Cemiplimab monotherapy for first line advanced NSCLC patients with PD-L1 expression ≥50%: 5-year outcomes of EMPOWER-Lung 1

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Background

- Previous data from the EMPOWER-Lung 1 study demonstrated a significant survival benefit for first-line cemiplimab monotherapy versus chemotherapy in patients with advanced non-small cell lung cancer (NSCLC) and programmed cell death-ligand 1 (PD-L1) expression ≥50%[1,2]

Objectives

- Here, we report the protocol pre-specified final overall survival (OS) and progression-free survival (PFS) analyses with 5-year follow-up.
- We also report outcomes of patients who continued cemiplimab at disease progression with the addition of chemotherapy.

Conclusions

- **At 5-year follow-up**
  - Cemiplimab monotherapy continued to show durable OS and PFS benefits versus chemotherapy in patients with advanced NSCLC with PD-L1 ≥50%.
  - Cemiplimab benefits increased with PD-L1 expression levels; patients with PD-L1 ≥90% derived the largest clinical benefits.
- **Addition of chemotherapy beyond progression**
  - The addition of chemotherapy to cemiplimab monotherapy beyond progression demonstrated meaningful clinical benefits (objective response rate [ORR], PFS, and OS), potentially providing a new treatment option for patients who progressed on first-line cemiplimab monotherapy.
  - These results increase our understanding of potential treatment strategy beyond progression for patients receiving first-line cemiplimab monotherapy for advanced metastatic NSCLC with PD-L1 ≥50%.

References

1. Sezer A, et al. *Lancet*. 2021;397:592–604.
2. Özgüroğlu M, et al. *Lancet Oncol*. 2023;24:989–1001.

Acknowledgements

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Scan the QR code for the **Supplementary Appendix**

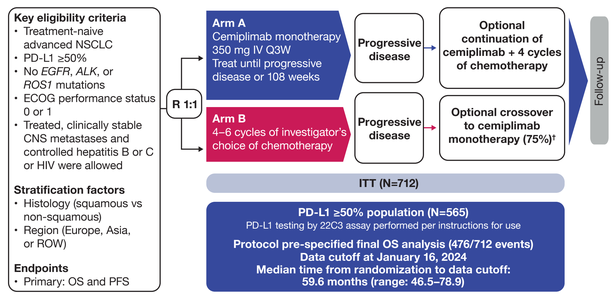
Disclosures

Saadettin Kilickap declares no conflicts of interest. Co-author disclosures are available via the QR code.

Methods

- EMPOWER-Lung 1 was a multicenter, open-label, randomized, phase 3 study of cemiplimab in patients with treatment-naive squamous or non-squamous NSCLC with PD-L1 expression in ≥50% of tumor cells (**Figure 1**).

Figure 1. EMPOWER-Lung 1 study design



†Crossover occurred in 75% of patients who had progressive disease in the cemiplimab arm.
ALK, anaplastic lymphoma kinase; CNS, central nervous system; ECOG, Eastern Cooperative Oncology Group; *EGFR*, epidermal growth factor receptor; HIV, human immunodeficiency virus; ITT, intention-to-treat; IV, intravenous; NSCLC, non-small cell lung cancer; OS, overall survival; PD-L1, programmed cell death-ligand 1; PFS, progression-free survival; Q3W, every 3 weeks; R, randomized; *ROS1*, c-ros oncogene 1; ROW, rest of the world.

- Patients were randomized 1:1 to cemiplimab (350 mg every 3 weeks for 2 years) or investigator's choice of chemotherapy.
- Primary endpoints were OS and PFS per blinded independent review committee (BIRC).
- For the post-progression analysis, response was assessed per BIRC against the last scan prior to the initial dose of chemotherapy.

Results

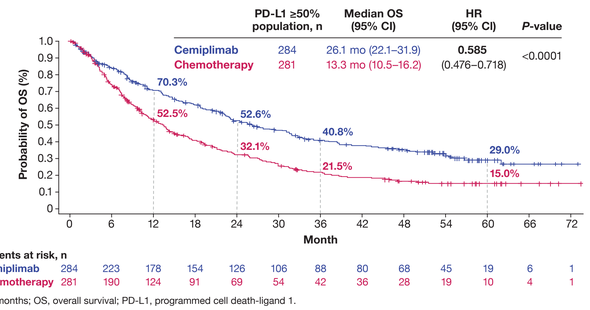
- Of 712 randomized patients, 565 had verified PD-L1 ≥50% (cemiplimab, n=284; chemotherapy, n=281). Median follow-up in this population was 57.3 months (range: 46.5–78.4).

Efficacy

5-year results

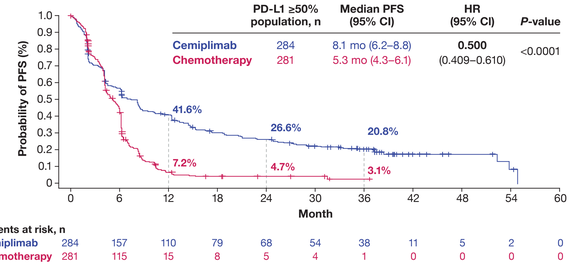
- Cemiplimab showed continued clinical benefits at 5 years (**Supplemental Table 1**).
- OS and PFS data at 5 years are shown in **Figures 2 and 3**.
- The OS and PFS in key subgroups were consistent with previous findings, and all estimates were in favor of cemiplimab (**Supplemental Figure 1**).
- ORR was 46.5% (95% CI: 40.6–52.5) for cemiplimab versus 20.6% (95% CI: 16.1–25.8) for chemotherapy. The median duration of response was 24.1 months for cemiplimab and 5.9 months for chemotherapy (**Supplemental Figure 2**).

Figure 2. Kaplan-Meier curves for OS through 5 years



mo, months; OS, overall survival; PD-L1, programmed cell death-ligand 1.

Figure 3. Kaplan-Meier curves for PFS through 5 years

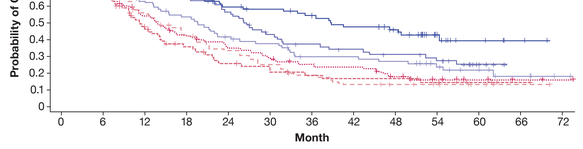


mo, months; PD-L1, programmed cell death-ligand 1; PFS, progression-free survival.

PD-L1 expression

- Improved cemiplimab activity was observed in patients with PD-L1 ≥90% (**Figure 4**).
- The 5-year OS probability for patients with PD-L1 ≥90% was 39.8%. Median PFS for these patients was 14.7 months (**Supplemental Table 2**) and the ORR (95% CI) was 60.6% (50.3–70.3) (**Supplemental Figure 3**).

Figure 4. Kaplan-Meier curves for OS with increasing PD-L1 expression



mo, months; OS, overall survival; PD-L1, programmed cell death-ligand 1.

Safety

- The safety profile at 5 years of either intervention was consistent with previous results.
- Grade ≥3 treatment-emergent adverse events (TEAEs) occurred in 45.8% (cemiplimab) and 51.6% (chemotherapy) of patients (**Table 1**).
- TEAEs occurring in ≥10% of patients in either arm are shown in **Supplemental Figure 4**.

Table 1. Cemiplimab safety profile

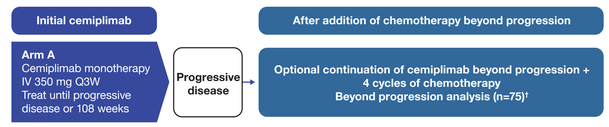
	Cemiplimab (n=356)		Chemotherapy (n=343)	
Duration of exposure, weeks, median (range)	36.0 (0.3–136.0)		18.0 (0.6–141.1)	
	Any grade	**Grade 3–5**	**Any grade**	**Grade 3–5**
TEAEs, regardless of attribution, n (%)				
Overall	330 (92.7)	163 (45.8)	329 (95.9)	177 (51.6)
Led to discontinuation	32 (9.0)	20 (5.6)	17 (5.0)	10 (2.9)
Led to death	36 (10.1)	36 (10.1)	33 (9.6)	33 (9.6)
Treatment-related TEAEs, n (%)				
Overall	224 (62.9)	65 (18.3)	310 (90.4)	137 (39.9)
Led to discontinuation	26 (7.3)	15 (4.2)	15 (4.4)	10 (2.9)
Led to death	10 (2.8)	10 (2.8)	7 (2.0)	7 (2.0)
Sponsor-identified immune-related TEAEs, n (%)				
Overall	83 (23.3)	17 (4.8)	12 (3.5)	2 (0.6)
Led to discontinuation	16 (4.5)	9 (2.5)	0	0
Led to death†	2 (0.6)	2 (0.6)	0	0

†Cause of death due to nephritis and myocarditis.
Adverse events are reported for all patients who received either intervention (safety analysis set). All events are listed as shown in the study safety report; hence, some events might reflect the same condition.
TEAEs, treatment-emergent adverse events.

Post-progression analysis

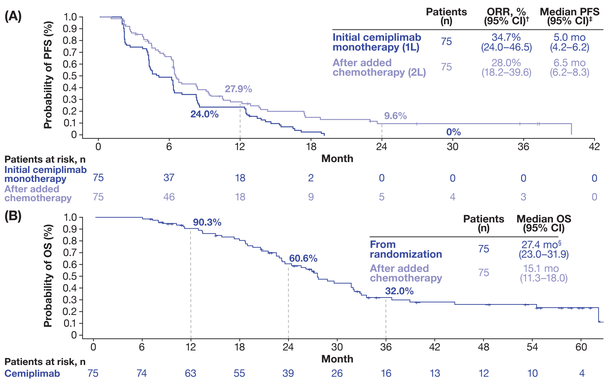
- Patients who progressed after cemiplimab monotherapy had the option to continue with the addition of four cycles of chemotherapy (n=75) (**Figure 5**). Demographics were similar to those receiving cemiplimab in the overall population (**Supplemental Table 3**).
- ORR, PFS, and OS data for this patient population at 5 years are shown in **Figure 6A** and **6B**.

Figure 5. Adding chemotherapy to cemiplimab beyond progression



†Patients included received ≥1 dose of chemotherapy and had ≥1 scan following progressive disease on cemiplimab; 1 patient did not have confirmed progressive disease.
IV, intravenous; Q3W, every 3 weeks.

Figure 6. A) ORR and PFS and B) OS with cemiplimab + chemotherapy beyond progression



†The tumor response during the period after added chemotherapy was assessed by BIRC against a new baseline, defined as the last scan prior to the initial dose of chemotherapy. PFS is defined as the time from randomization (for initial cemiplimab monotherapy) or from the new baseline (for the period after added chemotherapy) to the date of the first documented tumor progression or death due to any cause.
‡Includes median OS of 15.1 months after added chemotherapy.
BIRC, blinded independent review committee; mo, months; ORR, objective response rate; OS, overall survival; PFS, progression-free survival.

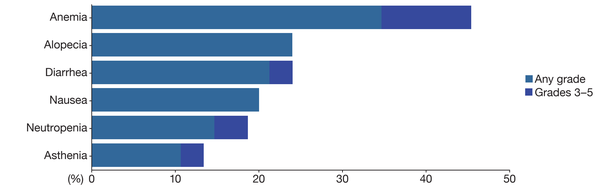
- Combination treatment with cemiplimab plus chemotherapy was generally well tolerated, with 27 patients (36.0%) experiencing grade ≥3 TEAEs (**Table 2**, **Figure 7**).

Table 2. TEAEs after adding chemotherapy to cemiplimab beyond progression

	After added chemotherapy (n=75)	
Duration of cemiplimab exposure, weeks, median (range)	26.7 (3.0–117.7)	
	Any grade	**Grade 3–5**
TEAEs, regardless of attribution, n (%)		
Overall	329 (95.9)	177 (51.6)
Led to discontinuation	17 (5.0)	10 (2.9)
Led to death	0	0

TEAE, treatment-emergent adverse event.

Figure 7. TEAEs in ≥10% of patients



TEAE, treatment-emergent adverse event.

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