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WCLC 2016 Late Publication Abstracts | Monday, December 5, 2016

ORAL ABSTRACT SESSIONS

SESSION OA03: IMMUNOTHERAPY CHECKPOINT INHIBITORS IN ADVANCED NSCLC MONDAY, DECEMBER 5, 2016 – 11:00-12:30

OA03.01 FIRST-LINE NIVOLUMAB MONOTHERAPY AND NIVOLUMAB PLUS IPILIMUMAB IN PATIENTS WITH ADVANCED NSCLC: LONG-TERM OUTCOMES FROM CHECKMATE 012

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Background: Nivolumab, a programmed death 1 (PD-1) immune checkpoint inhibitor antibody, has demonstrated improved efficacy and tolerability vs docetaxel in patients with advanced NSCLC that progressed on or after platinum-based chemotherapy and is approved in >50 countries in this patient population. We report efficacy and safety data from a phase 1 study (CheckMate 012; NCT01454102) evaluating first-line nivolumab in patients with advanced NSCLC. **Methods:** Patients (N=52) with advanced, chemotherapy-naive NSCLC (any histology) were treated with nivolumab monotherapy at 3 mg/kg IV Q2W until disease progression or unacceptable toxicity. Safety and tolerability was the primary study objective. Efficacy, as measured by objective response rate (ORR) and 24-week progression-free survival (PFS) rate per RECIST v1.1, was the secondary objective. Overall survival (OS) was an exploratory endpoint. **Results:** Treatment-related adverse events (TRAEs) were reported in 71% (any grade) and 19% (grade 3–4) of patients. The most frequent select TRAEs (those with potential immunologic causes) by category were skin, endocrine, and gastrointestinal (Table). With a median follow-up of 14.3 months (range, 0.2 to 30.1), the confirmed ORR was 23% (12/52) and 8% (4/52) of patients had complete responses. Of the 12 responses, 8 (67%) were ongoing at the time of database lock; median duration of response was not reached. Median OS was 19.4 months (range, 0.2–35.8+). The 24-week PFS rate was 41% (95% CI: 27–54); 18-month OS rate was 57% (95% CI: 42–70). Updated long-term data will be presented, including 2-year OS and will represent the longest follow-up to date for a PD-1/PD-L1 inhibitor for first-line advanced NSCLC. Updated data from patients treated with nivolumab plus ipilimumab (N = 77) will also be presented.

	Nivolumab monotherapy (N=52)
Safety	
Any grade / grade 3–4 TRAEs,[a] n (%)	37 (71) / 10 (19)
Any grade / grade 3–4 select TRAEs,[a,b] by category (≥10% of patients), n (%)	
Skin	13 (25) / 2 (4)
Endocrine	7 (14) / 0 (0)
Gastrointestinal	6 (12) / 1 (2)
Any grade / grade 3–4 TRAEs leading to discontinuation, n (%)	6 (12) / 6 (12)
Efficacy	
Confirmed ORR,[c] n (%) [95% CI]	12 (23) [13–37]
CR	4 (8)
PR	8 (15)
SD	14 (27)
PD	20 (38)
Unable to determine[d]	6 (12)
Median DOR, mo (range)	NR (4.2–25.8+)
Ongoing responders, n/N (%)	8/12 (67)
Median PFS, mo (range)	3.6 (<0.1+–28.0+)
24-week PFS, % (95% CI)	41 (27–54)
Median OS, mo (range)	19.4 (0.2–35.8+)
1-year OS, % (95% CI)	73 (59–83)
18-month OS, % (95% CI)	57 (42–70)

Efficacy and safety analyses, except for OS, were based on a March 2015 database lock; OS analyses were based on an August 2015 database lock.
[a]No grade 5 events were reported.
[b]AEs with a potential immunologic cause.
[c]Includes patients with initial observations of CR and PR that were subsequently confirmed by repeat scans performed no earlier than 4 weeks after the original observation.
[d]Includes patients who discontinued therapy because of disease progression before first assessment or patients only with assessments suggestive of, but that did not satisfy, the required minimum duration for SD.
CR = complete response; PR = partial response; SD = stable disease; PD = progressive disease; DOR = duration of response; NR = not reached.

Conclusion: First-line nivolumab monotherapy in patients with advanced NSCLC had a similar safety profile as previously reported in second-line NSCLC and other tumors, was well tolerated, and demonstrated durable efficacy.
Keywords: Nivolumab, NSCLC, monotherapy, survival

SESSION OA03: IMMUNOTHERAPY CHECKPOINT INHIBITORS IN ADVANCED NSCLC
MONDAY, DECEMBER 5, 2016 – 11:00-12:30

OA03.03 JAVELIN SOLID TUMOR: SAFETY AND CLINICAL ACTIVITY OF AVELUMAB (ANTI-PD-L1) AS FIRST-LINE TREATMENT IN PATIENTS WITH ADVANCED NSCLC

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Background: Avelumab* (MSB0010718C) is a fully human anti-PD-L1 IgG1 antibody that has shown antitumour activity in various malignancies. We report safety and clinical activity of avelumab as first-line therapy in a cohort of patients with non-small–cell lung cancer (NSCLC) from a phase 1b trial (NCT01772004). **Methods:** Patients with advanced NSCLC not previously treated systemically for metastatic or recurrent disease, without an activating *EGFR* mutation or *ALK* rearrangement, and not preselected for PD-L1 expression, received avelumab 10 mg/kg IV over 1 hour Q2W until progression, unacceptable toxicity, or study withdrawal. Objective response rate (ORR) and progression-free survival (PFS) were evaluated by RECIST v1.1. Adverse events (AEs) were graded by NCI-CTCAE v4.0. **Results:** As of 23 Oct 2015, 145 patients had received avelumab (median 10 weeks of treatment; range 2-30) and were followed for a median of 13 weeks (range 0-31). Median age was 70 years (range 41-90), ECOG PS was 0 (31.0%) or 1 (69.0%), and tumour histology was adenocarcinoma (63.4%) or squamous (26.9%) in most patients. Eighty-two patients (56.6%) had a treatment-related (TR) AE; those occurring in ≥10% were infusion-related reaction (IRR; n=24, 16.6%) and fatigue (n=21, 14.5%). Thirteen patients (9.0%) had a grade ≥3 TRAE; only IRR and fatigue occurred in >1 patient (each n=3, 2.1%). Four patients (2.8%) had a potential immune-mediated TRAE, all grade 1-2 (pneumonitis n=3, 2.1%; hypothyroidism n=1, 0.7%). There were no treatment-related deaths. Among 75 patients with ≥3 months' follow-up, unconfirmed ORR was 18.7% (95% CI: 10.6, 29.3) based on 1 complete response and 13 partial responses; 12 were ongoing. Thirty-four additional patients (45.3%) had stable disease as best response (disease control rate 64.0%). Updated analysis will be presented, including efficacy data with ≥3 months' follow-up in all patients and PD-L1 analysis. **Conclusion:** First-line avelumab monotherapy showed clinical activity and was well-tolerated in patients with EGFR-wildtype/ALK-negative NSCLC unselected for PD-L1 expression. A phase 3 trial of avelumab vs platinum-doublet in first-line NSCLC is in progress. *Proposed nonproprietary name.
Keywords: 1L NSCLC, phase i, avelumab, PD-L1

SESSION OA03: IMMUNOTHERAPY CHECKPOINT INHIBITORS IN ADVANCED NSCLC
MONDAY, DECEMBER 5, 2016 – 11:00-12:30

OA03.05 ANALYSIS OF EARLY SURVIVAL IN PATIENTS WITH ADVANCED NON-SQUAMOUS NSCLC TREATED WITH NIVOLUMAB VS DOCETAXEL IN CHECKMATE 057

Solange Peters[1], Frederico Cappuzzo[2], Leora Horn[3], Luis Paz-Ares[4], Hossein Borghaei[5], Fabrice Barlesi[6], Martin Steins[7], Enriqueta Felip[8], David Spigel[9], Cécile Dorange[10], Haolan Lu[10], Diane Healey[10], Teresa Kong Sanchez[10], Prabhu Bhagavatheeswaran[10], James Novotny Jr.[10], Brian Lestini[10], Julie Brahmer[11]

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Background: Nivolumab significantly improved OS versus docetaxel in patients with previously treated advanced non-squamous NSCLC (CheckMate 057; NCT01673867). Kaplan–Meier OS curves for nivolumab and docetaxel crossed at ~7 months, suggesting non-proportional hazards between arms. **Methods:** Post-hoc analyses were conducted to explore relationships between baseline patient/disease characteristics, including PD-L1 expression, and death within the first 3 months of treatment (3motx). Additionally, the association between PD-L1 expression level and magnitude of clinical benefit was explored. **Results:** During the first 3motx, risk of death (rDt) was numerically higher with nivolumab versus docetaxel (59 versus 44 deaths among 292 and 290 patients, respectively). Early deaths were most commonly attributed to disease progression (no treatment-related deaths occurred). At 3motx, 80% of nivolumab-treated patients (233/292) and 85% of docetaxel-treated patients (246/290) were alive. After 3motx, the rDt was consistently higher in the docetaxel arm. In univariate analyses, no single baseline factor, including PD-L1 expression, *EGFR* mutation, ECOG PS, or smoking status, reliably characterized the rDt within the first 3motx with nivolumab. Among patients alive >3 months, the OS HR (95% CI) favored nivolumab in the overall population (0.59 [0.47–0.74]) and PD-L1 non-expressors (PD-L1 expression <1%; 0.66 [0.45–0.97]). In a multivariate analysis, factors associated with higher rDt within the first 3motx on nivolumab versus docetaxel were ECOG PS=1, time since last treatment <3 months, and/or progressive disease as best response to prior treatment combined with lower or no PD-L1 expression. However, the majority of nivolumab-treated patients with these attributes (including PD-L1 non-expressors), did not die within the first 3motx and experienced subsequent benefit. PD-L1 expression was a continuum, ranging from 1 to 100%, with increasing expression associated with enhanced ORR/OS benefit from nivolumab. **Conclusion:** In CheckMate 057, the benefit–risk profile of nivolumab versus docetaxel was favorable across the overall patient population. During the first 3motx, a small difference in the number of deaths (n=15) was observed; thereafter the OS rate consistently favored nivolumab (2-year OS was >2-fold higher with nivolumab versus docetaxel). Patients with poorer prognostic factors and/or more aggressive disease combined with lower or no PD-L1 expression appeared to be at higher rDt within the first 3motx on nivolumab versus docetaxel. With the exception of PD-L1 status, these are recognized prognostic factors. While PD-L1 expression may help inform individual treatment decisions, PD-L1 status alone is not considered an appropriate biomarker for nivolumab treatment selection in pre-treated advanced NSCLC, but rather should be considered in the context of other patient/disease characteristics.
Keywords: Nivolumab, non-squamous NSCLC, overall survival, baseline characteristics

SESSION OA04: EPIDEMIOLOGY AND PREVENTION OF LUNG CANCER
MONDAY, DECEMBER 5, 2016 – 11:00-12:30

OA04.05 CHRONIC INFLAMMATION, NSAIDS AND THE RISK OF LUNG CANCER DEATH

Marisa Bittoni[1], David Carbone[2], Randall Harris[3]

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Background: Chronic inflammation appears to heighten the risk of lung cancer and, reciprocally, agents that reduce inflammation have been found to reduce this risk. Nevertheless, few prospective studies have examined associations between lung cancer and the intake of nonsteroidal anti-inflammatory drugs (NSAIDs). In the current study, we examined associations between fatal lung cancer and NSAIDs using prospective data from the Third National Health and Nutrition Examination Study. **Methods:** Baseline data on smoking, NSAIDs and other lifestyle variables were collected for 10,735 participants during 1988-1994, and cause-specific mortality status was ascertained through probabilistic record matching using the National Death Index through 2006. Cox proportional hazards regression models were used to estimate hazard ratios (HRs) to quantify associations between NSAID use and lung cancer death, with adjustment for current smoking and other variables. **Results:** During 18 years of follow-up, 269 individuals died from lung cancer of which 252 (93.6%) reported a history of cigarette smoking. Since all but 17 of the 269 fatal lung cancer cases occurred among current or former smokers, estimates of NSAID effects were ascertained from a sub-cohort of 5,882 individuals who reported a history of past or current cigarette smoking. Multivariate regression models revealed that regular use of ibuprofen reduced the risk of lung cancer death by 48% (HR=0.52, 95% CI=0.33-0.82, P<0.01). Main effects of other compounds tested (aspirin or acetaminophen) were

not statistically significant. **Conclusion:** Prospective data from NHANES III showed that among adults with a history of past or current smoking, ibuprofen intake was associated with a substantial (48%) reduction in the risk of dying from lung cancer. Effects of aspirin and acetaminophen were not statistically significant. These results suggest that regular use of certain NSAIDs may be beneficial for high-risk subgroups of smokers as a lung cancer prevention strategy.
Keywords: lung cancer, inflammation, NSAIDs, smoking

SESSION OA05: TREATMENT ADVANCES IN SCLC MONDAY, DECEMBER 5, 2016 – 11:00-12:30

OA05.01 PEMBROLIZUMAB IN PATIENTS WITH EXTENSIVE-STAGE SMALL CELL LUNG CANCER: UPDATED SURVIVAL RESULTS FROM KEYNOTE-028

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Background: Patients with extensive-stage disease (ED) small cell lung cancer (SCLC) have limited treatment options and poor survival following failure of platinum-based chemotherapy. Pembrolizumab, a humanized anti–programmed death 1 (PD-1) antibody, has demonstrated robust antitumor activity and a favorable safety profile in multiple tumor types. Here, we present updated safety and efficacy data, including survival, for patients with ED SCLC enrolled in the KEYNOTE-028 (ClinicalTrials.gov, NCT02054806) study. **Methods:** KEYNOTE-028 is a nonrandomized, multicohort phase 1b trial of pembrolizumab in patients with PD-L1–positive advanced solid tumors. Patients received pembrolizumab 10 mg/kg every 2 weeks for up to 2 years or until confirmed progression or intolerable toxicity, death, withdrawal of consent, or physician decision. Response was assessed per RECIST v1.1 by investigators every 8 weeks for the first 6 months and every 12 weeks thereafter. The primary end point was objective response rate (ORR; per RECIST v1.1, investigator assessed). Secondary end points included safety, tolerability, progression-free survival (PFS), and overall survival (OS). **Results:** 24 patients with ED SCLC and tumor PD-L1 positivity were enrolled and received ≥1 dose of pembrolizumab. At the data cutoff date (June 9, 2016), median follow-up duration was 9.8 months (range, 0.5-24.0 months); 3 patients (12.5%) remain on treatment. The ORR was 37.5% (95% CI, 18.8%-59.4%), including 1 complete and 8 partial responses in 24 evaluable patients. Median duration of response was 9.0 months (range, 1.9-19.9+ months). Median PFS was 1.9 months (95% CI, 1.7-5.9 months); the 6- and 12-month PFS rates were 29.8% and 24.8%, respectively. Median OS was 9.7 months (95% CI, 4.1 months-not reached); the 6- and 12-month OS rates were 66.0% and 35.7%, respectively. No new safety concerns were noted. Sixteen of 24 (66.7%) patients experienced treatment-related AEs. Two patients experienced grade 3-5 treatment-related AEs: 1 patient had blood bilirubin increased (grade 3) and 1 patient experienced grade 3 asthenia and grade 5 colitis. **Conclusion:** Pembrolizumab demonstrated promising antitumor activity in this pretreated, PD-L1–positive ED SCLC population. The responses were found to be durable and may have led to an OS benefit for the subset of patients who achieved objective responses with pembrolizumab.
Keywords: pembrolizumab, anti–PD-1 antibody, PD-L1, small cell lung cancer