Conclusion: Preliminary immunophenotyping data from the interim analysis showed significantly lower baseline immunosuppressive cell subsets in patients with preop-TRAE and decreased late activated $CD4^+$and $CD8^+$T cells from PB in patients with MPR.These results, together with additional LN IMMUNOME and cytokine analyses, may improve our understanding of immunophenotypic features associated with outcome, and changes induced by neoadjuvant atezolizumab in early stage NSCLC patients. **Keywords:** NSCLC, neoadjuvant anti-PD-L1 treatment, immunophenotyping

OA14.01
KEYNOTE-024 3-Year Survival Update: Pembrolizumab vs Platinum-Based Chemotherapy for Advanced Non–Small-Cell Lung Cancer

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Background: In the phase 3 KEYNOTE-024 trial (NCT02142738), first-line pembrolizumab significantly improved PFS (hazard ratio [HR] 0.50, $P<0.001$) and OS (HR 0.60, $P=0.005$) vs platinum-based chemotherapy in patients with advanced NSCLC, PD-L1 tumor proportion score (TPS) $\geq$50%, and no targetable *EGFR/ALK* alterations (median follow-up, 11.2 months). We present data with 3-years minimum follow-up. **Method:** Patients were randomized to pembrolizumab 200 mg Q3W for 2 years or platinum doublet (investigator's choice) for 4–6 cycles plus optional maintenance (nonsquamous), with stratification by ECOG PS (0/1), tumor histology (squamous/nonsquamous), and region (East Asia/non–East Asia). Patients in the chemotherapy arm could cross over to pembrolizumab upon disease progression if they met eligibility criteria. The primary endpoint was PFS; OS was a key secondary endpoint. Response per investigator by RECIST version 1.1 is reported. **Result:** 305 patients were randomized (pembrolizumab, n=154; chemotherapy, n=151). At data cutoff (February 15, 2019), median (range) follow-up was 44.4 (39.6–52.9) months. 210 patients had died (pembrolizumab, n=97; chemotherapy, n=113). 98 (64.9%) patients crossed over from chemotherapy to anti–PD-(L)1 therapy during/outside of the study. Median (95% CI) OS in the pembrolizumab arm was 26.3 (18.3–40.4) months vs 14.2 (9.8–18.3) months in the chemotherapy arm (HR, 0.65; 95% CI, 0.50–0.86). 36-month OS rate was 43.7% in the pembrolizumab arm vs 24.9% in the chemotherapy arm. Despite longer mean treatment duration in the pembrolizumab arm (11.1 vs 4.4 months), grade 3–5 treatment-related adverse events (AEs) were less frequent with pembrolizumab vs chemotherapy: 31.2% vs 53.3%. 38 patients in the pembrolizumab arm completed 2 years (35 cycles) of therapy. Among these, 34 were alive, 31 (81.6%) had an objective response (including 3 with complete response), and median duration of response was not reached (range, 4.2–46.7+ months). OS rate 12 months after completing pembrolizumab treatment (ie, ~36 months after initiating treatment) was 97.4% (95% CI, 82.8–99.6). Among the 38 patients who completed 2 years, 5 (13.2%) had treatment-related grade 3-4 AEs; no fatal treatment-related AEs occurred. 10 patients who completed 2 years (1 completed 34 cycles) and subsequently progressed received second-course pembrolizumab; 7 had an objective response, 8 remain alive. **Conclusion:** With >3 years' follow-up, first-line pembrolizumab monotherapy continued to provide durable long-term OS benefit vs chemotherapy despite a majority of patients assigned to chemotherapy crossing over to pembrolizumab. Pembrolizumab was associated with less toxicity than chemotherapy. Patients who completed 35 cycles of pembrolizumab had durable clinical benefit and most were alive at data cutoff. **Keywords:** non-small-cell lung cancer, Pembrolizumab, platinum

OA14.02
IMpower131: Final OS Results of Carboplatin + Nab-Paclitaxel ± Atezolizumab in Advanced Squamous NSCLC

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Background: IMpower131 (NCT02367794) is a randomised Phase III trial of atezolizumab + chemotherapy vs chemotherapy alone as first-line therapy in Stage IV squamous NSCLC. Here we report the final OS results (Arm B vs Arm C). **Method:** Enrolled patients were randomised 1:1:1 to Arm A (atezolizumab 1200 mg q3w + carboplatin AUC 6 q3w + paclitaxel 200 mg/m^2 q3w), Arm B (atezolizumab + carboplatin + nab-paclitaxel 100 mg/m^2 qw) or Arm C (carboplatin + nab-paclitaxel) for 4 or 6 cycles followed by atezolizumab maintenance therapy (Arms A and B) until loss of clinical benefit or progressive disease. Coprimary endpoints were investigator-assessed PFS and OS in the ITT population. Data cutoff: October 3, 2018. **Result:** 1021 patients were enrolled, with 343 in Arm B and 340 in Arm C. Median age was 65 years (range, 23-83 [Arm B] and 38-86 [Arm C]) and ≈80% of patients were male. The proportion of patients with high (14% vs 13%), positive (39% vs 37%) or negative (47% vs 50%) PD-L1 expression was similar between arms. Median OS in the ITT population was 14.2 months in Arm B vs 13.5 months in Arm C (HR, 0.88 [95% CI: 0.73, 1.05]; $P = 0.158$; Table), not crossing the boundary for statistical significance. In the PD-L1—high subgroup, median OS was 23.4 vs 10.2 months, respectively (HR, 0.48 [95% CI: 0.29, 0.81]; not formally tested). Treatment-related Grade 3-4 AEs and treatment-related SAEs occurred in 68.0% and 21.0% (Arm B) and 57.5% and 10.5% (Arm C) of patients; no new safety signals were identified, consistent with previous analyses. **Conclusion:** Final OS in Arm B vs C did not cross the boundary for statistical significance.

Clinically meaningful OS improvement was observed in the PD-L1–high subgroup, despite not being formally tested. No new or unexpected safety signals were reported.

	Arm B Atezolizumab + Carboplatin + Nab-Paclitaxel (n = 343)	Arm C Carboplatin + Nab-Paclitaxel (n = 340)	HR (95% CI)
Median OS, mo			
ITT	14.2	13.5	0.88 (0.73, 1.05); $P = 0.16$
PD-L1 high (TC3 or IC3)	23.4	10.2	0.48 (0.29, 0.81)
PD-L1 positive (TC1/2/3 or IC1/2/3)	14.8	15.0	0.86 (0.67, 1.11)
PD-L1 negative (TC0 or IC0)	14.0	12.5	0.87 (0.67, 1.13)
Median PFS, mo	6.5	5.6	0.75 (0.64, 0.88)
Confirmed ORR, n/N (%)[a]	170/342 (49.7)	139/339 (41.0)	—

[a] Patients were classified as missing or unevaluable when no post-baseline response assessments were available or all post-baseline response assessments were unevaluable. CI, confidence interval; HR, hazard ratio; IC, tumour-infiltrating immune cell; ITT, intention-to-treat; OS, overall survival; ORR, objective response rate; PD-L1, programmed death-ligand 1; PFS, progression-free survival; TC, tumour cell.
TC3 or IC3: PD-L1 expression on ≥50% of TC or ≥10% of IC; TC1/2/3 or IC1/2/3: PD-L1 expression on ≥1% of TC or IC; TC0 and IC0: PD-L1 expression on <1% of TC and IC.

Keywords: Atezolizumab, Chemotherapy, squamous NSCLC

OA14.03
Clinical Rationale and Preclinical Evidence for Chimeric Antigen Receptor (CAR) T Cell Therapy Clinical Trial in KRAS-Mutant Lung Cancer

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Background: Chimeric antigen receptor (CAR) T cells are engineered to express a synthetic receptor that redirects specificity to a tumor-associated antigen (TAA). Mesothelin (MSLN) is a TAA expressed by solid tumors, notably in mesothelioma and lung adenocarcinoma (ADC). Our group clinical trial of MSLN-targeted CAR T cells in mesothelioma demonstrated a favorable safety profile and evidence of antitumor activity. In this study, we evaluated the feasibility and utility of MSLN-targeted CAR T cell therapy in advanced, *KRAS*-mutant lung ADC. **Method:** Tissue microarray from stage I-III lung ADC tumors (n=1438) were reviewed by two pathologists, then stained for MSLN expression on cell-surface and cytoplasm. Of 327 patients with distant recurrences, adequate tissue was available from 34 autologous metastatic sites for MSLN expression evaluation. Healthy donor T cells were retrovirally transduced with a MSLN-targeted CAR. *In vitro* function against lung ADC cell lines with heterogenous MSLN expression resembling human tumors was assessed via chromium release assay, ELISA, and flow cytometry. *In vivo* antitumor efficacy (n=30) was evaluated by median survival and tumor bioluminescence in mice bearing lung ADC tumors. **Result:** The incidence of cell-surface MSLN expression was higher in metastases than matched primary tumors (65% vs 38%) and higher in *KRAS*-mutant than wild type tumors (42% vs 32%). CAR T cells secrete cytokines and lyse lung ADC cell lines in proportion to their cell-surface MSLN expression. No activity against MSLN-very low mesothelial or MSLN-negative lung ADC cell lines was observed. *In vivo*, a single dose of CAR T cells eradicates established primary and metastatic MSLN-high tumors without evidence of on-target off-tumor toxicity. **Conclusion:** Therapeutically-relevant cell surface MSLN expression is enriched in a population of *KRAS*-mutant lung ADC patients with poor prognosis and limited treatment options. MSLN-targeted CAR T cells exhibit antigen-specific and antigen density-dependent cytotoxicity against lung ADC cells *in vitro* and *in vivo* with no on-target, off-tumor toxicity to normal tissues. These results provide strong rationale for our upcoming MSLN-targeted CAR T cell therapy clinical trial in metastatic, *KRAS*-mutant lung ADC patients. **Keywords:** KRAS mutation, Non-Small Cell Lung Cancer, Immunotherapy

OA14.04
Five-Year Outcomes From the Randomized, Phase 3 Trials CheckMate 017/057: Nivolumab vs Docetaxel in Previously Treated NSCLC

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Background: Historically, outcomes for advanced non-small cell lung cancer (NSCLC) have been poor, with 5-year survival rates <5% with conventional chemotherapy. Nivolumab, a programmed death-1 (PD-1) inhibitor, was approved in 2015 for patients with previously treated advanced NSCLC based on two randomized phase 3 trials, CheckMate 017 (NCT01642004; squamous) and CheckMate 057 (NCT01673867; non-squamous), which demonstrated improved overall survival (OS) vs docetaxel. We report 5-year pooled efficacy and safety from these trials, representing the longest survival follow-up for randomized phase 3 trials of an immune checkpoint inhibitor in advanced NSCLC. **Method:** Patients (N = 854; CheckMate 017/057 pooled) with advanced NSCLC, ECOG performance status (PS) ≤1, and progression during or after first-line platinum-based chemotherapy, were randomized 1:1 to nivolumab 3 mg/kg Q2W or docetaxel 75 mg/m^2 Q3W until progression or unacceptable toxicity. After completion of the primary analyses, patients in the docetaxel arm no longer receiving benefit could cross over to receive nivolumab. OS was the primary endpoint for both studies. **Result:** At 5-year follow-up, 50 nivolumab patients and 9 docetaxel patients were alive. Baseline characteristics of 5-year survivors in both arms were similar to the overall population and patients who survived <1 year, except for a higher percentage of patients with