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327P Three years survival outcome and continued cemiplimab (CEMI) beyond progression with the addition of chemotherapy (chemo) for patients (pts) with advanced non-small cell lung cancer (NSCLC): The EMPOWER-lung 1 trial

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Background: In the EMPOWER-Lung 1 trial, CEMI monotherapy provided a significantly improved overall survival (OS) and an acceptable safety profile vs chemo in pts with newly diagnosed advanced NSCLC. We are reporting the 3-year survival data of the trial. Also, we are presenting the first efficacy data of pts who continued CEMI at progression (PD) with the addition of histology-specific chemo.

Methods: Pts were randomized 1:1 to CEMI 350 mg IV every 3 weeks for 2 years or investigator's choice of chemo. Pts randomized to CEMI with PD, confirmed by a blinded independent review committee (BIRC), were allowed to continue CEMI with the addition of up to 4 cycles of chemo. To be included in the post PD analysis, pts had to receive at least one dose of chemo and have at least one scan following PD on CEMI. Response to continued CEMI + chemo was assessed by BIRC against a new baseline, defined as the last scan prior to the initial dose of chemo.

Results: At median follow-up of 37.1 months (m; range: 24.0 : 56.5), median OS (mOS) was 23.4 m (19.4, 27.4) for CEMI pts (N=357) vs 13.7 m (11.2, 16.2) for chemo pts (N=355), with hazard ratio (HR) of 0.634 (0.524, 0.768); median progression free survival (mPFS) was 6.3 m (4.6, 8.3) vs 5.3 m (4.3, 6.0), HR 0.560 (0.470, 0.666). 64 pts continued CEMI + chemo as 2L therapy. Continued CEMI + chemo as 2L therapy resulted in a 31.3% objective response rate and a mOS of 15.1 m (11.3, 18.7), and was generally tolerated, with 19 pts (29.7%) experiencing serious treatment-emergent adverse event (TEAE), and 3 pts each with TEAE resulting in discontinuation of study treatment or death.

Conclusions: At 3 year follow-up, HRs of CEMI vs. chemo improved (vs at 13 m follow-up) for both PFS and OS despite 76% crossover rate, an exceptional finding in the NSCLC field. Continued CEMI + chemo as 2L therapy provided meaningful and durable ORR and OS benefits and these results compare favorably to historical data of pts receiving chemo alone as 2L therapy (after immune-checkpoint inhibitor monotherapy). This data is the first report from a Phase 3 study providing therapeutic advantage to pts who progress after 1L PD1 monotherapy.

Clinical trial identification: NCT03088540.

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328P Long-term follow-up of pembrolizumab plus chemotherapy in Chinese patients with metastatic squamous non-small cell lung cancer (NSCLC) from KEYNOTE-407

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Background: First-line pembrolizumab (pembro) + paclitaxel and carboplatin (chemo) improved outcomes vs placebo (pbo) + chemo in Chinese patients (pts) with metastatic squamous NSCLC enrolled in the KEYNOTE-407 global and China extension studies, consistent with the global study population. We report long-term outcomes in Chinese pts from these studies.

Methods: Eligible pts in both the phase 3, double-blind KEYNOTE-407 global (NCT02775435) and China extension (NCT03875092) studies were randomized 1:1 to pembro 200 mg or pbo Q3W for up to 35 cycles (~2 y) + 4 cycles of chemo. Eligible pts in the pbo + chemo group could cross over to pembro monotherapy upon PD. Primary endpoints were OS and PFS per RECIST v1.1 by BICR. No alpha was allocated to this analysis.

Results: 125 pts from mainland China were randomized to pembro + chemo (n = 65) or pbo + chemo (n = 60). Median time from randomization to data cutoff (February 23, 2022) was 44.9 (range, 41.9–57.7) mo. 38 pts from the pbo + chemo group crossed over to pembro on-study; 1 additional pt received subsequent anti–PD-(L)1 therapy off-study for an effective crossover rate of 65.0%. The HR for OS was 0.41 (95% CI, 0.27–0.63), with 3-y OS rates of 46.2% for pembro + chemo vs 16.7% for pbo + chemo; additional efficacy data are in the table. Grade 3–5 treatment-related AEs occurred in 53 (81.5%) vs 49 pts (81.7%), with no new grade 5 AEs since previous follow-up. In 19 pts who completed 35 cycles of pembro, ORR was 89.5%, median OS from the time of completing 35 cycles was not reached, and 2-y OS rate after completing 35 cycles (~4 y after randomization) was 89.2%.

Table: 328P

ITT Population	Pembrolizumab + Chemotherapy n = 65	Placebo + Chemotherapy n = 60
Median OS (95% CI), mo	29.6 (18.2–NE)	12.7 (9.4–17.3)
OS HR (95% CI)	0.41 (0.27–0.63)	
3-y OS rate, %	46.2	16.7
Median PFS[a] (95% CI), mo	8.3 (6.2–10.5)	4.2 (4.0–5.4)
PFS[a] HR (95% CI)	0.36 (0.25–0.54)	
3-y PFS[a] rate, %	15.1	0
ORR[a] (95% CI), %	78.5 (66.5–87.7)	43.3 (30.6–56.8)
Median DOR[a] (range), mo	7.1 (1.7+ to 46.2+)	3.5 (2.4–9.0)
DOR ≥3 y, %	19.7	0

BICR, blinded independent central review; NE, not estimable. "+" indicates no PD by time of last assessment. [a]Assessed per RECIST v1.1 by BICR.

Conclusions: Pembro + chemo maintained improvement in OS and PFS with manageable safety after longer follow-up in Chinese pts in KEYNOTE-407, consistent with the global study population. OS was prolonged in pts who completed 35 cycles of pembro. These data support first-line pembro + chemo as SOC in pts with metastatic squamous NSCLC.

Clinical trial identification: NCT02775435, NCT03875092.

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329P ORCHARD: Osimertinib + necitumumab in patients (pts) with advanced NSCLC whose disease progressed on first-line (1L) osimertinib

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Background: Osimertinib is a 3rd generation, irreversible, epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor (TKI) with CNS activity; it is the preferred 1L treatment in pts with EGFR-TKI-sensitising (EGFRm) advanced NSCLC. However, pts on 1L osimertinib may develop treatment resistance, commonly by secondary EGFR alterations. The ongoing Phase II ORCHARD platform study (NCT03944772) aims to characterise these resistance mechanisms and identify novel 2L combinations. Preclinical data demonstrated antitumour activity when combining osimertinib with an anti-EGFR monoclonal antibody (mAb). Here we report an interim analysis of safety and efficacy of osimertinib + necitumumab, a mAb that blocks the ligand binding site of EGFR, in pts with EGFRm advanced NSCLC and a secondary EGFR alteration post 1L osimertinib.

Methods: Pts with a secondary alteration in EGFR (amplification, L718 or G724 mutation, exon 20 insertion) determined by next generation sequencing on tissue collected post disease progression on 1L osimertinib, received osimertinib (80 mg, orally, once daily) + necitumumab (800 mg intravenously on Day 1 + 8 of a 3-week cycle). Primary endpoint: objective response rate (ORR); other endpoints: safety. Futility criterion was defined as <10% chance ORR is ≥45%. Data cutoff (DCO): 11 Feb 2022.

Results: Sixteen pts were treated (56% ≥65 years, 63% male, 63% white, 61% never smokers). At DCO, 11 pts (69%) had discontinued treatment and 13 were evaluable for confirmed response. ORR was 15% (n=2 confirmed partial responses, 80% CI 4.2, 36.0). Stable disease was reported in 5 pts (39%) and progressive disease in 5 pts (39%); 1 pt (8%) was non-evaluable. Recruitment was closed as futility criteria were met. Overall, 7/16 (44%) had one or more Grade ≥3 adverse event (AE); 5 (31%) had serious AEs, 2 (13%) had an AE with an outcome of death, 1 was possibly related to necitumumab. No cases of interstitial lung disease seen.

Conclusions: Osimertinib + necitumumab showed no new safety signals in this population; however, futility criterion was met and recruitment was closed. These results suggest that this combination may not have the requisite clinical activity for further clinical development in this pt population.

Clinical trial identification: NCT03944772.

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