

Estimating Recurrences Prevented and Costs Avoided with Atezolizumab in Early Non-Small Cell Lung Cancer in the United States

Zizi Elsis¹, Rishika Sharma², Nathaniel Smith², Sarika Ogale¹, Janet Lee¹

1 Genentech Inc., South San Francisco, CA, USA; 2 Maple Health Group, LLC, New York, NY, USA

INTRODUCTION

- Recurrences of non-small cell lung cancer (NSCLC) post-resection are common, with 45% of patients experiencing a recurrence within 5 years¹
- NSCLC recurrences are associated with significant morbidity and mortality. The 5-year survival of patients with recurrence post resection and adjuvant chemotherapy is only 35.6%¹
- NSCLC recurrences are also associated with a substantial economic burden, resulting in significant health care resource use¹
- Tecentriq® (atezolizumab [ATZ]) was FDA approved in October 2021 for use as adjuvant treatment following resection and platinum-based chemotherapy for adult patients with stage II to IIIA NSCLC whose tumors have PD-L1 expression on ≥1% of tumor cells
- ATZ demonstrated significant reduction compared to best supportive care (BSC) in the rate of recurrence and death among patients enrolled in the phase 3 clinical trial IMPower010 (NCT02486718)²
- The aim of this study was to estimate the population-level health and economic benefits associated with ATZ as adjuvant treatment for early NSCLC (eNSCLC) patients in the United States (US)

PATIENTS AND METHODS

- A Monte-Carlo simulation model was built to estimate the cumulative number of recurrences and deaths prevented by treating patients with early-stage NSCLC with ATZ versus BSC in the US
- The model was static and included a cohort of patients treated during a one-year period and followed over a 5-year time horizon
- The base case population were adult patients with resected stage II-III A ALK/EGFR-positive or negative NSCLC with PD-L1 expression of ≥1%
- The difference between recurrence and mortality outcomes for ATZ versus BSC determined the clinical impact of ATZ
- Economic impact was calculated based on the cost of recurrence management including direct, indirect and terminal care costs
- The modeled number of patients was calculated through an epidemiological cascade in which the overall US population^{3,4} was stratified to align with the FDA label of ATZ in patients with eNSCLC⁵ (Table 1)
- Recurrence and mortality rates for BSC were estimated from disease-free and overall survival (DFS and OS) Kaplan-Meier (KM) curves from the IMPower010 trial where possible (median follow-up 32.2 months)²
 - Clinical trial DFS and OS data was supplemented with data from a real-world retrospective observational study¹
 - Mortality events were excluded from the DFS curves to isolate recurrence events
- Hazard ratios (HR) from the IMPower010 trial were applied to the BSC KM curves to calculate the rate of recurrence and mortality for ATZ and were assumed to be constant from years 1 to 5.
- Cost inputs were largely taken from published literature including a large retrospective US commercial claims analysis⁶ (Table 1) and were inflated to 2021 USD
- Probabilistic model inputs were included as distributions
 - Variance parameters (95% CI) were used for sourced inputs where reported; otherwise ±10% variance was assumed

Key Epidemiology, Clinical, and Cost Model Inputs

Table 1. Model inputs, distributions, and data sources (base case analysis)

	Input	95% CI	Distribution for Simulations	Source		
					Mean	
Epidemiology Inputs						
Demographic (aged >20 years)	76.26%	68.63%, 83.89%	Beta	US Census ³		
eNSCLC incidence rate	0.01309%	0.01298%, 0.1319%	Normal	SEER Stat ⁴		
Stages II-III A	87.76%	84.47%, 89.79%	Beta	Felip ²		
Proportion of patients with resectable tumors	80.60%	72.54%, 88.66%	Beta	GNE Data ⁷		
Proportion of patients receiving adjuvant chemotherapy	44.70%	40.23%, 49.17%	Beta	Maclean ⁸		
Proportion of patients tested for PD-L1	77.00%	69.30%, 84.70%	Beta	Velcheti ⁹		
PD-L1 ≥1%	53.23%	50.15%, 56.32%	Beta	IMPower010 ⁷		
Clinical Inputs						
Recurrence Rates						
Year 1	25.29%	19.51%, 31.07%	Normal	Felip ²		
Year 2	39.02%	32.48%, 45.55%				
Year 3	51.78%	44.29%, 59.27%				
Year 4	53.73%	47.55%, 56.65%				
Year 5	55.10%	50.10%, 60.20%				
% locoregional	ATZ	49.32%	37.85%, 60.78%	Beta	IMPower010 ⁷	
	BSC	44.12%	34.48%, 53.57%			
% distant	ATZ	38.36%	27.20%, 49.51%			
	BSC	39.22%	29.74%, 48.69%			
% locoregional and distant	ATZ	12.33%	6.00%, 19.87%	Log-Normal	Felip ²	
	BSC	16.67%	9.43%, 23.90%			
Mortality Rate						
Year 1	5.05%	2.14%, 7.96%	Normal	IMPower010 ⁷		
Year 2	13.02%	8.52%, 17.51%				
Year 3	21.47%	15.67%, 27.27%				
Year 4	27.37%	20.03%, 34.70%				
Year 5	38.80%	30.70%, 42.90%				
ATZ DFS Hazard Ratio	0.66	0.50, 0.88	Log-Normal	Felip ²		
ATZ OS Hazard Ratio	0.77	0.51, 1.17				
Cost Inputs						
Office visits	Localized	\$34,649	\$31,245, \$38,052	Log-Normal	GNE Data ⁷	
	Metastatic	\$62,455	\$61,897, \$62,922			
Outpatient	Localized	\$43,520	\$39,802, \$47,238			
	Metastatic	\$78,947	\$78,166, \$79,166			
ER visits	Localized	\$608	\$556, \$660			
	Metastatic	\$1,510	\$1,459, \$1,562			
Localized	\$61,730	\$39,802, \$47,238	Beta			IMPower010 ⁷
Metastatic	\$122,223	\$119,713, \$124,733				
Other	Localized	\$4,080	\$3,731, \$4,428			
	Metastatic	\$8,727	\$8,410, \$9,045			
Proportion using CIT post-recurrence	ATZ	11.0%	3.8%, 18.1%			
	BSC	35.3%	26.0%, 44.6%			
Proportion using chemotherapy post-recurrence	ATZ	54.8%	43.4%, 66.2%			
	BSC	46.1%	36.4%, 55.8%			
Cancer immunotherapy cost		\$165,086	\$148,577, \$181,159			
Chemotherapy cost		\$4,130	\$3,717, \$4,543			
Terminal care cost		\$86,904	\$84,221, \$89,594	Log-Normal	Sheehan ¹⁰	
Proportion of patients working		62.23%	56.00%, 68.45%	US Bureau of Labor Statistics ¹¹		
Proportion of patients taking leave	Short-term	38.00%	34.20%, 41.80%	Beta	Andreas ¹²	
	Long-term	10.00%	26.00%, 44.60%			
% Male		66.90%	60.21%, 73.59%	Log-Normal	US Bureau of Labor Statistics ¹³	
Daily wage	Male	\$219.00	\$197.10, \$240.90			
	Female	\$178.00	\$160.20, \$195.80			

Abbreviations: ATZ, atezolizumab; BSC, best supportive care; CI, confidence interval; CIT, cancer immunotherapy; DFS, disease-free survival; eNSCLC, early non-small cell lung cancer; ER, emergency room; OS, overall survival; PD-L1, programmed death ligand 1

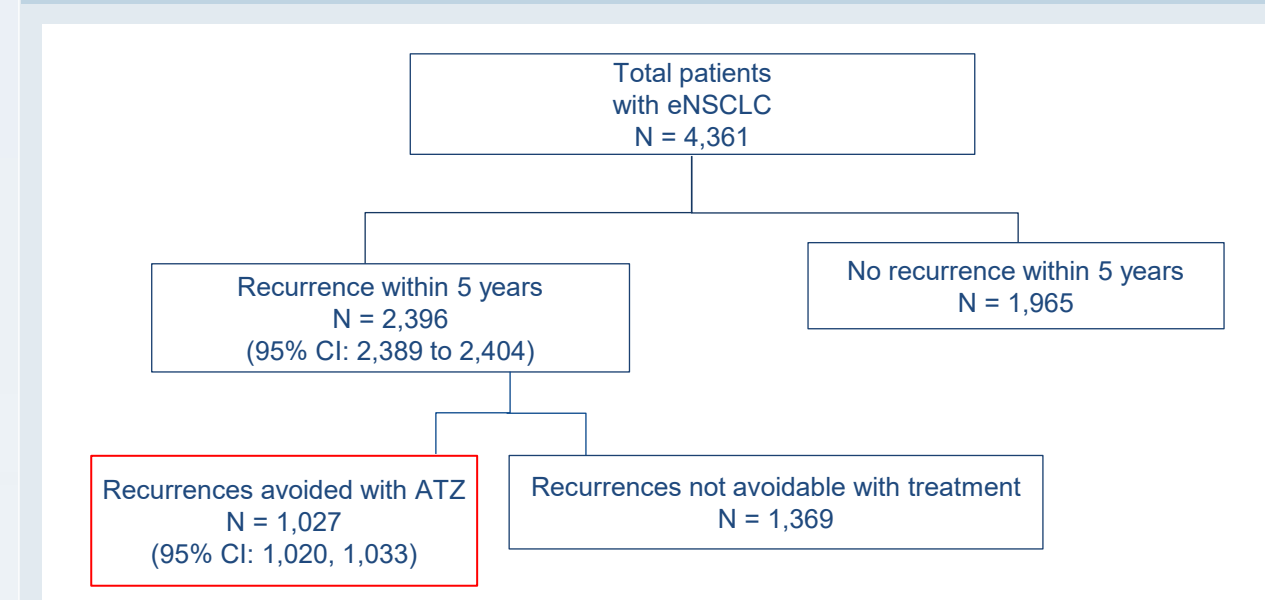
- With each simulation the input values were selected from a beta (for proportions) or a normal distribution (for other continuous variables) or a log-normal distribution for HR and cost data to ensure all randomized values are positive.
- Model outcomes were reported as the mean values and estimated confidence intervals of 5,000 Monte Carlo simulations
- One scenario analysis was explored by increasing the proportion of patients receiving adjuvant chemotherapy post-resection

RESULTS

Base Case Analysis

- In the base case there was an estimated 4,361 patients, 2,396 of which had a recurrence in 5 years when treated with BSC (Figure 1)

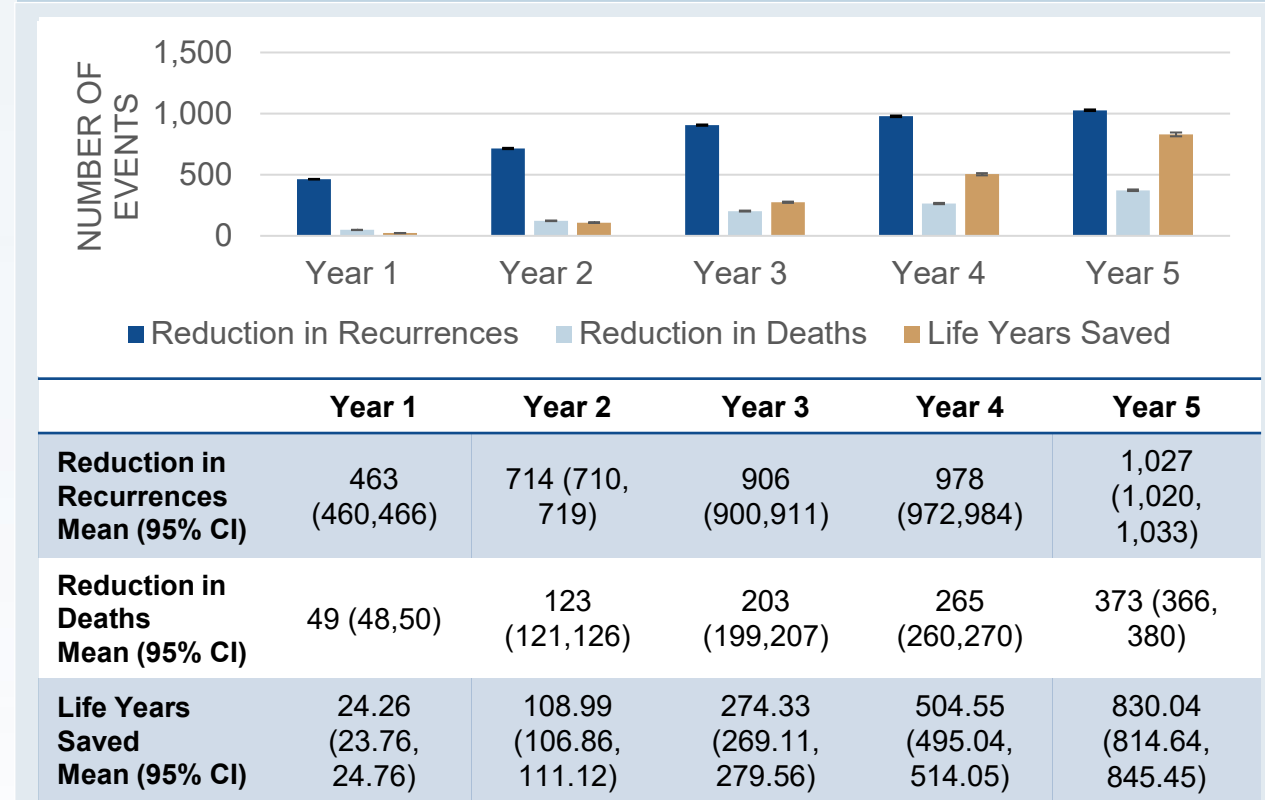
Figure 1. Number of patients with eNSCLC and recurrences avoided with ATZ over 5 years



- Treatment with ATZ led to a mean reduction in the number of recurrences by 1,027 (Figure 2), of which 418 were distant and 229 were both locoregional and distant recurrences over 5 years

- In addition, the use of ATZ resulted in avoidance of 373 deaths over 5 years (Figure 2)
- Reduced mortality events resulted in a total of approximately 830 life years saved over 5 years among the base case cohort of patients (Figure 2)

Figure 2. Cumulative recurrence and death outcomes, mean (95% CI)

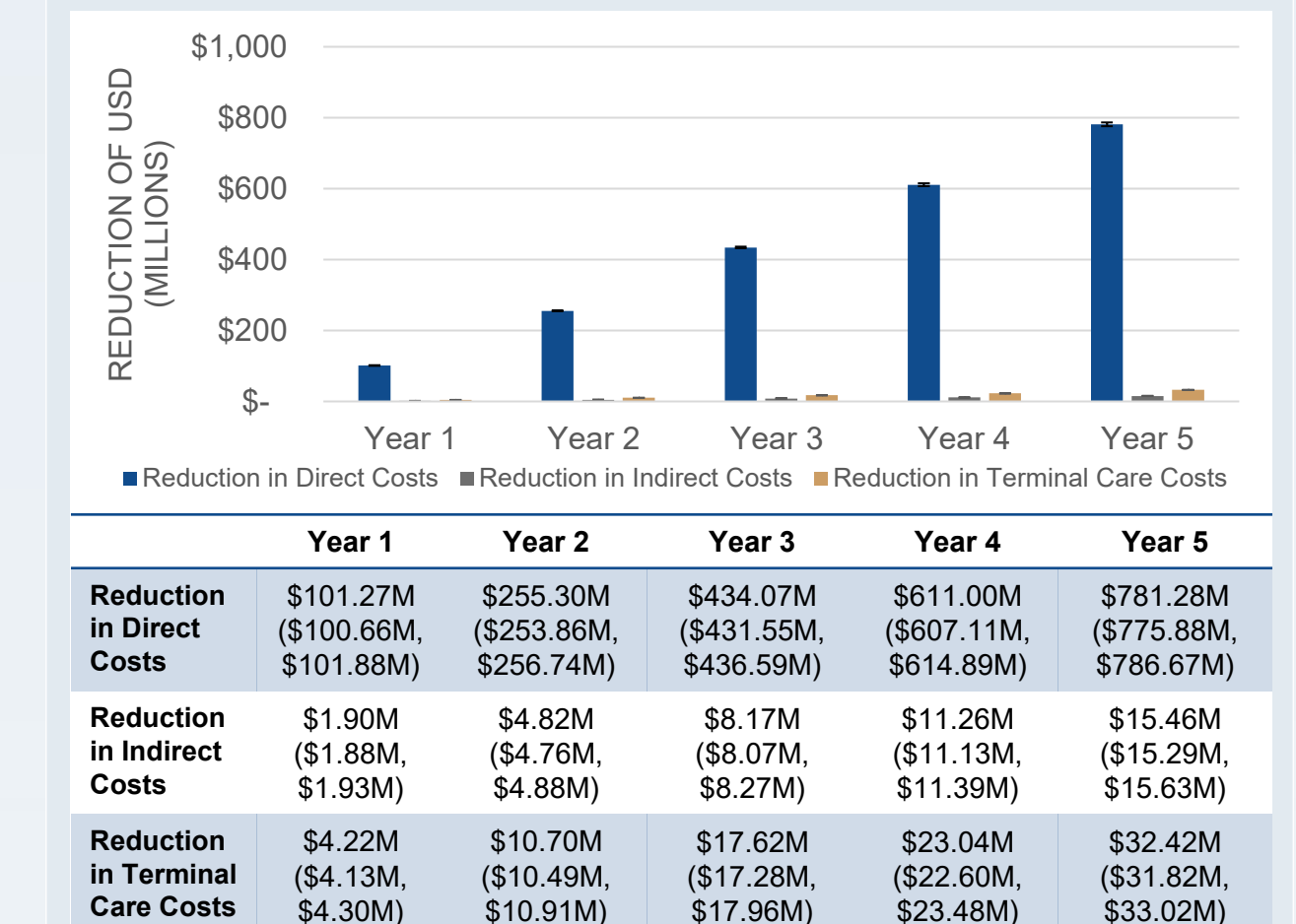


Abbreviations: CI, confidence interval

- In economic terms, treatment with ATZ was associated with a reduction of approximately \$781 million in direct medical costs over 5 years (Figure 3)

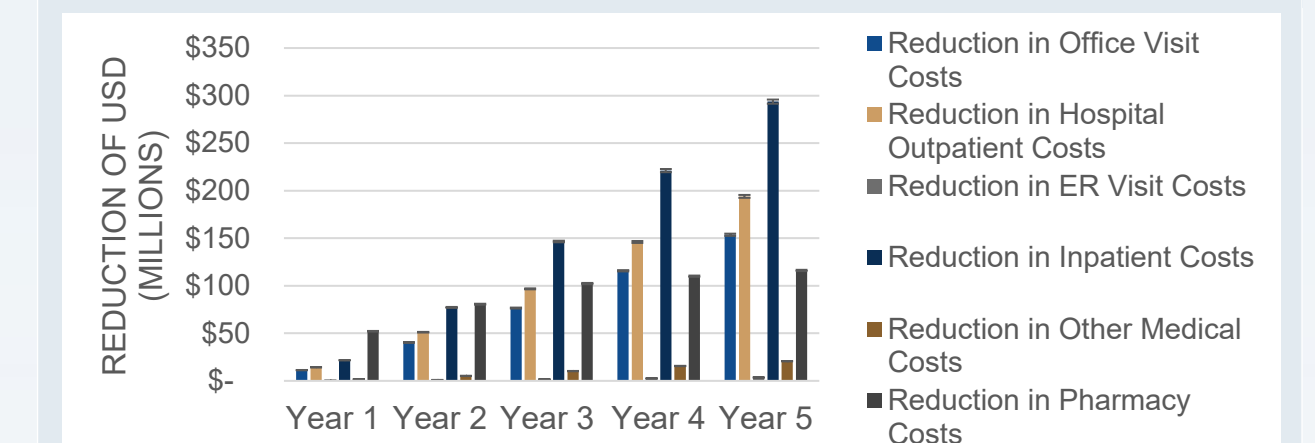
- The greatest cost reductions were seen from inpatient visit costs (~\$249 million) and hospital outpatient costs (~\$194 million) (Figure 4)
- Considering the proportion of patients working, ATZ saved approximately \$15 million by reducing patients' short-term and long-term leave (Figure 3)
- The cost of terminal care was reduced by approximately \$32 million (Figure 3)

Figure 3. Cumulative cost outcomes, mean (95% CI)



Abbreviations: CI, confidence interval

Figure 4. Cumulative direct medical costs, mean (95% CI)



Abbreviations: CI, confidence interval; ER, emergency room

Scenario Analysis

- Increasing the patient population who have received adjuvant chemotherapy by 10% yielded greater reductions in recurrence and death events with ATZ treatment (1,135 recurrences and 400 deaths avoided) driven by the larger population numbers
- With an increased adjuvant chemotherapy population, cost reductions for direct, indirect, and terminal care costs amounted to \$867 million, \$17 million, and \$35 million, respectively (Table 2)

Table 2. Scenario analyses clinical and cost outcomes (mean and 95% CI)

Scenario	Estimated No. of Patients	Reduction in Recurrences	Reduction in Deaths	Reduction in Direct Costs	Reduction in Indirect Costs	Reduction in Terminal Care Costs
Base Case	4,361	1,027 (1,020, 1,033)	373 (366, 380)	\$781,278,450 (\$775,882,245, \$786,674,656)	\$15,461,269 (\$15,289,248, \$15,633,290)	\$32,419,567 (\$31,816,556, \$33,022,577)
Adjuvant Chemo. Proportion (+10%)	4,797	1,135 (1,128, 1,142)	400 (392, 408)	\$866,926,785 (\$861,070,640, \$872,782,931)	\$16,793,487 (\$16,601,567, \$16,985,408)	\$34,763,943 (\$34,095,172, \$35,432,715)

Abbreviations: CI, confidence interval; No., number; Chemo., chemotherapy

LIMITATIONS

- Cost of recurrence in eNSCLC is not well-established in the literature and assumed model cost inputs were compiled from various sources
- Real-world recurrence rates may be different from those observed in clinical trials given potential differences in the real-world setting
- The overall survival data from the IMPower010 are not mature, therefore results regarding reduction of deaths and potential life-years saved should be interpreted with caution
- To address some of these limitations, a Monte Carlo simulation was used to account for uncertainty using a probabilistic model of 5,000 simulations determining mean and 95% CI outcomes.

CONCLUSION

- This analysis estimated the health and economic benefits associated with ATZ in eNSCLC in the US
- In the base case, ATZ use in 4,361 patients would prevent 1,027 recurrences and 373 deaths over 5 years, yielding a total of 830 life years saved
- In economic terms, ATZ would be associated with approximately \$800 million savings in direct, indirect, and terminal care costs over 5 years
- ATZ represents a valuable new therapeutic option for the adjuvant treatment of resected early-stage NSCLC that could prevent a significant number of recurrence events and prolong overall survival, with important clinical, humanistic, and economic consequences for patients, physicians, payers and society.

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AUTHOR EMAIL

- Zizi Elsis: zelsis@uw.edu

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DISCLOSURES

- Study funded by Genentech, Inc.