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WCLC 2016 Late Publication Abstracts | Wednesday, December 7, 2016

PLENARY SESSIONS

SESSION PL04A: PLENARY SESSION: IMMUNE CHECKPOINT INHIBITORS IN ADVANCED NSCLC WEDNESDAY, DECEMBER 7, 2016 – 08:45-09:40

PL04A.01 HEALTH-RELATED QUALITY OF LIFE FOR PEMBROLIZUMAB VS CHEMOTHERAPY IN ADVANCED NSCLC WITH PD-L1 TPS ≥50%: DATA FROM KEYNOTE-024

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Background: In KEYNOTE-024 (NCT02142738), pembrolizumab provided superior progression-free survival (PFS) over platinum-based chemotherapy as first-line therapy for patients with advanced non-small cell lung cancer (NSCLC) with PD-L1 expression on ≥50% of tumor cells (ie, PD-L1 tumor proportion score [TPS] ≥50%) and no sensitizing EGFR or ALK aberrations (HR 0.50, P < 0.001). Despite a 44% crossover rate from chemotherapy to pembrolizumab, pembrolizumab also significantly improved overall survival (OS) (HR 0.60, P = 0.005). Any-grade (73% vs 90%) and grade 3-5 (27% vs 53%) treatment-related adverse events were less frequent with pembrolizumab. Health-related quality of life (HRQoL) is an important consideration for anticancer therapy, particularly in the first-line setting. We present data from the prespecified exploratory patient-reported outcomes (PRO) analysis of KEYNOTE-024. **Methods:** 305 patients were randomized to pembrolizumab 200 mg Q3W or investigator-choice platinum-doublet chemotherapy plus optional pemetrexed maintenance therapy for nonsquamous disease. The EORTC QLQ-C30 and QLQ-LC13 were administered at cycles 1-3 and every 9 weeks thereafter. The key PRO end points were change from baseline to week 15 in the QLQ-C30 global health status/QoL score and time to deterioration in the QLQ-LC13 composite of cough, chest pain, and dyspnea. PROs were analyzed for all patients who received study treatment and completed ≥1 PRO instrument (n = 299). **Results:** Across treatment arms, PRO compliance was >90% at baseline and ~80% at week 15. Least squares (LS) mean (95% CI) change from baseline to week 15 in QLQ-C30 global health status/QoL score was 6.95 (3.29 to10.58) for pembrolizumab (n = 151) and –0.88 (–4.78 to 3.02) for chemotherapy (n = 148). The difference in LS means was 7.82 (95% CI 2.85-12.79; nominal 2-sided P = 0.002). The proportion of improved global health status/QoL score at week 15 was 40.0% for pembrolizumab and 26.5% for chemotherapy. Fewer patients in the pembrolizumab arm had deterioration in the QLQ-LC13 composite of cough, dyspnea, and chest pain (30% vs 39%), and time to deterioration was also prolonged with pembrolizumab (HR 0.66, 95% CI 0.44-0.97; nominal 2-sided P = 0.029). **Conclusions:** Pembrolizumab was associated with a clinically meaningful improvement in HRQoL compared with platinum-based chemotherapy. Combined with the superior PFS and OS and manageable safety profile, these data suggest pembrolizumab may be a new standard of care for first-line treatment of PD-L1–expressing advanced NSCLC.

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PL04A.02 OAK, A RANDOMIZED PH III STUDY OF ATEZOLIZUMAB VS DOCETAXEL IN PATIENTS WITH ADVANCED NSCLC: RESULTS FROM SUBGROUP ANALYSES

Shirish Gadgeel[1], Fortunato Ciardiello[2], Achim Rittmeyer[3], Fabrice Barlesi[4], Diego Cortinovis[5], Carlos Barrios[6], Toyoaki Hida[7], Keunchil Park[8], Dariusz Kowalski[9], Manuel Cobo Dols[10], Joseph Leach[11], Jonathan Polikoff[12], Christina Matheny[13], Pei He[13], Marcin Kowanetz[13], Daniel Chen[13], Daniel Waterkamp[13], Marcus Ballinger[13], Alan Sandler[13], David R. Gandara[14], Joachim Von Pawel[15]

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Background: Atezolizumab inhibits PD-L1 binding to its receptors PD-1 and B7.1, thereby restoring tumor-specific T-cell immunity. Primary analysis of the Phase III OAK study in previously-treated NSCLC revealed superior survival for atezolizumab vs docetaxel in the ITT population (mOS, 13.8 vs 9.6 months; HR, 0.73) and in patients expressing ≥1% PD-L1 on TC or IC (TC1/2/3 or IC1/2/3; mOS, 15.7 vs 10.3; HR, 0.74). Here we present further subgroup analyses. **Methods:** OAK evaluated atezolizumab vs docetaxel in an unselected NSCLC population who had failed prior platinum-containing chemotherapy. Patients were stratified by PD-L1 expression, prior chemotherapy regimens and histology, and randomized 1:1 to atezolizumab (1200 mg) or docetaxel (75 mg/m^2) IV q3w. PD-L1 expression by IHC and mRNA was centrally evaluated by VENTANA SP142 IHC assay and Fluidigm, respectively. Data cutoff, July 7, 2016. **Results:** For the first 850 of 1225 randomized patients (primary study population), OS was improved with atezolizumab vs docetaxel regardless of histology and this benefit was observed across PD-L1 subgroups within each histology (Table). PD-L1 gene expression showed a similar association with OS as PD-L1 IHC. In nonsquamous patients ORR was 14.4% vs 15.2%; in squamous patients ORR was 11.6% vs 8.2% (atezolizumab vs docetaxel). OS benefit vs

docetaxel was seen across subgroups including patients with treated baseline brain metastases (n=85; mOS 20.1 vs 11.9 mo; HR 0.54, 95% CI 0.63-0.89) and never smokers (n=156; mOS 16.3 vs 12.6 mo, HR 0.71, 95% CI 0.47-1.08). Further secondary endpoints and exploratory biomarker analyses for these subgroups and by age and *EGFR/KRAS* status will be presented. **Conclusion:** OAK demonstrated clinically relevant improvements with atezolizumab in the ITT population, including in both histology subgroups regardless of PD-L1 expression (measured by IHC or tumor gene expression), and among other subgroups including never smokers and in patients with baseline brain metastases.

	OS				
	Atezolizumab		Docetaxel		HR[a] 95% CI
	n	Median, mo	n	Median, mo	
Nonsquamous					
TC3 or IC3	49	22.5	47	8.7	0.35 (0.21-0.61)
TC2/3 or IC2/3	89	18.7	99	11.3	0.61 (0.42-0.88)
TC1/2/3 or IC1/2/3	171	17.6	162	11.3	0.72 (0.55-0.95)
TC0 and IC0	140	14.0	150	11.2	0.75 (0.57-1.00)
All	313	15.6	315	11.2	0.73 (0.60-0.89)
Squamous					
TC3 or IC3	23	17.5	18	11.6	0.57 (0.27-1.20)
TC2/3 or IC2/3	40	10.4	37	9.7	0.76 (0.45-1.29)
TC1/2/3 or IC1/2/3	70	9.9	60	8.7	0.71 (0.48-1.06)
TC0 and IC0	40	7.6	49	7.1	0.82 (0.51-1.32)
All	112	8.9	110	7.7	0.73 (0.54-0.98)

[a]Unstratified HRs.
TC=tumor cell, IC=tumor-infiltrating immune cell

Keywords: NSCLC, atezolizumab, Immunotherapy

SESSION PL04A: PLENARY SESSION: IMMUNE CHECKPOINT INHIBITORS IN ADVANCED NSCLC
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PL04A.03 DURVALUMAB IN ≥3RD-LINE LOCALLY ADVANCED OR METASTATIC, EGFR/ALK WILD-TYPE NSCLC: RESULTS FROM THE PHASE 2 ATLANTIC STUDY

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Background: Treatment with anti-PD-1/PD-L1 antibodies has demonstrated meaningful clinical benefit in patients with advanced NSCLC. Patients that progress after 2 lines of chemotherapy have few treatment options and poor outcomes. Durvalumab is an engineered human IgG1 mAb targeting programmed cell death ligand-1 (PD-L1). **Methods:** ATLANTIC (NCT02087423) is a Phase 2, open-label, single-arm trial in patients with locally advanced or metastatic Stage IIIB–IV NSCLC (WHO PS 0 or 1; ≥2 prior systemic treatment regimens, including one platinum-based). There was no maximum number of prior treatments. The study initially enrolled all-comers and then was restricted to patients with PD-L1 high tumours (≥25% of tumour cells with membrane staining). The study includes three cohorts; here we report final results in Cohorts 2 and 3 that had *EGFR/ALK* wild-type or unknown status. Patients enrolled in Cohort 3 had ≥90% of tumour cells with PD-L1 staining. The primary endpoint is ORR (RECIST v1.1), based on independent central review. Secondary endpoints include DCR, DoR, PFS, OS, and safety (CTCAE v4.03). **Results:** As of 3 June 2016, in Cohorts 2/3, 265/68 patients (median age 62/61 years, 67/72% PS 1, 21/29% squamous histology; mean of 3.2/2.6 prior therapies) had received durvalumab (10 mg/kg i.v. q2w). Responses were durable; in Cohort 2, patients with PD-L1 ≥25%, the ORR was similar in patients with squamous and non-squamous histology.

	Cohort 2		Cohort 3
	PD-L1 high (≥25%)	PD-L1 low/ negative (<25%)	PD-L1 ≥90%
	n=146	n=93	n=68
ORR,* % (95%CI)	16.4 (10.8-23.5)	7.5 (3.1-14.9)	30.9 (20.2-43.3)
DCR, % (95%CI)	28.8 (21.6-36.8)	20.4 (12.8-30.1)	38.2 (26.7-50.8)
mDoR, months (25^{th}, 75^{th} percentile)	12.3 (7.5-NR)	NR (7.2-NR)	NR; 18/21 responders progression free at DCO
	n=149	n=94	n=67
mPFS, months (95%CI)	3.3 (1.9-3.7)	1.9 (1.8-1.9)	2.4 (1.8-5.5)
mOS, months (95%CI)	10.9 (8.6-13.6)	9.3 (5.9-10.8)	NR (5.9-NC)
1-year OS, % (95%CI)	47.7 (39.3-55.5)	34.5 (25.0-44.1)	50.8 (36.9-63.2)
mFollow-up for OS, months	9.4	9.3	7.0

*Confirmed response per independent central review. DCO=data cutoff; DCR=disease control rate (complete response, partial response or stable disease ≥24 weeks); DoR=duration of response; m=median; NC=not calculated; NR=not reached; ORR=objective response rate; OS=overall survival; PFS=progression-free survival

Most AEs were low grade and resolved with treatment delay and/or immunosuppressive interventions. Overall, 10.2% of patients had Grade ≥3 treatment-related AEs and 2.7% had treatment-related AEs leading to discontinuation. **Conclusion:** Durvalumab was active and led to durable responses in a heavily pretreated metastatic NSCLC population; activity was numerically greater for patients whose tumours exceeded the 25% PD-L1 cutoff. The tolerability profile was manageable. Results are consistent with other anti-PD-1/PD-L1 therapies in metastatic, relapsed NSCLC and support further development of durvalumab.
Keywords: durvalumab, Checkpoint blockade, Immunotherapy, MEDI4736

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PL04A.04 MULTICENTRIC FRENCH HARMONIZATION STUDY FOR PD-L1 IHC TESTING IN NSCLC

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Background: PD-L1 immunohistochemistry (IHC) is considered as a predictive biomarker for most anti PD-1/PDL-1 therapies in non-small cell lung cancer, but different assays were used in clinical trials. Several studies have compared 4 assays (22C3, 28-8, SP142, SP263) performed in central laboratories on dedicated platforms. In order to harmonise and make PD-L1 testing widely available on most IHC platforms and centers, we compared PD-L1 Dako (22C3, 28-8) and Ventana (SP263) assays and laboratory-developed tests

(LDT). **Methods:** IHC with five anti-PD-L1 clones (28-8, 22C3, E1L3N, SP142 and SP263) was performed concomitantly on 41 NSCLC surgical specimens in 7 centers. The IHC platforms used were Ventana BenchMark Ultra (2 centers), Leica Bond (2 centers) or Dako Autostainer Link 48 (3 centers). For each matching platform, 22C3, 28.8 and SP263 assays were performed. For non-matching platforms and other antibodies, LDT were developed in each center and harmonised based on tonsil tissue staining. A total of 35 stainings were performed across different platforms and antibodies for each case. Seven thoracic pathologists trained to PD-L1 scoring in expert courses participated. Each pathologist analysed 6 cases and compared the stainings obtained with the 5 antibodies on all platforms. Tumor cell and immune cell D-L1 stainings were scored semi-quantitatively as recommended in PD-L1 Dako and Ventana assays. For statistical analysis, 1, 5, 25, 50% and 1, 5, 10% thresholds were used for tumor cells and immune cells, respectively. **Results:** 28-8, 22C3 and SP263 assays were highly concordant for tumor cell and immune cell stainings across the 5 Dako or Ventana platforms (R2=0.886 to 0.953). LDT demonstrated various levels of concordance as compared to those 3 assays. Notably, LDT using SP263 clone were the most concordant across all platforms for both immune cell and tumor cell stainings, whereas some selected LDT with clones 28-8, 22C3 and E1L3N, but not SP142, showed a good correlation with the 3 assays regarding tumor cells only. **Conclusion:** 28-8, 22C3 and SP263 assays gave comparable results across dedicated platforms for tumor cells staining, as well as some selected LDT protocols using 28-8, 22C3, SP263 and E1L3N clones. These results will be further validated at the national level in order to provide recommendations for the use of assays and LDT for PD-L1 testing in NSCLC.

Keywords: harmonization, Immunohistochemistry, LDT, PD-L1 testing