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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

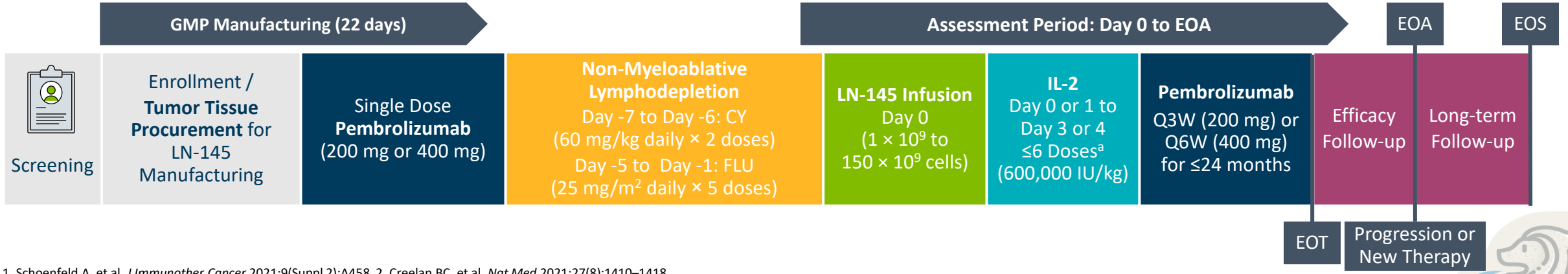
Introduction

- 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[1,2]
- 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.

[a]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 (%)[a]	7 (36.8)
Median prior lines of systemic therapy by prior therapy subgroup, n (min, max)	1 (0, 4)
Treatment-naïve (n=5)[b]	0 (0, 1)
Post-chemotherapy (n=7)[c]	1 (1, 3)
EGFR-mutated post-TKI (n=7)[d]	2 (1, 4)
Nonsquamous histologic cell type, n (%)[e]	18 (94.7)
Driver mutation-positive, n (%)[f]	13 (68.4)
EGFR	7 (36.8)
KRAS[g]	6 (31.6)
NTRK	1 (5.3)
PD-L1 tumor proportion score, n (%)[h]	
<1%	**13 (68.4)**
1-49%	2 (10.5)
≥50%	4 (21.1)
Median number of target and nontarget lesions, n (min, max)	4 (2, 10)
Median target lesion SOD, mm (min, max)	**61.0 (13, 218)**
Anatomic site of TTPS, n (%)[i]	
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, $\times 10^9$ cells (min, max)	23.5 (2.8, 57.6)

Table 2. Non-hematologic TEAEs in ≥30% of Patients[j]

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

[a]12 patients (63.2%) were former smokers. [b]ICI-naïve patients who are treatment naïve in metastatic setting (n=5); 1 patient received neoadjuvant chemotherapy. [c]ICI-naïve patients who received prior chemotherapy (n=7). [d]ICI-naïve *EGFR*-mutated patients who received prior TKI therapy (n=7). [e]1 patient (5.3%) had squamous cell carcinoma. [f]Genes assessed include *BRAF*, *EGFR*, *ALK*, *ROS1*, *KRAS*, and *NTRK*; some patients did not have all genes assessed. [g]1 patient had a *KRAS* G12C mutation. [h]As adjudicated between site-reported and central-laboratory data; 8 of the patients with PD-L1–negative disease were *EGFR* wild-type. [i]6 patients (26.3%) had other site, including bone, liver, skin/subcutaneous, buttock, post chest wall, and pleura (n=1 each). [j]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.

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

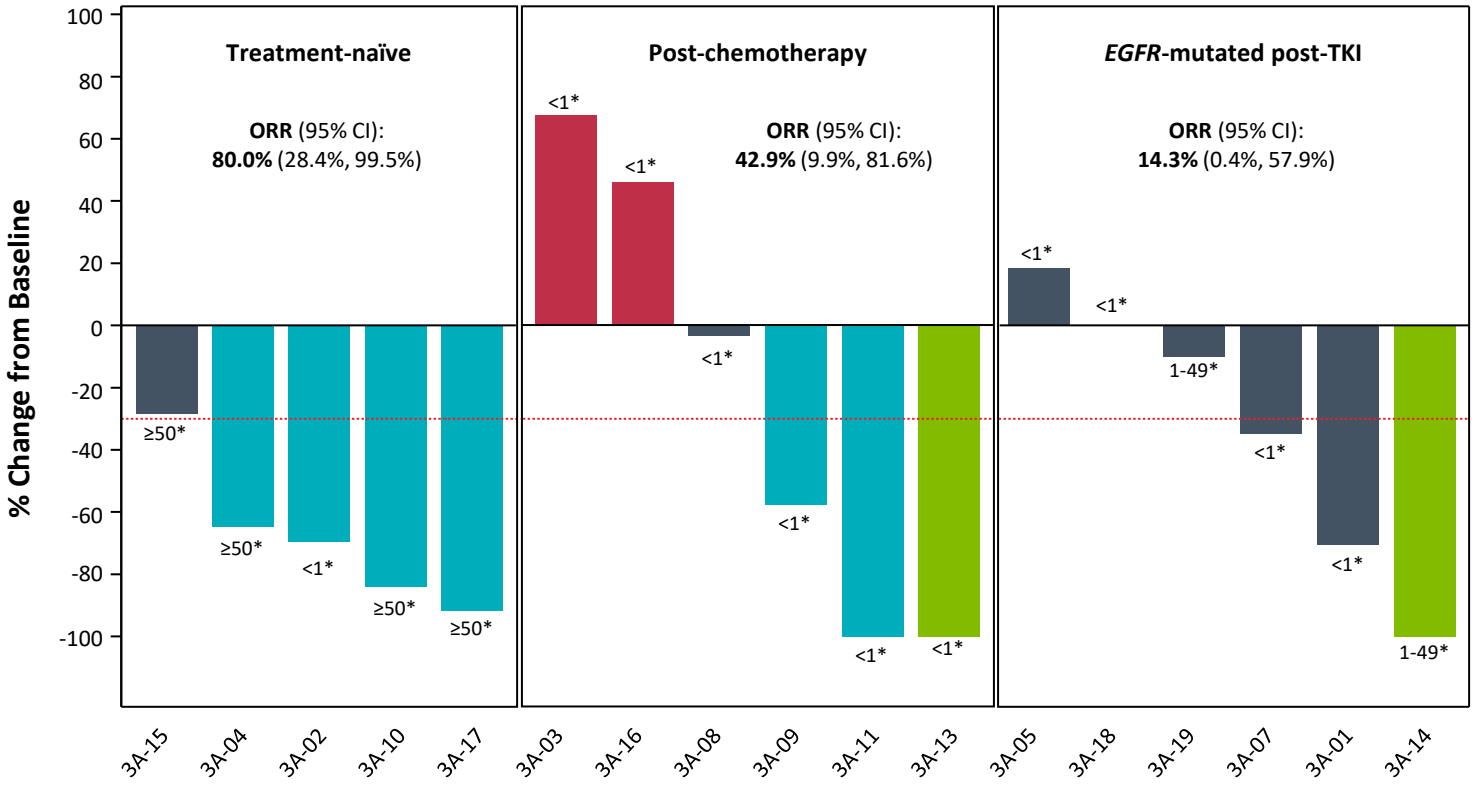


Table 4. Best Overall Response

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)

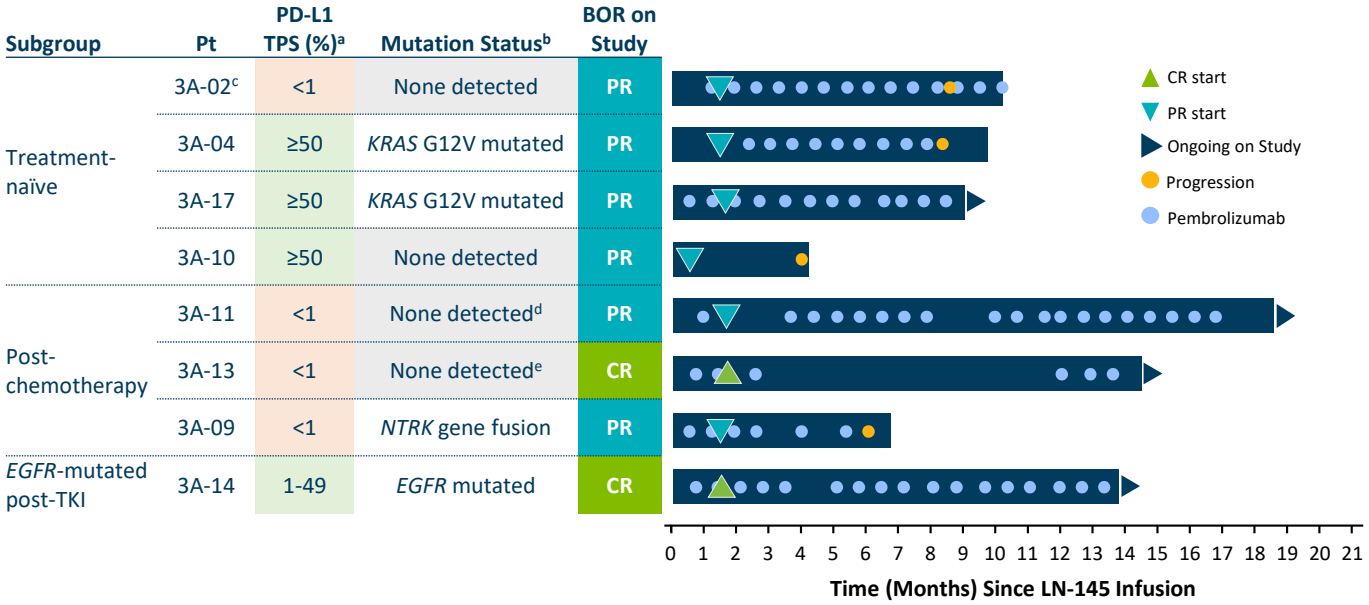
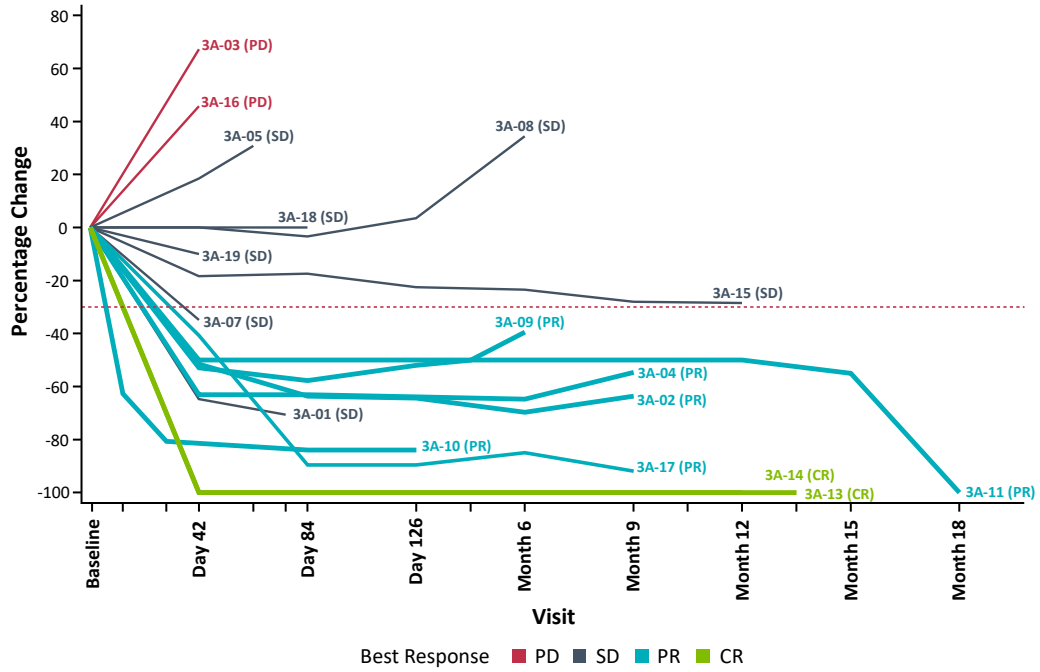


Figure 4. Percentage Change from Baseline in Target Lesion SOD



- 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**)

[a]As adjudicated between site-reported and central-laboratory data. [b]The following genes were tested: *BRAF*, *EGFR*, *ALK*, *ROS1*, *KRAS*, and *NTRK*. [c]Patient received prior neoadjuvant chemoradiotherapy. [d]*ROS1*, *NTRK* not assessed. [e]*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*

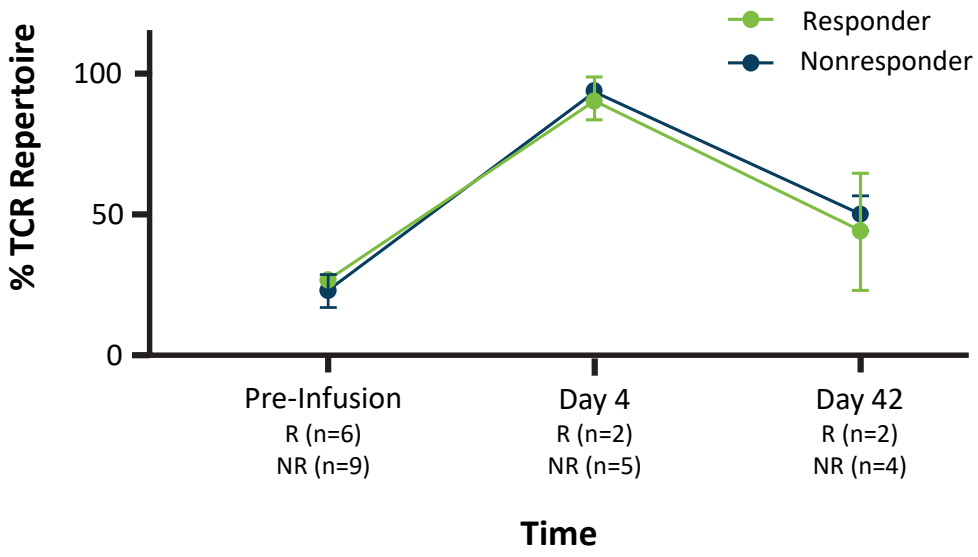
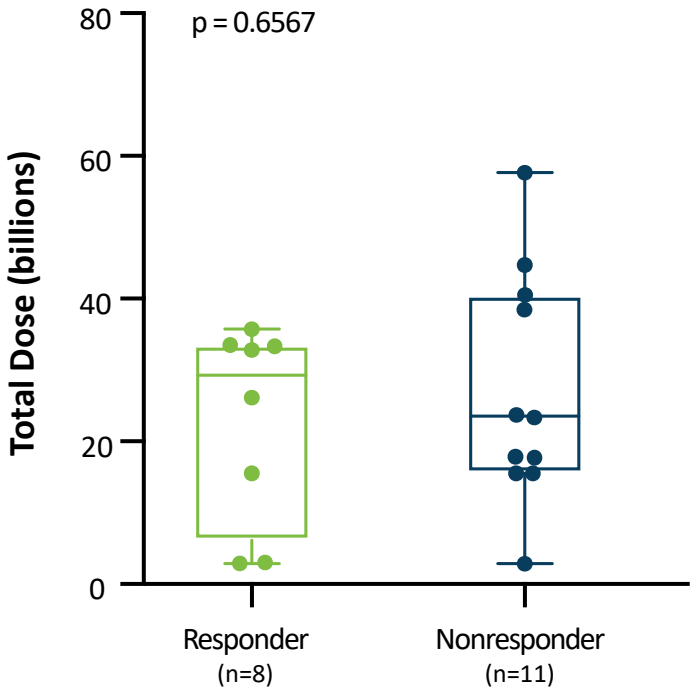


Figure 6. Total Cell Dose



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

ICI, immune checkpoint inhibitor; mNSCLC, metastatic non-small cell lung cancer; ORR, objective response rate; PD-L1, programmed death ligand-1; TKI, tyrosine kinase inhibitor; TPS, tumor proportion score.