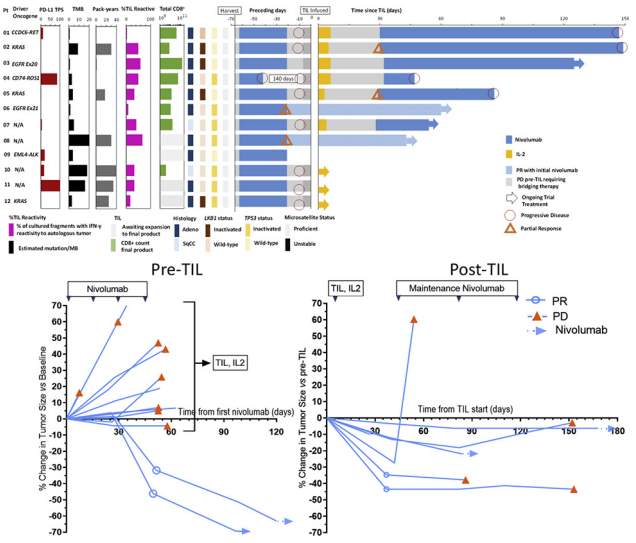
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Background: Adoptive transfer of tumor infiltrating lymphocytes (TIL) can cause durable regression by recognition of neoantigens unique to the patient. NSCLC TIL has synergistic preclinical activity with nivolumab, and we hypothesized it may induce remissions in anti-PD1-refractory patients. We initiated a phase I trial with the primary objective to characterize the safety and preliminary activity of the combination. **Method:** Metastases from patients with Stage 4 NSCLC were resected, morselized, cultured, and tested for autologous reactivity. Reactive TIL fragments were pooled and cryopreserved. Patients received nivolumab over 8 weeks. Patients with progressive disease (PD) proceeded to lymphodepletion cyclophosphamide/fludarabine (Cy/Flu), TIL, and IL-2. Tumor whole exome sequencing, transcriptomics, and LC-MS/MS peptide sequencing was performed. TCR-Vß rearrangements were analyzed from tumor, TIL, and pre-/post-infusion peripheral lymphocytes. **Result:** Of 14 patients enrolled to date, 13 had successful *ex vivo* TIL expansion from resected metastases. TIL had high proliferative capacity, expanding to median 81 billion $CD3^+$ cells infused per patient (range 27—138 billion) and median 27% of fragments were autologously reactive (range 0-67%). Demographics: median age 54 (range 44-74), median TMB 4 mutations/MB (range 0.9—25), median PD-L1 proportion-score 0% (range 0—100%), and 4 had *LKB1* allelic inactivation. Predicted neoantigens correlated with variants on proteomic sequencing. Outcomes: 9 patients had confirmed PD on nivolumab, and proceeded to receive Cy/Flu/TIL/IL-2. No unexpected serious adverse reactions (SUSARs) were identified. Of these 9 patients, 7 had reduction in sum of target lesions at Day+28 CT scan (Figure 1). Peripheral lymphocytes expanded at Days 2-7 in the majority of patients. In patients tested to date, TIL clonotypes persisted through Day+100, and $CCR7^+CD95^+CD45RA^+$ stem cell-like memory (T_{SCM}) cells were increased at post-infusion timepoints. **Conclusion:** Adoptive cell transfer with TIL and nivolumab for NSCLC had acceptable toxicity and preliminary activity in this ongoing trial. **Keywords:** Tumor-specific neoantigen testing, Phase I NSCLC trials, Adoptive cell transfer of tumor infiltrating lymphocytes (TIL)



OA05.05
Avelumab vs Docetaxel for Previously Treated Advanced NSCLC: Primary Analysis of the Phase 3 JAVELIN Lung 200 Trial

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Background: Avelumab is a human anti—PD-L1 IgG1 monoclonal antibody that is an approved treatment for metastatic Merkel cell carcinoma (various regions) and platinum-treated advanced urothelial carcinoma (US). We report findings from a global, open-label, phase 3 trial of avelumab vs docetaxel in patients with advanced NSCLC after platinum failure (NCT02395172). **Method:** Patients with stage IIIB/IV or recurrent NSCLC with disease progression after platinum doublet therapy were randomized 1:1 to avelumab 10 mg/kg Q2W or docetaxel 75 mg/m^2 Q3W, stratified by PD-L1 status (PD-L1+/PD-L1—) and histology (squamous/nonsquamous). The primary endpoint was overall survival (OS) in the PD-L1+ population (expression on ≥1% of tumor cells, assessed using the PD-L1 IHC 73-10 assay). **Result:** Between April 2015 and February 2017, 792 patients were randomized to receive avelumab or docetaxel, including 264 and 265 with PD-L1+ tumors, respectively; 0.8% vs 7.5% did not receive study treatment. Median follow-up in the avelumab and docetaxel arms was 18.9 and 17.8 months; 15.5% vs 1.5% remained on treatment at data cutoff (November 22, 2017). In the avelumab and docetaxel arms, 39.8% vs 47.5% received subsequent anticancer therapy after discontinuation, including checkpoint inhibitors in 5.7% vs 26.4%, respectively. In the PD-L1+ population, median OS in the avelumab and docetaxel arms was 11.4 vs 10.3 months (hazard ratio [HR], 0.90 [96% CI, 0.72-1.12]; P=0.1627, 1-sided). Pre-planned exploratory analyses based on higher PD-L1 cutoffs showed increased OS with avelumab vs docetaxel, including PD-L1-high (≥80% cutoff, 29% of patients; 17.1 vs 9.3 months; HR, 0.59 [95% CI, 0.42-0.83]; P=.0022, 2-sided) and PD-L1-medium/high (≥50% cutoff, 40% of patients; 13.6 vs 9.2 months; HR, 0.67 [95% CI, 0.51-0.89]; P=0.0052, 2-sided) subgroups. In the PD-L1+ population (≥1% cutoff), ORR was 18.9% vs 11.7% (odds ratio, 1.76 [95% CI, 1.08-2.86]; P=0.0105, 1-sided); median duration of response was not reached with avelumab (95% CI, 9.9-not estimable [NE]) vs 6.9 months with docetaxel (95% CI, 3.5-NE). Overall rates of treatment-related adverse events (AEs) were lower with avelumab than docetaxel, including all grades (63.9% vs 85.8%) and grade ≥3 (9.9% vs 49.3%). Immune-related AEs occurred in 16.5% of avelumab-treated patients (grade ≥3 in 2.8%). **Conclusion:** Avelumab showed increasing clinical activity in patients who had platinum-treated NSCLC with higher tumor

PD-L1 expression; however, the trial did not meet its primary objective of improving OS vs docetaxel in PD-L1+ tumors (≥1% cutoff). OS findings may have been confounded by subsequent checkpoint inhibitor therapy in the docetaxel arm. **Keywords:** Phase 3, avelumab, docetaxel

OA05.06

CheckMate 227: Patient-Reported Outcomes of First-Line Nivolumab + Ipilimumab in High Tumor Mutational Burden Advanced NSCLC

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Background: The randomized, open-label, multipart phase 3 study CheckMate 227 (NCT02477826) demonstrated a significant progression-free survival benefit (co-primary endpoint) with first-line nivolumab + ipilimumab versus histology-based, platinum-doublet chemotherapy in patients with advanced non-small cell lung cancer (NSCLC) and high tumor mutational burden (TMB; ≥10 mutations/Mb). Patient-reported outcomes (PROs) for this population within CheckMate 227 are presented. **Method:** Eligible chemotherapy-naïve patients had stage IV or recurrent NSCLC, ECOG performance status 0–1, and no known sensitizing *EGFR/ALK* alterations. PROs were assessed as an exploratory endpoint; this analysis included patients with high TMB randomized to nivolumab+ipilimumab or chemotherapy; specific outcomes included proportion of patients with disease-related symptom deterioration by 12 weeks and time to deterioration in symptoms (by Lung Cancer Symptom Scale [LCSS] Average Symptom Burden Index [ASBI]), and assessment of quality of life and overall health status (by EuroQoL-5 Dimension [EQ-5D] utility index [UI] and visual analog scale [VAS]). PROs were evaluated each cycle (Q2W, nivolumab+ipilimumab; Q3W, chemotherapy) for the first 6 months, every 6 weeks thereafter during treatment, and at follow-up visits 1/2. EQ-5D was also assessed during survival follow-up. **Result:** PRO completion rates were ~90% at baseline and >80% for nearly all on-treatment assessments. Among patients with high TMB, fewer patients in the nivolumab+ipilimumab (n=139) versus chemotherapy (n=160) groups reported symptom deterioration by week 12, irrespective of whether they were still on therapy or had discontinued (22.3% versus 35.0%; absolute risk reduction: 12.7% [95% CI: 2.4–22.5]). Time to first deterioration (TTD) using common assessment time points (on/off treatment) was delayed with nivolumab+ipilimumab versus chemotherapy for the LCSS ASBI (hazard ratio [HR]: 0.40; 95% CI: 0.26–0.63) and 3-Item Global Index (3-IGI; HR: 0.56; 95% CI: 0.38–0.82). The estimated benefit in TTD generally favored nivolumab+ipilimumab for individual symptoms in the ASBI and each item in the 3-IGI (HRs: 0.48–0.74), except for hemoptysis (HR: 1.20), which exhibited very low burden; an advantage for nivolumab+ipilimumab was also seen in the EQ-5D VAS (HR: 0.62; 95% CI: 0.42–0.92) and UI (HR: 0.50; 95% CI: 0.34–0.73). Mean changes from baseline with nivolumab+ipilimumab showed early and clinically meaningful improvements in LCSS ASBI/3-IGI and EQ-5D VAS/UI; for patients treated with chemotherapy, symptoms and quality of life remained stable (LCSS ASBI/3-IGI, EQ-5D UI) or improved following completion of chemotherapy (EQ-5D VAS). **Conclusion:** Nivolumab+ipilimumab demonstrated early and sustained improvements in health-related quality of life versus chemotherapy in patients with advanced NSCLC and high TMB. **Keywords:** NSCLC, first-line nivolumab, Patient-reported outcomes

OA05.07

IMpower132: PFS and Safety Results with 1L Atezolizumab + Carboplatin/Cisplatin + Pemetrexed in Stage IV Non-Squamous NSCLC

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Background: In addition to the combination of atezolizumab (anti–PD-L1)+platinum+taxane±bevacizumab, non-squamous NSCLC patients may derive benefit from adding atezolizumab to platinum+pemetrexed. The randomized Phase III IMpower132 study (NCT02657434) evaluated first-line pemetrexed+carboplatin or cisplatin±atezolizumab in patients with stage IV non-squamous NSCLC without *EGFR* or *ALK* driver mutations. **Method:** Patients were randomized 1:1 to receive 4 or 6 cycles of carboplatin AUC 6 mg/mL/min or cisplatin 75 mg/m^2 + pemetrexed 500 mg/m^2 Q3W alone (arm PP) or in combination with atezolizumab 1200 mg Q3W (arm APP), followed by pemetrexed (arm PP) or atezolizumab + pemetrexed (arm APP) maintenance. Atezolizumab could be continued beyond disease progression per protocol guidelines. PFS and OS were co-primary endpoints. Efficacy by PD-L1 expression was an exploratory endpoint. Here, we present investigator-assessed PFS per RECIST v1.1 (final analysis), OS (interim analysis) and safety data. **Result:** 292 pts were enrolled in arm APP and 286 pts in arm PP. 43% and 40% in arms APP and PP, respectively, had ECOG PS 0. At the data cutoff (22 May 2018), median follow-up was 14.8 mo overall. PFS analysis showed a statistically significant improvement between arm APP vs PP (median PFS 7.6 vs 5.2 mo; HR=0.596; 95% CI: 0.494, 0.719; $P<0.0001$). Interim analysis showed a numerical but non-statistically significant OS improvement (Table). Efficacy results were consistent across all key clinical subgroups. Grade 3-4 TRAEs occurred in 53.6% of patients (APP) vs 39.1% (PP). 7.2% of patients (APP) vs 5.1% (PP) had a Grade 5 AE, 3.8% (APP) vs 2.6% (PP) were treatment related. 48.5% of patients (APP) vs 38.0% (PP) experienced AEs of special interest specific to atezolizumab. **Conclusion:** IMpower132 met its co-primary endpoint of investigator-assessed PFS in the ITT. Interim OS data (not fully mature) showed numerical improvement. Atezolizumab+pemetrexed+carboplatin or cisplatin was well tolerated, and no new safety signals were identified. **Keywords:** atezolizumab, 1L NSCLC, chemotherapy