35, 68)
Never tobacco use, n (%) <sup>a</sup>	7 (36.8)
Median prior lines of systemic therapy by prior therapy subgroup, n (min, max)	1 (0, 4)
Treatment-naïve (n=5) <sup>b</sup>	0 (0, 1)
Post-chemotherapy (n=7) <sup>c</sup>	1 (1, 3)
<i>EGFR</i> -mutated post-TKI (n=7) <sup>d</sup>	2 (1, 4)
Nonsquamous histologic cell type, n (%) <sup>e</sup>	18 (94.7)
Driver mutation-positive, n (%) <sup>f</sup>	13 (68.4)
<i>EGFR</i>	7 (36.8)
<i>KRAS</i> <sup>g</sup>	6 (31.6)
<i>NTRK</i>	1 (5.3)
PD-L1 tumor proportion score, n (%) <sup>h</sup>	
<1%	<b>13 (68.4)</b>
1-49%	2 (10.5)
≥50%	4 (21.1)
Median number of target and nontarget lesions, n (min, max)	4 (2, 10)
<b>Median target lesion SOD, mm (min, max)</b>	<b>61.0 (13, 218)</b>
Anatomic site of TTPS, n (%) <sup>i</sup>	
Lung	8 (42.1)
Lymph node	5 (26.3)
Median time from TTPS to LN-145 infusion, d (min, max)	39.0 (34, 84)
Median LN-145 dose, ×10 <sup>9</sup> cells (min, max)	23.5 (2.8, 57.6)

<sup>a</sup>12 patients (63.2%) were former smokers. <sup>b</sup>ICI-naïve patients who are treatment naïve in metastatic setting (n=5); 1 patient received neoadjuvant chemotherapy. <sup>c</sup>ICI-naïve patients who received prior chemotherapy (n=7). <sup>d</sup>ICI-naïve *EGFR*-mutated patients who received prior TKI therapy (n=7). <sup>e</sup>1 patient (5.3%) had squamous cell carcinoma. <sup>f</sup>Genes assessed include *BRAF*, *EGFR*, *ALK*, *ROS1*, *KRAS*, and *NTRK*; some patients did not have all genes assessed. <sup>g</sup>1 patient had a *KRAS* G12C mutation. <sup>h</sup>As adjudicated between site-reported and central-laboratory data; 8 of the patients with PD-L1–negative disease were *EGFR* wild-type. <sup>i</sup>6 patients (26.3%) had other site, including bone, liver, skin/subcutaneous, buttock, post chest wall, and pleura (n=1 each). <sup>j</sup>Per CTCAE v4.03; TEAEs include AEs that occur from the earlier of the first dose of pembrolizumab or LN-145 infusion, up to 30 days after the later of the last dose of pembrolizumab or LN-145 infusion or start of a new anticancer therapy. AE, adverse event; IL-2, interleukin 2; PD-L1, programmed death ligand-1; SOD, sum of diameters; TEAE, treatment-emergent adverse event; TKI, tyrosine kinase inhibitor; TTPS, tumor tissue procurement surgery.

**Table 2. Non-hematologic TEAEs in ≥30% of Patients<sup>j</sup>**

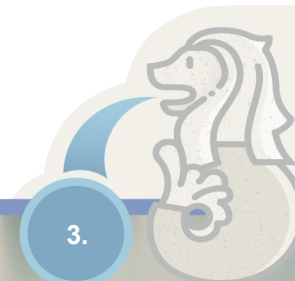
Preferred Term, n (%)	Cohort 3A (N=19)	
	Any grade	Grade 3/4
Pyrexia	15 (78.9)	1 (5.3)
Hypoxia	14 (73.7)	11 (57.9)
Chills	13 (68.4)	0
Dyspnea	12 (63.2)	4 (21.1)
Fatigue	10 (52.6)	3 (15.8)
Cough	9 (47.4)	0
Diarrhea	9 (47.4)	0
Hypotension	9 (47.4)	3 (15.8)
Nausea	9 (47.4)	1 (5.3)
Febrile neutropenia	8 (42.1)	8 (42.1)
Hypoalbuminemia	8 (42.1)	1 (5.3)
Sinus tachycardia	8 (42.1)	0
Hypophosphatemia	7 (36.8)	6 (31.6)
Hypertension	7 (36.8)	2 (10.5)
Peripheral edema	7 (36.8)	1 (5.3)
Constipation	6 (31.6)	0
Hyponatremia	6 (31.6)	2 (10.5)
Hyperglycemia	6 (31.6)	1 (5.3)
Maculopapular rash	6 (31.6)	0
Musculoskeletal chest pain	6 (31.6)	0

**Table 3. Grade 3/4 Hematologic Lab Abnormalities**

Preferred Term, n (%)	Cohort 3A (N=19) Grade 3/4
Neutropenia	19 (100)
Leukopenia	19 (100)
Lymphopenia	19 (100)
Thrombocytopenia	17 (89.5)
Anemia	15 (78.9)

**Data cutoff:** 26 June 2023

- Patients were **largely PD-L1–negative**, with **high burden of disease (Table 1)**
- TEAEs were consistent with the underlying disease and the known safety profiles of non-myeloablative lymphodepletion and IL-2 (**Table 2; Table 3**)
- No Grade 5 TEAE was reported



# Results: Clinical Efficacy in ICI-naïve mNSCLC Responses (RECIST v1.1) Observed Independent of PD-L1 Status

Figure 2. Best Percentage Change from Baseline in Target Lesion SOD for Evaluable Patients

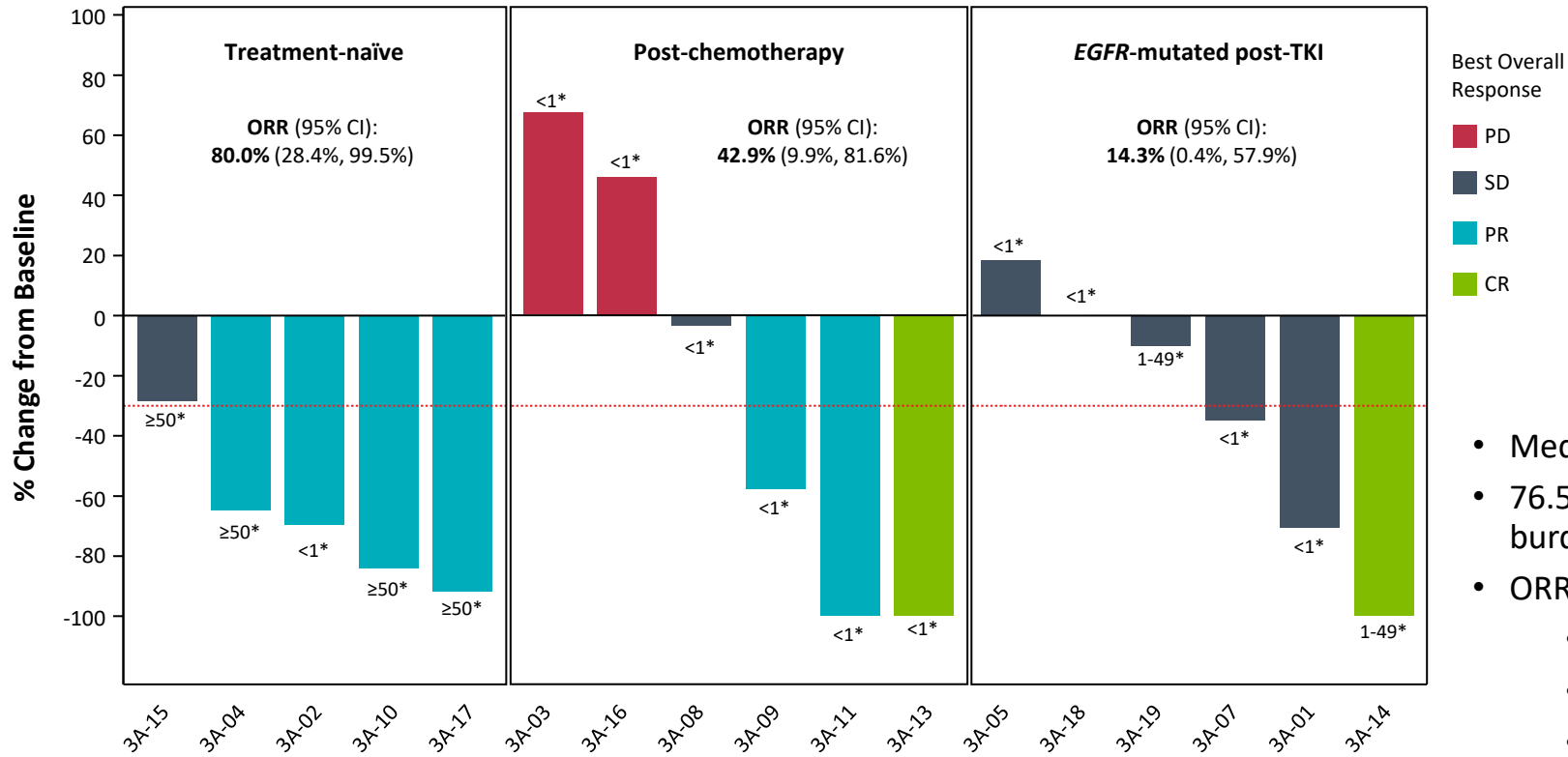


Table 4. Best Overall Response

Best Overall Response	Cohort 3A (N=19)	
	n/N	% (95% CI)
ORR	8/19	42.1 (20.3, 66.5)
DCR	15/19	78.9 (54.4, 93.9)
CR	2/19	10.5
PR	6/19	31.6
SD	7/19	36.8
PD	2/19	10.5
NE	2/19	10.5

- Median study follow-up was 18.2 months
- 76.5% of patients experienced reduction in tumor burden (**Figure 2**)
- ORR was 42.1% (**Table 4**); ORRs by prior therapy were:
  - Treatment-naïve: 80.0% (4/5)
  - Post-chemotherapy: 42.9% (3/7)
  - EGFR-mutated post-TKI: 14.3% (1/7)
- Treatment-naïve or post-chemotherapy: 58.3% (7/12)

\*PD-L1 status (%) as adjudicated between site-reported and central-laboratory data.

CR, complete response; DCR, disease control rate; ICI, immune checkpoint inhibitor; mNSCLC, metastatic non-small cell lung cancer; NE, non-evaluable; ORR, objective response rate; PD-L1, programmed death ligand-1; PD, progressive disease; PR, partial response; SD, stable disease; SOD, sum of diameters; TKI, tyrosine kinase inhibitor.



# Results: Clinical Efficacy in ICI-naïve mNSCLC

## Durable Responses Were Observed

Figure 3. Time to Response and Time on Efficacy Assessment for Confirmed Responders (PR or Better)

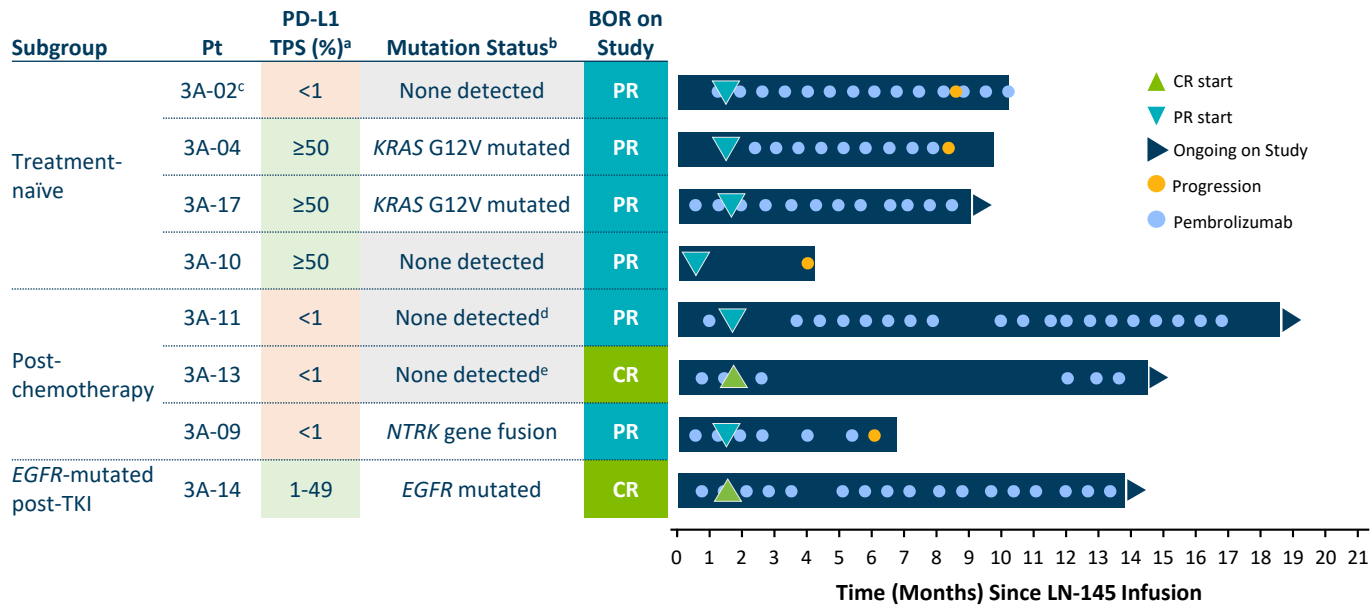
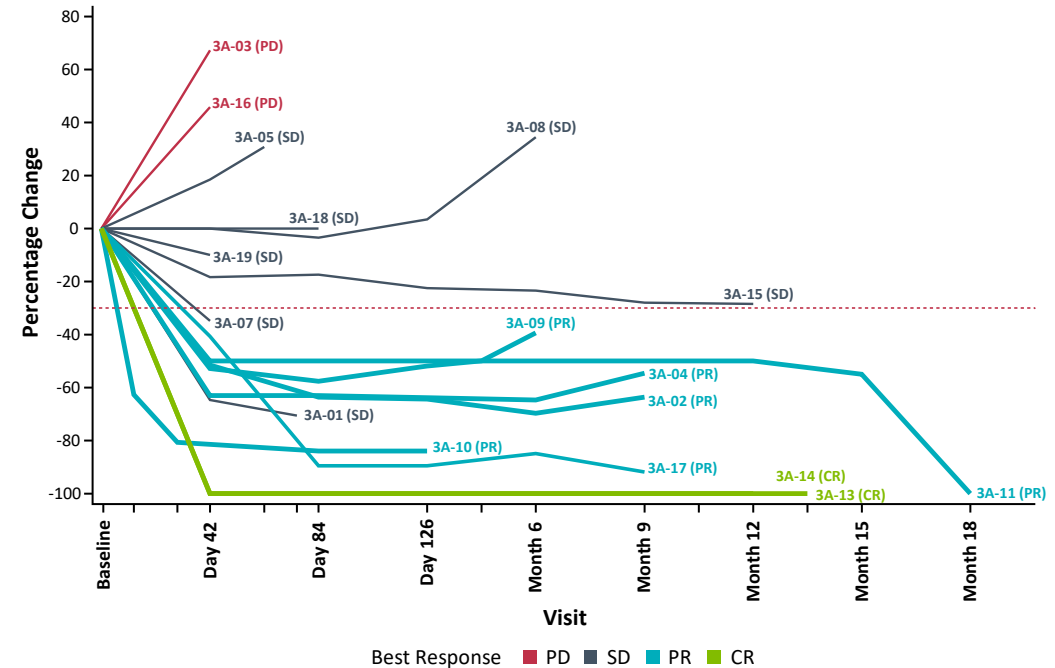


Figure 4. Percentage Change from Baseline in Target Lesion SOD



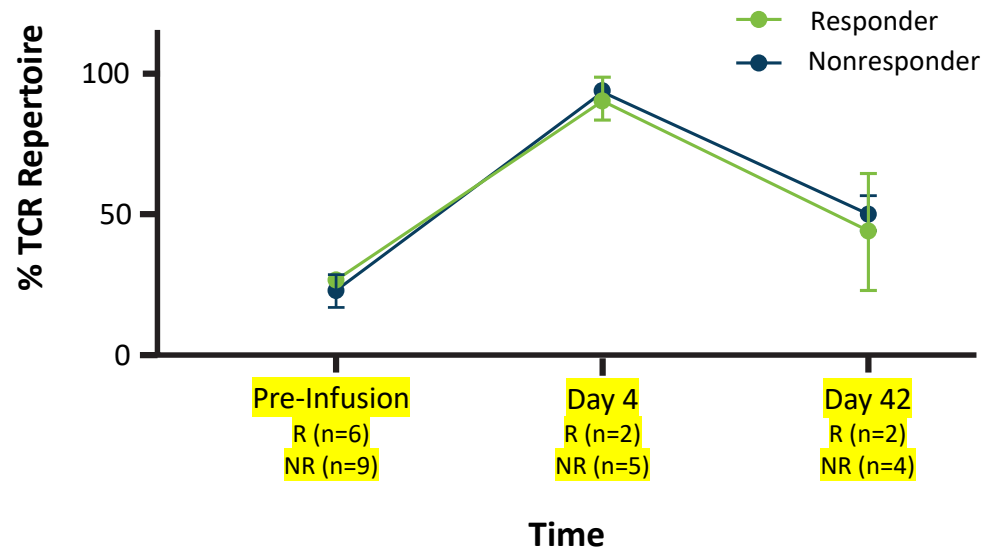
- 4 responses occurred in 8 patients with *EGFR* wild-type, PD-L1–negative disease (50%) (Figure 3)
- Responses deepened over time in a subgroup of patients (Figure 4)

<sup>a</sup>As adjudicated between site-reported and central-laboratory data. <sup>b</sup>The following genes were tested: *BRAF*, *EGFR*, *ALK*, *ROS1*, *KRAS*, and *NTRK*. <sup>c</sup>Patient received prior neoadjuvant chemoradiotherapy. <sup>d</sup>*ROS1*, *NTRK* not assessed. <sup>e</sup>*NTRK* not assessed. BOR, best overall response; CR, complete response; ICI, immune checkpoint inhibitor; mNSCLC, metastatic non-small cell lung cancer; PD-L1, programmed death ligand-1; PR, partial response; SOD, sum of diameters; TKI, tyrosine kinase inhibitor; TPS, tumor proportion score.

# Infused TCR Clonotypes Over Time and Cell Dose

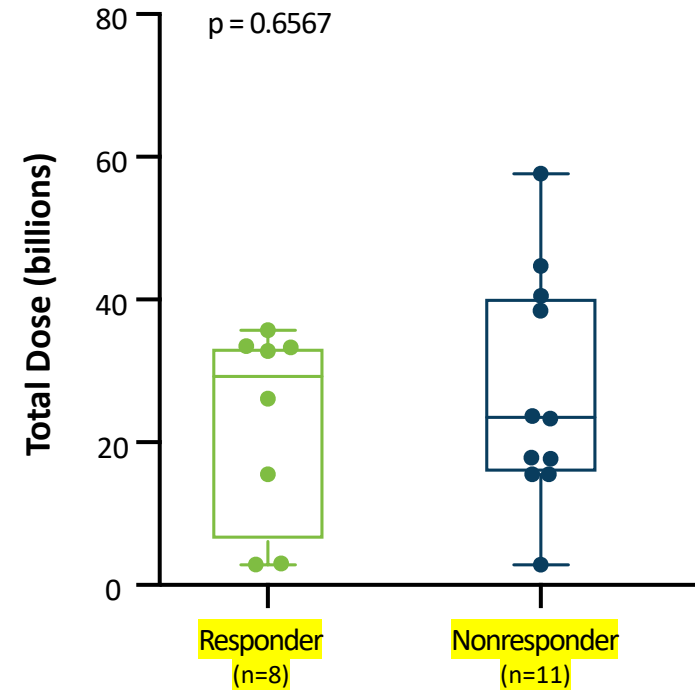
## Infused TIL Persist in Peripheral Blood and Cell Dose Did Not Differ By Response

Figure 5. Persistence of Infused TIL\*



- Clones from the infused TIL product persisted similarly in responders and nonresponders (**Figure 5**)

Figure 6. Total Cell Dose



- Total cell dose infused was similar among responders and nonresponders (**Figure 6**)

\*Bars represent standard error.

NR, nonresponder; R, responder; TCR, T-cell receptor; TIL, tumor-infiltrating lymphocyte.



# Trial Conclusions

## TIL Cell Therapy Activity May Be Independent of PD-L1 Status in ICI-naïve mNSCLC

- In patients with ICI-naïve mNSCLC, activity of LN-145 plus pembrolizumab was greater than what has previously been reported for LN-145 monotherapy or pembrolizumab alone and was not limited by PD-L1 TPS
  - Overall, the ORR was 42.1%
    - Treatment-naïve: 80.0% (4/5)
    - Post-chemotherapy: 42.9% (3/7)
    - *EGFR*-mutated post-TKI: 14.3% (1/7)
    - Treatment-naïve or post-chemotherapy: 58.3% (7/12)
    - *EGFR* wild-type, PD-L1–negative disease: 50.0% (4/8)
  - No new safety signals were observed with pembrolizumab addition to the LN-145 regimen
- Durable and deepening responses (up to 15.4 months and ongoing) were observed and TIL clones persisted after infusion
- No difference was observed in cell dose infused for responders and nonresponders
- These results support further clinical investigation of LN-145 in ICI-naïve mNSCLC and inform design of a phase 3 study of LN-145 added to front-line standard of care therapy for patients with mNSCLC

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