Cost-Effectiveness of Atezolizumab Monotherapy Versus Pembrolizumab Monotherapy for First-Line Treatment of Metastatic Non-Small Cell Lung Cancer

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PRESENTED AT:

INTRODUCTION & OBJECTIVE

INTRODUCTION

- Atezolizumab is a PD-L1 inhibitor FDA-approved as first-line (1L) monotherapy for metastatic non-small cell lung cancer (mNSCLC) patients whose tumors have high PD-L1 expression ($\geq$ 50%) without EGFR or ALK mutations. Approval was based on clinical benefit evaluated relative to chemotherapy in IMpower110, a multicenter, international, randomized, open-label trial in stage IV NSCLC patients whose tumors express PD-L1 and who had received no prior chemotherapy for metastatic disease [1].

- Pembrolizumab, a PD-1 inhibitor, has also been approved as a 1L monotherapy for mNSCLC patients with high PD-L1 expression in the US [2-5].

- Atezolizumab and pembrolizumab are the preferred category 1 treatments recommended by the National Comprehensive Cancer Network (NCCN), and these are the most commonly used treatments in the US for the PD-L1 high population [6].

OBJECTIVE

- To evaluate the cost-effectiveness of 1L atezolizumab versus pembrolizumab monotherapy for mNSCLC patients with high PD-L1 expression from a US payer perspective.

MODEL APPROACH

- An area under the curve model (AUC, also known as a partitioned survival model) was developed in Microsoft Excel 2016 to estimate the cost-effectiveness of atezolizumab monotherapy compared to pembrolizumab monotherapy as 1L treatment in the target population.

- The model structure includes three mutually exclusive health states, progression-free (PF) (starting state), progressive disease (PD), and death (**Figure 1**).
  - From the initial PF state, patients transition in annual cycles to PD where they receive subsequent therapies or death based on underlying progression-free survival (PFS) and overall survival (OS) data for the designated intervention.
  - Patients who progress can remain in the PD state or transition to the death state but can never go back to the PF state. All patients eventually enter the absorbing death state.

- The base case time horizon was 20 years (lifetime), and a 3% discount rate was applied to costs and outcomes according to US guidelines [7].

Figure 1. Model Structure

PF: progression-free; PD: progressed disease
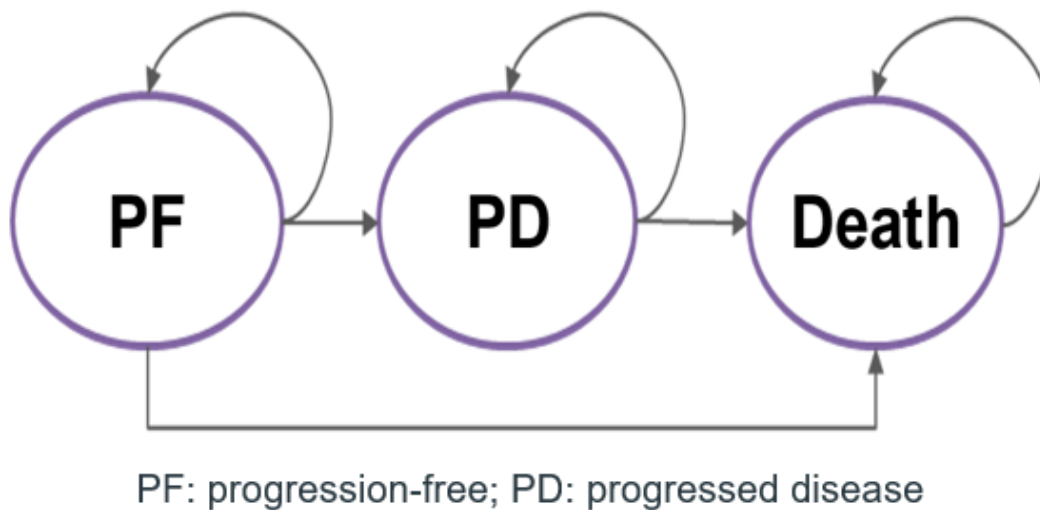
MODEL INPUTS

CLINICAL INPUTS

- For the atezolizumab arm, PFS and OS were obtained from the IMpower110 clinical trial, including 205 PD-L1 high chemotherapy-naive patients with stage IV mNSCLC randomized 1:1 to receive atezolizumab monotherapy or platinum-based chemotherapy [1].

- Using IMpower110 data, parametric functions (Weibull, exponential, log-normal, log-logistic, generalized gamma, and Gompertz) were fit to the Kaplan-Meier PFS and OS curves to extrapolate survival across the 20-year time horizon. In the base case, the log-logistic distribution was used for atezolizumab PFS and OS curves based on statistical tests (Akaike information criterion and the Bayesian information criterion), visual inspection, and clinical plausibility of the extrapolated results.

- Clinical outcomes for the pembrolizumab arm were derived from indirect comparisons between atezolizumab (IMpower110) and pembrolizumab (KEYNOTE-024 and KEYNOTE-042) based on a network meta-analysis (NMA) of published cancer immunotherapy agents [1-5]. Additional agents in the NMA included chemotherapy, nivolumab and nivolumab plus ipilimumab. The hazard ratio (HR) derived from the NMA was used to generate the PFS and OS curves for pembrolizumab monotherapy.

- Treatment duration for atezolizumab and pembrolizumab was based on the PFS curves for each treatment; patients remained on 1L treatment until progression, which is in-line with the labeled use for both treatments.

- Grade ≥3 treatment-related adverse events (AEs) affecting ≥1% of the study population for atezolizumab and pembrolizumab were included in the base case analysis. AE data for atezolizumab monotherapy were obtained from the IMpower110 study [8]. The respective grade ≥3 treatment-related AEs for pembrolizumab were sourced from the KEYNOTE-024 study because this study reported AEs in the same subgroup of patients as IMpower110 (PD-L1 high) [3].

RESOURCE USE & COST INPUTS

- Drug dosing for atezolizumab, pembrolizumab, and subsequent therapies in PD was based on the product prescribing information. The average patient's weight and total body surface area were also accounted for where applicable for drug dosing and were based on IMpower110 data [8].

- The unit cost for the drugs (Wholesale Acquisition Cost [WAC], accessed March 2020), drug administration, health state, and terminal care costs are reported in **Table 1** [9]. As a conservative assumption, the base case of the economic model assumes full vial sharing (i.e., no wastage) for the administration of all weight-based drugs in the model. In the base case analysis, terminal care costs were applied once for the last week of life.

- The costs of the PD health state include subsequent lines of therapy after 1L treatment discontinuation, where treatment patterns in PD were obtained from the IMpower110 study (**Table 2**) [8].

- The costs to manage each AE were estimated using published data from Wong et al. where applicable, and Centers for Medicare and Medicaid Services (CMS) physician fee schedule were applied to clinically-guided resource use assumptions for AEs not included in the published study [10,11].

Table 1. Drug, administration, and health state costs

Cost Category	Cost
Drug Cost Per Cycle (dose per cycle)^ [9]	
Atezolizumab (1200 mg)	$9,194.03
Pembrolizumab (200 mg)	$9,724.08
Pemetrexed (500 mg/m^2)	$1,342.97
Gemcitabine (1000 mg/m^2)	$22.98
Carboplatin (400 mg/m^2)*	$11.89
Cisplatin (75 mg/m^2)	$40.85
Paclitaxel (200 mg/m^2)	$59.91
Bevacizumab (15 mg/kg)	$8,593.80
Drug Administration Costs [12]	
Outpatient infusion administration (single agent, up to 1 hour)	$142.55
Outpatient infusion (additional drug, up to 1 additional hour)	$69.29
Weekly Health State and Terminal Care Costs ($) [15,16]**	
Health state costs – PF ($)	$373.05
Health state costs – PD ($)	$465.38
Terminal care costs ($)	$2,055.00

^ All treatments are assumed to be administered every three weeks (Q3W) in accordance with product prescribing information. WAC costs were access March 2020 .
*Carboplatin cost per cycle is based on AUC 6 dosing.
**Weekly health state costs are limited to supportive care costs; treatment costs are excluded.

Table 2. Treatment patterns in progression

Post-immunotherapy treatment	Proportion of patients on each treatment* [8]	Mean duration of therapy (months)
Pemetrexed	19%	18.0**
Gemcitabine	21%	18.0**
Carboplatin	28%	18.0**
Cisplatin	9%	18.0**
Paclitaxel	17%	18.0**
Bevacizumab	6%	11.6^

* The IMpower110 study collected data on the utilization of post-discontinuation therapies. It was not possible to distinguish combination therapies because treatments were coded separately.
** Assumption based on 6 cycles of chemotherapy in progression
^ Obtained from IMpower150 [16]

HEALTH UTILITY INPUTS

- Health utilities were incorporated into the model using overall utility values from IMpower110 based on EQ-5D-3L [8]. Progression data from the IMpower110 trial was used to estimate utilities by progression status (pre-progression [base case value = 0.75] and after progression [base case value = 0.71).

BASE CASE RESULTS

- In the base case, treatment with atezolizumab versus pembrolizumab resulted in an increase of 0.57 life-years (LYs, with 0.16 additional LYs in the PF state and 0.41 LYs in the PD state. This translates to 0.41 incremental quality-adjusted LYs (QALYs) for patients treated with atezolizumab (**Table 3**)

- The longer survival for patients receiving atezolizumab led to an increase in 1L treatment and supportive care costs:
    - Additional time spent in the PF state was associated with a $10,693 increase in 1L atezolizumab treatment costs.
    - In PD, atezolizumab patients faced higher supportive care costs ($61,328) compared to pembrolizumab patients ($51,390) due to living an extra 0.41 years in this state.

- When considering incremental costs and effects, atezolizumab had an ICER of $39,392 per LY gained and $54,549 per QALY gained relative to pembrolizumab.

Table 3. Base case results

|	Atezolizumab Monotherapy	Pembrolizumab Monotherapy	Incremental (Atezo vs Pembro)
Mean time in PF (years)	1.83	1.66	0.16
Mean time in PD (years)	2.53	2.12	0.41
Total life years	4.35	3.78	0.57
Mean QALYs in PF	1.38	1.25	0.12
Mean QALYs in PD	1.79	1.50	0.29
Total QALYs	3.17	2.76	0.41
Mean cost of PF ($)	307,442	294,701	12,892
Mean first-line treatment costs ($)	295,468	284,775	10,693
Mean drug administration costs ($)	4,581	4,175	406
Mean adverse event costs ($)	1,430	323	1,107
Mean PF supportive care costs ($)	5,963	5,428	535
Mean cost of PD ($)	65,515	55,610	9,906
Mean PD supportive care cost ($)	61,328	51,390	9,938
Mean subsequent therapy costs ($)	4,188	4,220	-32
Terminal/palliative care cost ($)	1,634	1,700	-66
Mean total cost ($)	374,592	352,011	22,581
Cost per life year gained ($)			**39,392**
Cost per QALY gained ($)			**54,549**

Abbreviations: PF = progression-free; PD= progressed disease; QALYs=quality-adjusted-life-years

SENSITIVITY & SCENARIO ANALYSIS RESULTS

ONE-WAY SENSITIVITY ANALYSIS

- In the one-way sensitivity analysis (OWSA), input parameters were varied by 20% to ascertain the key drivers of the cost-effectiveness results. Parameters included in the OWSA were supportive care costs (PF and PD), terminal care costs, administration costs, discount rates for costs and effects, adverse event management costs, and adverse event costs for post-discontinuation therapy.

- When varying discount rates for costs and effects by 20%, the ICER for atezolizumab compared to pembrolizumab varied by as much as 77% and 72%, respectively (**Figure 2**). The ICER varied 54% when evaluating the low and high estimates for PD supportive care costs. When varying other parameters by 20%, the ICER did not vary more than 4%, demonstrating that results were robust to variation in most parameters.

Figure 2. One-way Sensitivity Analysis - Tornado Diagram of ICER
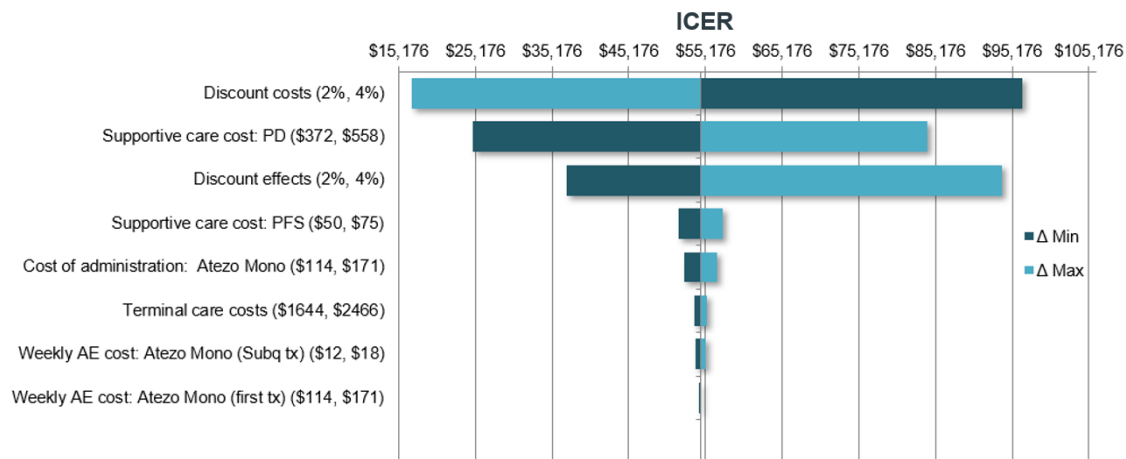
PROBABILISTIC SENSITIVITY ANALYSIS

- In the probabilistic sensitivity analysis (PSA), 1,000 iterations of the model were completed where each iteration varied all included model parameters with parameter uncertainty (PFS and OS extrapolations, AE rates, and health state utilities) within logical ranges described by appropriate distributions. All costs were excluded from the PSA as these parameters were either direct list prices or did not have reported uncertainty.

- The PSA demonstrated that atezolizumab had a 51% probability of being cost-effective at a WTP threshold of US$150,000/QALY (**Figure 3**).

- These findings are driven by the uncertainties around the survival extrapolations and the relatively small difference between the two treatments (atezolizumab and pembrolizumab) in terms of efficacy.

Figure 3. Cost-effectiveness acceptability curve for atezolizumab monotherapy versus pembrolizumab monotherapy
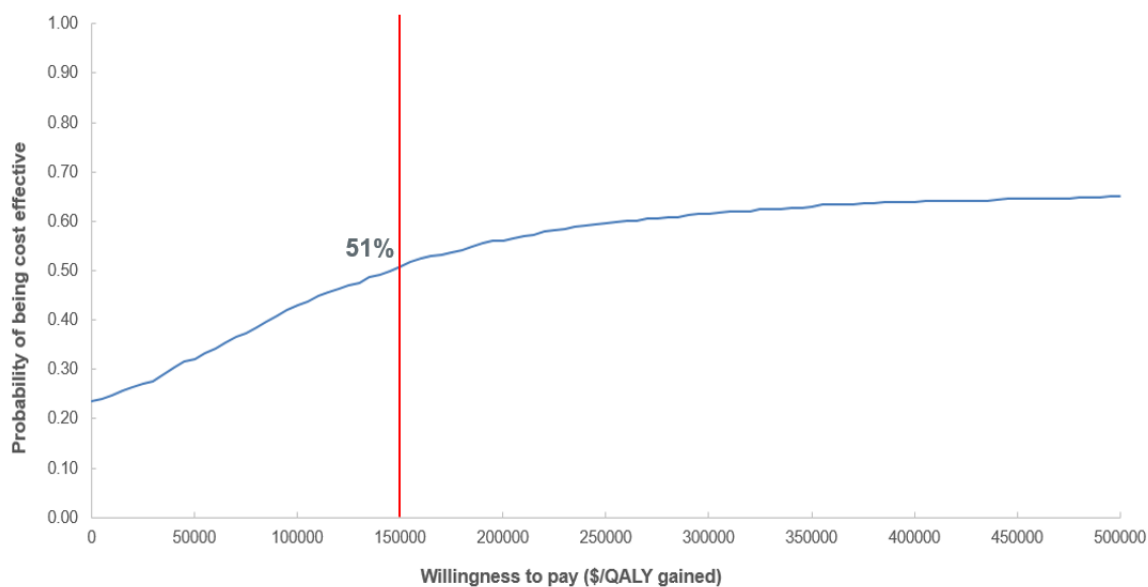
SCENARIO ANALYSIS

- A scenario analysis was conducted to test the sensitivity of the results to model assumptions. The scenario used results from an NMA that was limited to indirect comparisons between IMpower110, Keynote-024, and Keynote-042 trials [1, 3-5, 13-14]. In addition, this scenario used US-based utilities, WAC costs updated to reflect the most recent list WAC prices (accessed April 2021), and terminal care costs were applied for one month rather than one-week costs. Results remained well below a commonly-cited $150,000/QALY US WTP threshold, at $52,633.
    - When compared to the base case, incremental LYs and QALYs associated with atezolizumab increased, driven by less favorable PFS and OS pembrolizumab data from the more focused NMA.
    - These increased LY gains resulted in increased incremental costs in PFS and PD. The updated drug costs, terminal care costs, and health state utilities in this scenario had a minimal impact on results.

CONCLUSIONS & REFERENCES

DISCUSSION AND CONCLUSIONS

- Our base case analysis indicates that atezolizumab monotherapy is likely to be cost-effective in the US relative to pembrolizumab monotherapy in 1L PD-L1 high mNSCLC patients, with an ICER of $54,549/QALY gained over a 20-year (lifetime) time horizon.

- This favorable ICER was driven by LY and QALY gains associated with atezolizumab in PF and PD due to its improved PFS and OS relative to pembrolizumab based on a network meta-analysis.

- The cost-effectiveness results were consistent (i.e. ICERs remained below $150,000 WTP threshold) across deterministic one-way sensitivity analyses and scenario analyses. In the PSA, uncertainty in the survival extrapolations resulted in a 51% probability of atezolizumab being cost-effective at the $150,000/QALY WTP threshold.

- As is the case with most cost-effectiveness analyses, results based on clinical trial data with limited sample sizes may increased uncertainty around model inputs and may not always be generalizable to a real-world setting.

- In addition, due to the lack of a head-to-head comparison of atezolizumab monotherapy and pembrolizumab monotherapy, an indirect comparison was necessary through an NMA to derive the PFS and OS curves for pembrolizumab.

- Despite these limitations, this study provides an estimate of comparative effectiveness and cost-effectiveness of atezolizumab monotherapy compared to pembrolizumab monotherapy for first-line treatment in the PD-L1 high mNSCLC population in the US.

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