Abstract number 1133
Poster number EP04.01-017

Cost-Effectiveness of Atezolizumab for Adjuvant Treatment of Patients With Stage II-IIIA PD-L1+ Non-Small Cell Lung Cancer

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BACKGROUND

- Lung cancer is the second most common cancer and is responsible for the most cancer-related deaths worldwide among both men and women[1]
- Non-small cell lung cancer (NSCLC) accounts for the majority (88%) of all lung cancer cases, and approximately half of all patients are diagnosed with Stage I–III disease, or early NSCLC (eNSCLC)[2,3]
- Lobectomy with or without neoadjuvant or adjuvant treatment is the primary treatment option for operable patients with eNSCLC, and chemotherapy has been the standard of care for adjuvant treatment of resectable stage IB-IIIA eNSCLC[4]
- Improvements in overall survival have been modest for patients with eNSCLC receiving adjuvant chemotherapy,[5] with high rates of recurrence, especially for stage II-IIIA disease[6]
- Atezolizumab demonstrated a significant disease-free survival (DFS) benefit vs best supportive care (BSC) and was approved by the Food and Drug Administration in the US as adjuvant treatment following resection and platinum-based chemotherapy for adults with Stage II-IIIA (American Joint Committee on Cancer, 7th edition) NSCLC and PD-L1 expression on ≥1% of tumor cells (PD-L1+) based on the randomized, open-label, Phase III IMpower010 clinical trial (NCT02486718)[7,8]

OBJECTIVE

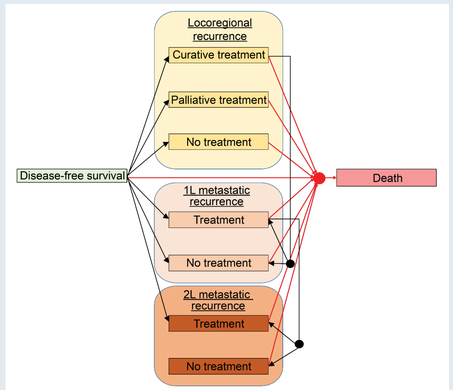
- To evaluate the cost-effectiveness of atezolizumab vs BSC following adjuvant chemotherapy in resected patients with Stage II-IIIA PD-L1+ NSCLC in the US

METHODS

Table 1. Base case model attributes

Model attribute	Description
Perspective	US commercial payer
Target population	Adults (≥18 years) with Stage II-IIIA PD-L1+ NSCLC following resection and platinum-based chemotherapy
Intervention	Atezolizumab
Comparator	Best Supportive Care
Structure	Markov model (Figure 1)
Time horizon	Lifetime
Annual discount rate	3.0%
Cycle length	1 month, with half cycle corrections

Figure 1. Model structure



1L, first line. 2L, second line.

Clinical inputs

- Atezolizumab dosage (1200 mg every 3 weeks) and treatment duration (median, 10.4 months; range, 0-16; mean, 8.2 months; SD, 3.9) were based on IMpower010 (data cutoff: 21 January 2021; follow-up duration, 32 months)[7,8]
- DFS curves from IMpower010 were extrapolated for both treatment arms using log-logistic distribution, and the following adjustments were made to ensure they predict proportions of patients in this health state over time that reflect reality:
  - Cure adjustment: a maximum of 91.5% of patients can be cured within 5 years
  - Treatment effect of atezolizumab assumed to cease at Year 5
  - Mortality adjustment: probability of death among cured patients is 25% greater than the general population using a standardized mortality ratio of 1.25
- After accounting for probability of death (atezolizumab, 17%; BSC, 3%), the remainder of the event probability is assigned to locoregional recurrence (atezolizumab, 49%; BSC, 42%) or metastatic recurrence (atezolizumab, 51%; BSC, 58%) based on IMpower010
- Transition probabilities between health states were derived from the literature or clinical trials[9,10]
- Atezolizumab patients can re-challenge with immunotherapy if recurrence occurs ≥17 months after atezolizumab initiation (≈6 months after the end of 16 cycles). If recurrence occurs <17 months after atezolizumab initiation, patients were re-treated with chemotherapy
- Up to 4 treatment options are available for locoregional or metastatic recurrence based on clinical practice guidelines and market share data[11]
- Unpublished clinical inputs were validated with a clinical expert

Costs

- Drug costs associated with treatment of eNSCLC and recurrences were based on wholesale acquisition costs[12] for the base case, and average selling price[13] for the Medicare scenario
- Adverse event (AE) management costs were included for treatment of grade ≥3 AEs; monthly costs were calculated based on the weekly probability of each AE according to those observed in clinical trials[7, 9, 10], and costs were sourced from the Healthcare Utilization Project (HCUP)[15]
- Drug administration and other costs included in the model are presented in Table 2

Table 2. Costs inputs

Cost	CPT code	Commercial	Medicare
Drug administration costs			
Outpatient infusion, single agent up to 1 hour	96413	$510.65[11]	$140.16[14]
Outpatient infusion, additional hour	96415	$191.93[11]	$29.76[14]
Outpatient infusion, additional drug up to 1 additional hour	96417	$254.08[11]	$68.17[14]
Other costs			
Radiation therapy	–	$297 per fraction[15]	
CT scan, chest	–	$522[16]	$178[17]
End-of-life care	–	$64,336[18]	$79,631[19]

CMS, Center for Medicare & Medicaid Services; CPT, Current Procedural Terminology; CT, computed tomography; PFS, Physician Fee Schedule.

Utilities

- Since IMpower010 did not collect patient-reported outcomes, health state utilities were derived from EQ-5D scores published in the literature and in the IMpower150 trial (Table 3)

Table 3. Health state utility values based on EQ-5D scores

Health state	Base case value	Population	Tariff
Disease-free survival	0.76[20]	Canada	US
Locoregional recurrence, curative	0.73[21]	Europe, Canada, Australia, Turkey	UK
Locoregional recurrence, palliative	0.62[22]	The Netherlands	Not specified
1L metastatic recurrence	0.71[10]	–	US
2L metastatic recurrence	0.67[10]	–	US
1L metastatic recurrence, 2L recurrence not treated	0.62[22]	The Netherlands	Not specified

Analysis

- The primary outcome was incremental cost effectiveness ratio (ICER), which was calculated as the difference in costs divided by the difference in quality-adjusted life-years (QALYs)
- One-way sensitivity analysis (using 20th and 80th percentile values) and probabilistic sensitivity analysis were performed to test the robustness of model results and to identify influential parameters
- A scenario analysis was performed using Medicare-specific costs and assuming an average patient age of 65 years to reflect the Medicare population perspective

RESULTS

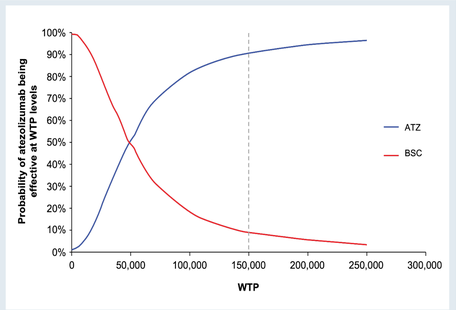
- At a willingness-to-pay (WTP) threshold of $150,000, atezolizumab was cost-effective at $46,859 per QALY in the base case (Table 4)
  - Relative to BSC, atezolizumab leads to an increase of 1.391 life-years or 1.045 QALYs
- Results from the scenario analysis indicated that atezolizumab was also cost-effective in the Medicare population

Table 4. Cost-effectiveness results

	Cost	QALYs	ICER
Base case (commercial)			
Atezolizumab	$288,639	6.839	
BSC	$239,683	5.794	
Incremental	$48,956	1.045	$46,859
Scenario analysis (Medicare)			
Atezolizumab	$276,479	6.302	
BSC	$229,097	5.325	
Incremental	$47,382	0.977	$48,512

- Atezolizumab was cost-effective in 91% of iterations at a WTP threshold of $150,000 (Figure 2)

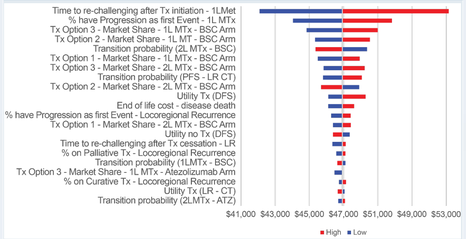
Figure 2. Cost-effectiveness acceptability curve



ATZ, atezolizumab; BSC, best supportive care.

- Results were most sensitive to time to immunotherapy rechallenge in the 1L metastatic health state (Figure 3)

Figure 3. One-way sensitivity analysis



ATZ, atezolizumab; BSC, best supportive care; MTx, metastatic treatment; Tx, treatment.

LIMITATIONS

- The extrapolation of DFS across time was based on 32 months of median follow-up data, which leads to uncertainty around the incremental benefit of the intervention after the trial follow-up period
- Some clinical inputs, including health utilities, were unavailable from IMpower010 and were derived from the published literature, which may have introduced bias related to differences between underlying study populations
- Additional non-drug treatment costs potentially associated with locoregional and metastatic recurrence were not included in the base case analysis, providing conservative results as the inclusion of additional costs would increase the cost of recurrence and decrease the observed ICER further

CONCLUSIONS

- At a WTP threshold of $150,000, atezolizumab is cost-effective vs BSC for the adjuvant treatment of resected patients with PD-L1+ Stage II-IIIA NSCLC, supporting utilization of this regimen as the new standard of care in this setting

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ACKNOWLEDGMENTS

- This study is sponsored by Genentech Inc, a member of the Roche Group
- Medical writing/editorial support for this poster, furnished by Jeff Frimpter, MPH, of Health Interactions, Inc, was provided by Genentech Inc, a member of the Roche Group

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DISCLOSURES

- MD Research: Merck, Genentech, CellSight, Novartis, Abbvie, United Therapeutics, Verily, Varian, Celgene (also NIH grants: U01 CA231851-01 [PI: Krasnow] and RO1 CA206540-01 [PI: Sage]); Consulting/Advisory board: Beigene, Astra Zeneca, Sanofi/Genzyme, Eurofins, Janssen
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