

Cost-effectiveness analysis of PD-L1 testing associated with Pembrolizumab for the treatment of advanced NSCLC in China

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1. Introduction

Lung cancer is the leading cause of cancer-related deaths in China, and pembrolizumab has significantly improved clinical outcomes in advanced non-small cell lung cancer (NSCLC). Pembrolizumab is approved in advanced NSCLC as monotherapy for patients with PD-L1 TPS $\geq 1\%$ and in combination with chemotherapy for patients regardless of PD-L1 expression. Due to high costs and availability of several treatment options in the first-line setting, it is important to identify cost-effective treatment strategies. Therefore, this cost-effectiveness analysis aimed to assess the value of PD-L1 testing associated with pembrolizumab for the treatment of advanced NSCLC in China.

2. Methods

A cost-effectiveness analysis was performed by constructing a three-state partitioned survival model to compare pembrolizumab treatment strategies for advanced NSCLC, with or without PD-L1 testing, from the perspective of the Chinese healthcare system. In the PD-L1 testing group, patients were stratified by PD-L1 tumor proportion score (TPS) $\geq 50\%$, $1\% \leq \text{TPS} < 50\%$, or TPS $< 1\%$ and received pembrolizumab monotherapy, pembrolizumab plus chemotherapy, or chemotherapy alone, respectively. In the non-PD-L1 testing group, all patients received pembrolizumab plus chemotherapy. (Figure 1)

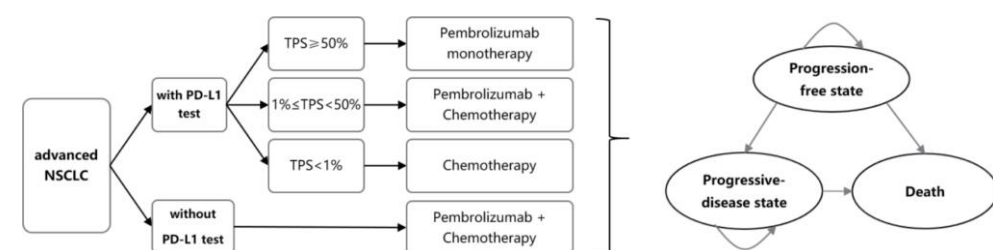


Figure 1 Model structure for advanced NSCLC selecting pembrolizumab related regimen with/without PD-L1 test

Model inputs were obtained from published literature and a healthcare price database, and clinical outcomes were derived from two randomized clinical trials, KEYNOTE-042 Chinese cohort study and KEYNOTE-189 study. Costs for PD-L1 testing, pembrolizumab, chemotherapy, subsequent therapy, adverse events, supportive care, and terminal care were included. Costs and outcomes were discounted at a rate of 5% per year and half-cycle correction was applied. The net monetary benefit (NMB) was estimated for the PD-L1 testing group versus the non-PD-L1 testing group.

3. Results

3.1 Baseline results

Using PD-L1 testing to guide treatment in patients with advanced NSCLC led to cost savings of \$53,914.71 and a reduction in QALYs of 0.234, resulting in a positive NMB of \$50,973.98 at a willingness-to-pay (WTP) threshold of \$12,551.50/QALY (GDP per capita in China, 2021). (Table 1)

Table 1 Summary of Cost and utilities results in base case analysis of pembrolizumab-based regimen with PD-L1 test vs. combination treatment without

	With PD-L1 test	Without PD-L1 test
Costs(\$)		
PFS state	56,449.39	109,837.69
PD state	14,723.92	15,250.33
Total costs	71,173.31	125,088.02
Incremental costs	-53,914.71	
Utilities(QALYs)		
PFS state	0.632	0.815
PD state	0.249	0.299
Total utilities	0.880	1.114
Incremental Utilities	-0.234	
ICER(\$/QALYs)	Less effective and less costly	
NMB(\$)	50,973.98	

3.2 Sensitivity analysis

One-way sensitivity analysis demonstrated that the cost of pembrolizumab, efficacy of pembrolizumab plus chemotherapy on patients with PD-L1 TPS $< 1\%$, and the proportion of patients with TPS $< 1\%$ had the most influence on the NMB result. (Figure 2) Probabilistic sensitivity analysis showed a 100% probability that the PD-L1 testing approach was cost-effective at a WTP threshold of one- and three-times GDP per capita in China. (Figure 3)

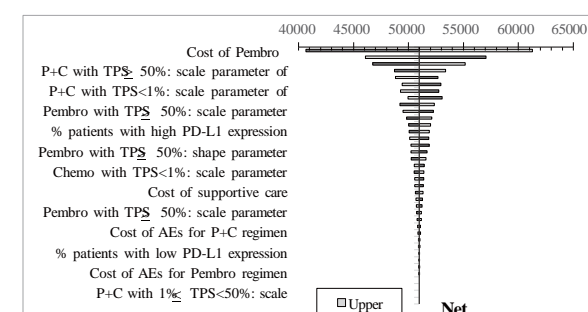


Figure 2 Tornado diagram for the net benefit of pembrolizumab-based regimen with PD-L1 test vs. combination treatment without PD-L1 test

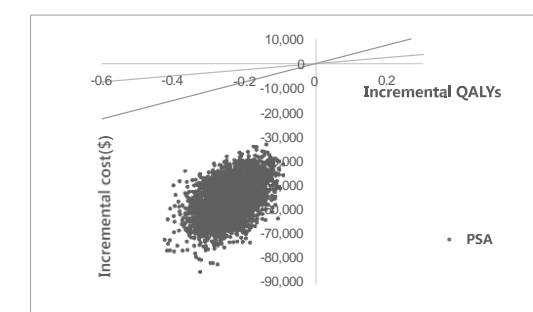


Figure 3 Probabilistic sensitivity analysis results of pembrolizumab-based regimen with PD-L1 test vs. combination treatment without PD-L1 test

3.3 Scenario analyses

Scenario analysis 1 included a price reduction for pembrolizumab consistent with an available patient assistance program (PAP). Scenario analysis 2 modified the PD-L1 testing group so that patients with TPS $< 1\%$ received pembrolizumab plus chemotherapy in accordance with new clinical guidelines in China. (Table 2)

Table 2 Cost-effectiveness of scenario analyses of pembrolizumab-based regimen with PD-L1 test vs. combination treatment without PD-L1 test

	Scenario 1: Cost reduction of Pembro		Scenario 2: Modified regimen of TPS $< 1\%$	
	With test	Without test	With test	Without test
Total costs(\$)	41,126.86	61,585.65	115,537.66	125,088.02
Incremental costs(\$)	-20,458.78		-9,550.36	
Total utilities(QALY)	0.880	1.114	1.056	1.114
Incremental Utilities(QALY)	-0.234		-0.058	
ICER(\$/QALYs)	Less effective and less costly		Less effective and less costly	
NMB(\$)	17,518.05		8,817.59	

4. Discussion

The base-case and scenario analyses showed that selecting treatments based on PD-L1 TPS expression was less effective and less costly than treating all patients with pembrolizumab plus chemotherapy without PD-L1 testing and resulted in a positive net monetary benefit. The cost of pembrolizumab contributed the most to the negative incremental cost in both base-case and scenario analyses. The negative incremental utilities revealed differences in clinical efficacy among therapies

There are several limitations in the analysis. First, local clinical data was not available for all inputs. KN189 was used to estimate the clinical efficacy of pembrolizumab combination therapy and chemotherapy and this could contribute to differences in OS and PFS data due to patient heterogeneity. Second, due to the lack of head-to-head data comparing pembrolizumab monotherapy with combination therapy, the relative efficacy for high PD-L1 expression remains uncertain.

5. Conclusions

Using a PD-L1 testing strategy to guide first-line pembrolizumab treatment in patients with advanced NSCLC is cost-effective compared to a non-PD-L1 testing strategy at a WTP threshold of \$12,551/QALY for China.

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