378MO EMPOWER-Lung 1: Phase III first-line (1L) cemiplimab monotherapy vs platinum-doublet chemotherapy (chemo) in advanced non-small cell lung cancer (NSCLC) with programmed cell death-ligand 1 (PD-L1) ≥50%

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Background: EMPOWER-Lung 1 is a multicentre, open-label, global, phase III study of cemiplimab, an anti–PD-1, in patients (pts) with treatment-naïve stage IIIB, IIIC or IV squamous or non-squamous NSCLC with PD-L1 expressed in ≥50% of tumour cells.

Methods: Pts were randomised 1:1 to receive cemiplimab 350 mg Q3W IV or investigator's choice of chemo. Crossover (CO) from chemo to cemiplimab was allowed following progression. The primary endpoints were overall survival (OS) and progression-free survival (PFS) per blinded Independent Review Committee. A pre-specified interim analysis was performed after 50% of OS events. Data are presented per intention-to-treat (ITT) and in a PD-L1 ≥50% ITT population which comprised only pts with PD-L1 ≥50% by 22C3 per instruction for use (after recommended retesting in some pts). Data cut-off was 1 March 2020.

Results: In the ITT population (median follow-up: 13.1 months), median OS was 22.1 months (95% CI: 17.7—not evaluable [NE]) with cemiplimab (n=356) vs 14.3 months (95% CI: 11.7—19.2) with chemo (n=354; HR, 0.68; 95% CI: 0.53—0.87; P=0.002). Median PFS was 6.2 months (95% CI: 4.5—8.3) with cemiplimab vs 5.6 months (95% CI: 4.5—6.1) with chemo (HR, 0.59; 95% CI: 0.49—0.72; P<0.0001). In the PD-L1 ≥50% ITT population (median follow-up: 10.8 months), median OS was not reached (95% CI: 17.9—NE) with cemiplimab (n=283) vs 14.2 months (95% CI: 11.2—17.5) with chemo (n=280; HR, 0.57; 95% CI: 0.42—0.77; P=0.0002). Median PFS was 8.2 months (95% CI: 6.1—8.8) with cemiplimab vs 5.7 months (95% CI: 4.5—6.2) with chemo (HR, 0.54; 95% CI: 0.43—0.68; P<0.0001). CO rate to cemiplimab was 73.9%. In the ITT population, cemiplimab was associated with higher response rate (36.5% vs 20.6%), longer median duration of response (21.0 months vs 6.0 months) and lower rates of Grade ≥3 adverse events regardless of attribution (37.2% vs 48.5%) compared to chemo.

Conclusions: In this study, 1L cemiplimab monotherapy significantly improved OS and PFS vs chemo in pts with advanced NSCLC with PD-L1 ≥50%, despite high CO rate, providing rationale for cemiplimab as a new treatment option for this patient population.

Clinical trial identification: NCT03088540.

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379MO Durvalumab (D) ± tremelimumab (T) + platinum-etoposide (EP) in 1L ES-SCLC: Characterization of long-term clinical benefit and tumour mutational burden (TMB) in CASPIAN

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Background: In the phase III CASPIAN trial, 1L D+EP significantly improved OS vs EP (HR 0.73 [95% CI 0.59–0.91; p=0.0047]) in pts with ES-SCLC, with sustained benefit after >2 yr median follow-up (HR 0.75 [95% CI 0.62–0.91; nominal p=0.0032]). Landmark analyses indicated 22% of pts were alive at 24m with the addition of D±T to EP. Here we assess the clinical characteristics and outcomes of pts deriving long-term benefit, as well as the relationship between TMB and efficacy outcomes in the ITT population.

Methods: 805 pts with ES-SCLC were randomised 1:1:1 to D+EP, D+T+EP, or EP. Exploratory subgroup analyses defined long-term clinical benefit as PFS ≥12m. Tumour tissue was mandated at screening, if available. TMB was assessed in tissue (tTMB) using the FoundationOne CDx platform.

Results: 45 (17%), 42 (16%), and 12 (5%) pts treated with D+EP, D+T+EP, and EP had PFS ≥12m, respectively (data cutoff 27 Jan 2020). In all arms, the PFS ≥12m subgroup had a higher incidence of favorable prognostic factors (more women and pts with PS 0, fewer pts with brain/liver metastases). In the D+EP arm, pts with PFS ≥12m received more D (median 25 vs 7 cycles) and had improved ORR (96% vs 63%), median DoR (NR vs 4m) and OS at 24m (77% vs 11%) compared with the PFS <12m subgroup (Table). Similar results were observed with EP and when both IO arms were combined. Safety and additional efficacy outcomes in the subgroups will be presented. Across all 3 arms, 283 pts (35% of ITT) were evaluable for tTMB. tTMB was not predictive of a differential treatment effect for D±T+EP vs EP (OS, PFS, or ORR).

Table: 379MO

	D+EP		IO arms combined	
	PFS ≥12m n=45	PFS <12m n=220	PFS ≥12m n=87	PFS <12m n=444
Ongoing durvalumab at DCO, n (%)	27 (60)	5 (2)	50 (57)	12 (3)
Durvalumab cycles, median (range)	25 (6—37)	7 (1—28)	25 (2—37)	6 (1—33)
Male, %	60	73	63	75
Never / ever smoker, %	9 / 91	8 / 92	9 / 91	7 / 93
PS 0 / 1, %	47 / 53	35 / 65	48 / 52	36 / 64
Brain mets, %	7	11	3	14
Liver mets, %	20	44	23	46
ORR, n/N (%)	43/45 (96)	139/220 (63)	82/87 (94)	256/443 (58)
Median DoR, m (95% CI)	NR (18—NE)	4 (3.5—5)	NR (24—NE)	4 (4—5)
OS at 24m, % (95% CI)	77 (61—87)	11 (7—16)	82 (72—89)	11 (8—14)