Cost-effectiveness of cemiplimab plus chemotherapy versus pembrolizumab plus chemotherapy as the first-line treatment for advanced non-small cell lung cancer

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BACKGROUND

- Lung cancer is the leading cause of cancer death in the U.S., comprising about 1 in 5 of all cancer deaths.[1] Non-small cell lung cancer (NSCLC) accounts for 85% of lung cancer cases, with approximately 70% of patients diagnosed at an advanced or metastatic stage.[2,3]
- Immunotherapy has notably improved survival for advanced NSCLC patients, yet its high treatment costs pose significant financial burdens on both patients and the healthcare system.[4-6]
- Pembrolizumab, as a programmed cell death protein 1 (PD-1) receptor inhibitor, combined with chemotherapy (PEM-CHEM), has been considered the preferred first-line treatment for advanced NSCLC patients from a U.S. healthcare perspective.[7]
- Cemiplimab, as a new generation of PD-1 inhibitor, combined with chemotherapy (CEM-CHEM) is a new treatment for advanced NSCLC.

OBJECTIVE

To evaluate the cost-effectiveness of CEM-CHEM versus PEM-CHEM as the first-line treatment for patients with advanced NSCLC from a U.S. healthcare payer perspective.

METHODS

Model Structure

- From the healthcare payer perspective, we constructed a partition survival model (PSA) to simulate costs, quality of life, toxic effects, disease progression, and survival for advanced NSCLC patients treated with CEM-CHEM and with PEM-CHEM (Figure 1). We utilized monthly time units and a 10-year overall time horizon.

Figure 1: Partition survival model

PFS: progression-free survival PD: processed disease

Survival and Cost Inputs

- The overall survival (OS) and PFS transformed probabilities for patients treated with CEM-CHEM and PEM-CHEM were derived from EMPOWER-Lung 3, KEYNOTE-407, and KEYNOTE-189 trials, respectively.[8-10] Kaplan-Meier (KM) survival curves were extracted and modeled with best-fitted parametric models among exponential, Weibull, Gamma, Gompertz, log-logistic, and log-normal distributions.

Figure 2: Fitted PFS model

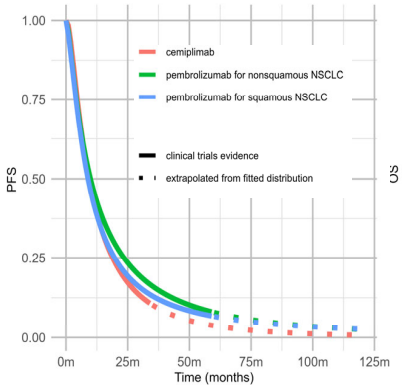
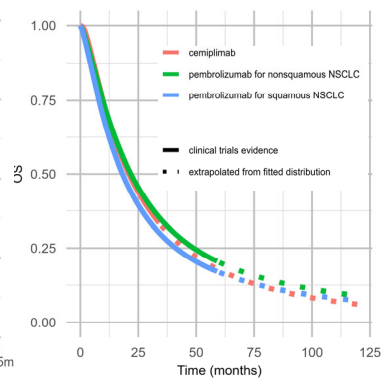


Figure 3: Fitted OS model



- The direct medical expenses, including costs of therapeutic drugs, intravenous injection administration, follow-up care, managing severe adverse events (AEs), and death-related expenses, were obtained from the literature.[11-17]
- The weighted average of cost and disutility associated with grade ≥ 3 AEs with more than 5% incidence in updated clinical trial reports were calculated and inputted in the PSA model.

Table 1: Associated costs and disutility of adverse events

Adverse Event	Probability[8-10]	Disutility[18-20]	Cost in 2024 USD[21,22]
CEM-CHEM			
Anemia	0.109	-0.073	26104
Neutropenia	0.064	-0.35	22137
PEM-CHEM (Nonsquamous)			
Anemia	0.19	-0.073	26104
Diarrhea	0.052	-0.22	21272
Asthenia	0.067	-0.29	1195
Neutropenia	0.168	-0.35	22137
PEM-CHEM (Squamous)			
Anemia	0.158	-0.073	26104
Thrombocytopenia	0.083	-0.108	29245
Neutropenia	0.23	-0.35	22137
Weighted Average			
CEM-CHEM		0.0304	4262
PEM-CHEM*		0.122	10880

*: Squamous and non-squamous NSCLC are weighted as 0.429 and 0.571 (same histology distribution in EMPOWER-Lung 3 trial for CEM-CHEM)

Analysis

- Total costs and total quality-adjusted life-years (QALYs) gained of CEM-CHEM and PEM-CHEM, and incremental cost-effectiveness ratio (ICER) were calculated.
- In scenario analysis 1, the incidence of severe AEs for PEM-CHEM and CEM-CHEM were derived in the same follow-up period in three trials.[23,24] In scenario analysis 2, the extrapolated OS curve after 60 months using real-world advanced NSCLC survival rates from the U.S. Surveillance, Epidemiology, and End Results (SEER) dataset were also used to test the uncertainties of the results.[25]
- One-way deterministic sensitivity analysis of cost, health utilities, and severe AEs-related disabilities, and probabilistic sensitivity analysis with 10,000 simulations were performed.

RESULTS

- The base-case and sensitivity analyses consistently showed that CEM-CHEM was a dominant alternative, compared to PEM-CHEM (Table 1).

Table 1: Base-case and scenario sensitivity analyses results

	Treatment	Total cost ($)	Total QALYs	Incremental cost ($)	Incremental QALY	ICER ($/QALY)
Base-case	PEM-CHEM	232,843	1.709	—	—	—
	CEM-CHEM	202,167	1.728	-30,676	0.018	-1,694,882
scenario 1	PEM-CHEM	237,170	1.713	—	—	—
	CEM-CHEM	202,167	1.727	-30,521	0.014	-2,188,250
scenario 2	PEM-CHEM	230,947	1.693	—	—	—
	CEM-CHEM	201,863	1.725	-29,084	0.032	-910,013

RESULTS

- One-way deterministic sensitivity analysis showed that the disutility of AEs for PEM-CHEM, the cost of PEM and CEM, and the utility in PFS stage significantly influenced ICER results (Figure 4).

Figure 4: Tornado diagram of one-way sensitivity analyses

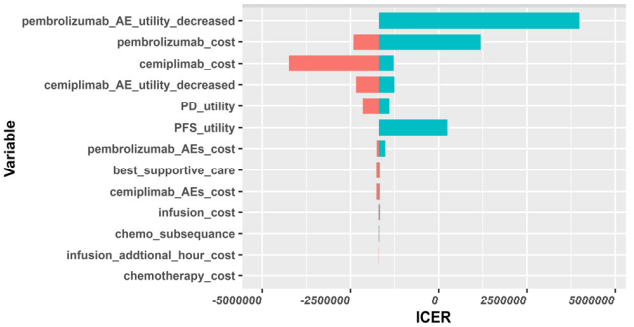
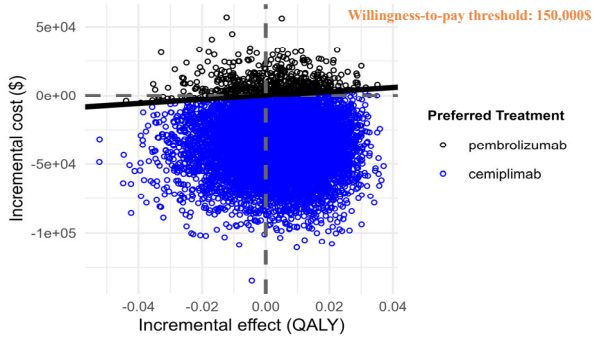


Figure 5: The probabilistic sensitivity analysis scatter plot



DISCUSSION

- Our study showed that using a CEM-CHEM regimen would result in lower costs and more QALY gained than using a PEM-CHEM regimen as a first-line treatment for patients with advanced NSCLC in the U.S.
- Additionally, the greater QALYs gained with CEM-CHEM were primarily due to its better safety profile, as fewer severe AEs were observed in clinical trials.
- However, the uncertainties of the results due to the disutility of AEs for PEM-CHEM, the costs of PEM and CEM, and the utility in the PFS stage should be further examined.

CONCLUSION

- Based on the CEA results, CEM-CHEM is a dominant treatment regimen, compared to PEM-CHEM for patients with advanced NSCLC from a U.S. healthcare perspective.

REFERENCE AND SUPPLIMENTAL MATERIALS