Cost Effectiveness Analysis of Nivolumab Plus Ipilimumab vs. Pembrolizumab Plus Chemotherapy for the First-Line Treatment of Non-squamous, Advanced Non-Small Cell Lung Cancer in the USA

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OBJECTIVES

Immunotherapy used with or without chemotherapy has demonstrated significant clinical outcomes for non-small cell lung cancer (NSCLC) patients. The CheckMate-227 trial has shown that nivolumab plus ipilimumab (Nivo+Ipi) indicates significant survival benefits as first-line treatment for non-squamous, advanced NSCLC patients. The KeyNote-189 trial has also concluded that pembrolizumab plus chemotherapy (Pembro+Chemo) achieves efficacy for patients with the same disease characteristics as in CheckMate-227. The paper studied the cost-effectiveness of nivolumab plus ipilimumab vs. pembrolizumab plus chemotherapy as the first-line treatment for non-squamous, advanced NSCLC for adult patients from the US payer's perspective.

METHODS

A Markov model was built to analyze the cost-effectiveness of nivolumab plus ipilimumab in the first-line treatment of metastatic NSCLC. The health outcomes were estimated in quality-adjusted life-years (QALYs) and were obtained from the literature. The cost information was from Veteran Affairs (VA) catalogue Federal Supply Schedule (FSS) price in 2021. In addition to the base case incremental cost-effectiveness ratio (ICER) and incremental net monetary benefit (INMB), probabilistic and one-way sensitivity analyses were also conducted to examine the impact of uncertainties on the results.

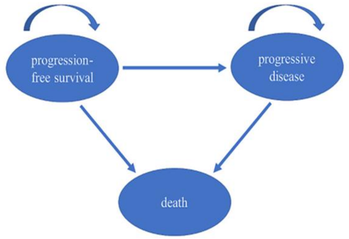

Figure 1. State transition diagram

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RESULTS

- **Base Case Analysis**

In the base case, nivolumab plus ipilimumab indicated total costs of $135,529 and total QALY of 0.87, while pembrolizumab plus chemotherapy yielded total costs of $223,324 and total QALY of 1.00. The incremental costs and QALYs by using nivolumab plus ipilimumab were ($87,795.30) and (0.13) for the advanced NSCLC patients regardless of PD-L1 expression, which led to an ICER of $674,610.82 per QALY and an INMB of $68,273.98 at the willingness to pay threshold of $150,000/ QALY.

Table 1. Key Model Parameters

Parameter Description	Point Estimates	Min	Max
Utility, PFS - Nivo+Ipi	0.784	0.740	0.828
Utility, PFS - Pembro+Chemo	0.652	0.431	0.833
Utility, PD - Nivo+Ipi	0.473	0.166	0.568
Utility, PD - Pembro+Chemo	0.470	0.184	0.773
Median OS (Month) - Nivo+Ipi	17.100	15.200	19.900
Median OS (month) - Pembro+Chemo	22.000	19.500	25.200
Median PFS (month) - Nivo+Ipi	5.100	4.200	5.700
Median PFS (month) - Pembro+Chemo	9.000	8.100	9.900
Drug acquisition cost - Nivo+Ipi	15377.120	12301.696	18452.544
Drug acquisition cost - Pembro+Chemo	15230.670	12184.536	18276.804

Table 2. Base case results at WTP $150,000/QALY

	Total costs ($)	Total QALY	ACER ($/QALY)	NMB ($)
Nivo + Ipi	135529.32	0.87	155355.72	-4672.2301
Pembro + Chemo	223324.62	1.00	222762.64	-72946.207

Nivo+Ipi vs Pembro+Chemo	
Δ Cost ($)	-87795.30
Δ QALY	-0.13
ICER ($/QALY)	674610.82
INMB ($)	68273.98

- **Sensitivity Analysis**

The average ICER computed from the 1000 iterations run in probabilistic sensitivity analyses was $230,707 per QALY, with an average QALY gain of (0.21) and an incremental cost of ($88,331). Fig. 2 showed the ICER scatter plot and Fig. 3 showed the cost-effectiveness acceptability curve. At a willingness-to-pay level of $150,000 per QALY, the probability of nivolumab plus ipilimumab being cost-effective was approximately 87.3% (Fig. 3). When parameters varied from the deterministic estimates, the INMB results were the most sensitive around the utility of progressive disease state for both groups, followed by drug acquisition cost for both groups (Fig. 4).

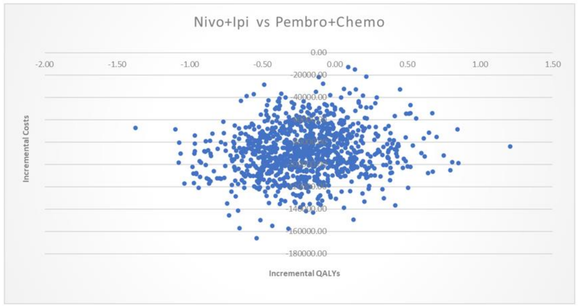

Figure 2. ICER scatter plot

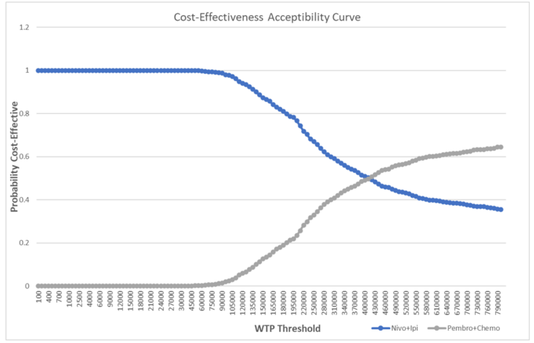

Figure 3. CEAC curve

DISCUSSION

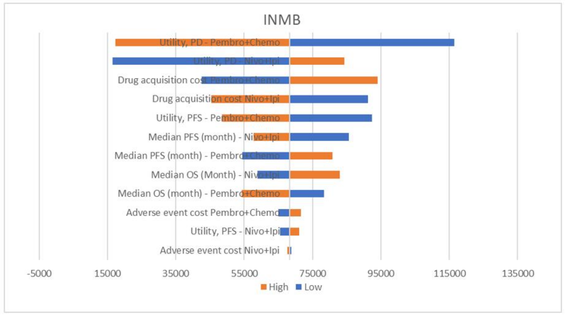

Figure 4. Tornado diagram: INMB

There are several limitations of this analysis governed by data availability and model assumptions. Firstly, we did not have access to patient-level data and thus we relied solely on the aggregate survival data reported from the clinical trials to model patient survival. Secondly, drug acquisition costs of the study were extracted from VA FSS schedule, which might not reflect the real-world costs for US payers. We conducted sensitivity analysis around +-20% of the point estimates to complement this problem. Furthermore, there was not a consensus from the literature on the utility of patients who received second-line subsequent therapies for both arms. We thus assumed patients' second-line utility the same as the first-line utility in the progressive disease state. Overall, the study is the first cost-effectiveness analysis in the literature of the two treatment arms, which are representative of the first treatments approved for combo-immunotherapy (CI) and immune-chemotherapy (IO), respectively. The analysis would be instrumental for the US payer to allocate first-line treatment resources for advanced, NSCLC patients.

CONCLUSIONS

Nivolumab plus ipilimumab was not found to be cost-effective at the willingness to pay threshold of $150,000 per QALY as compared with pembrolizumab plus chemotherapy for non-squamous, metastatic NSCLC patients.