

A Cost-Utility Analysis of Atezolizumab in the Second-Line Treatment of Metastatic Urothelial Carcinoma

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INTRODUCTION

- Metastatic urothelial carcinoma (MUC) portends a poor prognosis with 5-year survival rates of less than 5%.¹
- Systemic cytotoxic chemotherapy in the first- and second-line setting has been associated with modest gains in survival.²⁻³
- Cytotoxic chemotherapy also portends risks of serious adverse events for the older and co-morbid patient characteristic of the MUC population.⁴
- Immunotherapy with atezolizumab offered promise for improving patient outcomes for MUC patients in the second-line with a positive Phase II trial.⁵
- However, the IMvigor211 Phase III trial failed to demonstrate an overall survival (OS) benefit for atezolizumab, as compared to cytotoxic chemotherapy.
- Given lower rates of adverse events (AE) and thus potential improved tolerability for patients, there may still be investment value for atezolizumab.
- Accordingly, a cost-utility analysis was conducted for the use of atezolizumab in the second-line treatment of MUC.

METHODS

- A partitioned survival model was used to evaluate atezolizumab, as compared to chemotherapy (docetaxel/paclitaxel) for the second-line treatment of MUC.
- Perspective: Canadian public healthcare system
- Health outcomes of interest: life-year gains (LYG) and quality-adjusted life-years (QALY).
- All cost and health outcomes discounted at 1.5%.
- Progression and survival estimates derived from digitized progression-free survival and OS Kaplan-Meier curves from IMvigor211 trial data. Best-fit parametric curves (as per Akaike Information Criterion) used to extrapolate survival beyond trial timeline.
- Health state utility estimates derived from IMvigor211 trial data.
- Costs for systemic therapy (second-line + post-progression), select AE (anemia + febrile neutropenia) and end-of-life care were included (2018 Canadian dollars), as estimated in the published literature and from the Canadian Institute for Health Information patient cost estimator.
- Base case analysis evaluated the IMvigor211 intention-to-treat population (i.e. no biomarker stratification) over a life-time horizon of 10-years.
- Scenario analyses included: a) analyses stratified by biomarker stratification [i.e. programmed death ligand-1 (PD-L1)]; b) within trial time horizon (i.e. 2 years)
- One-way sensitivity analysis for costs of systemic therapy, probabilities/cost of AE and health state utilities performed to address variable influence.

RESULTS

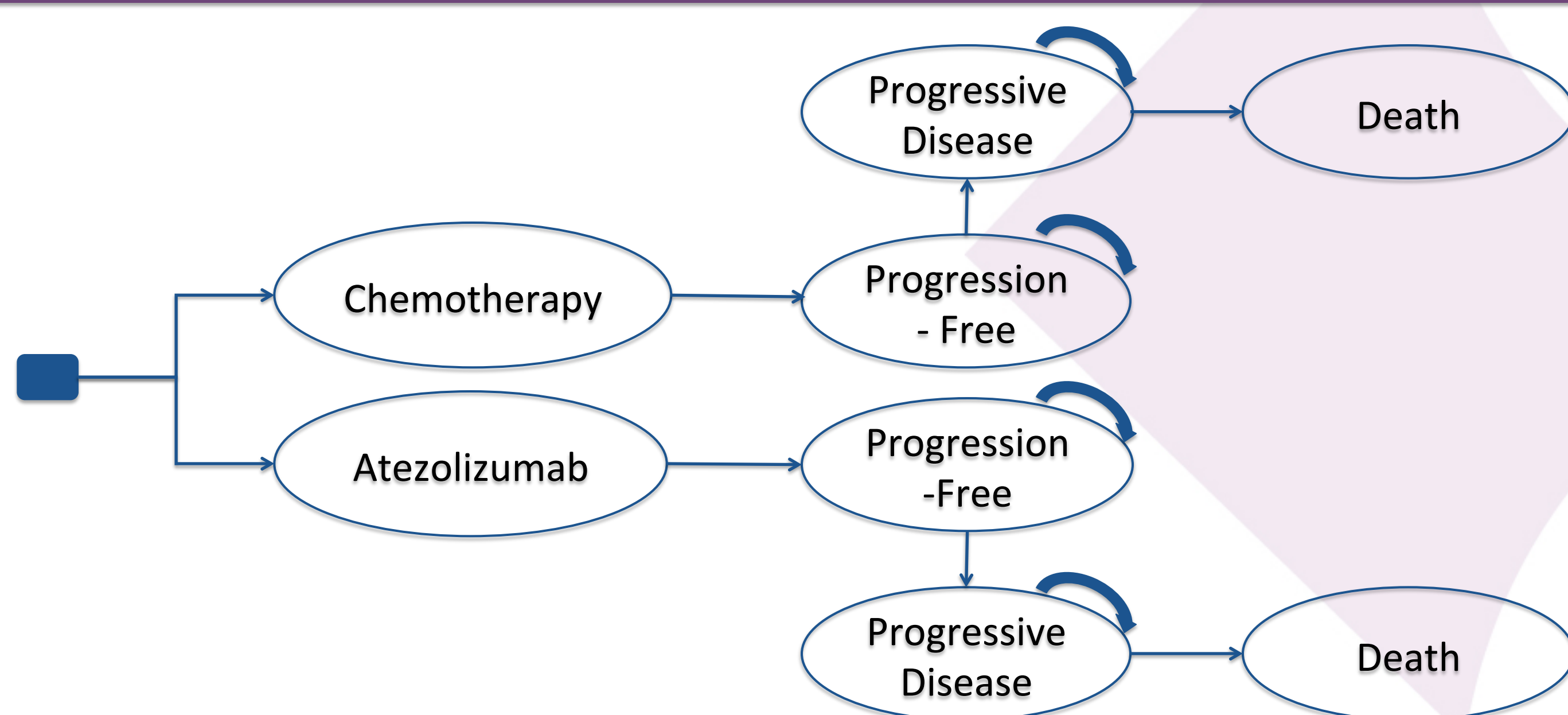


FIGURE 1. Partitioned Survival Model

TABLE 1. Base Case Analysis

Variable	Atezolizumab	Chemotherapy	Incremental
Cost (CAD\$)	61,248	11,117	50,131
Progression-Free	57,526	8,595	48,931
Progressive Disease	3,722	2,522	1,200
Life-Year Gain	1.37	1.08	0.29
Progression-Free	0.49	0.52	-0.03
Progressive Disease	0.88	0.56	0.32
Quality-Adjusted Life-Years	0.79	0.62	0.17
Progression-Free	0.30	0.32	-0.02
Progressive Disease	0.49	0.30	0.19
Cost per LYG (CAD\$/LYG)			172,865
Cost per QALY (CAD\$/QALY)			294,888

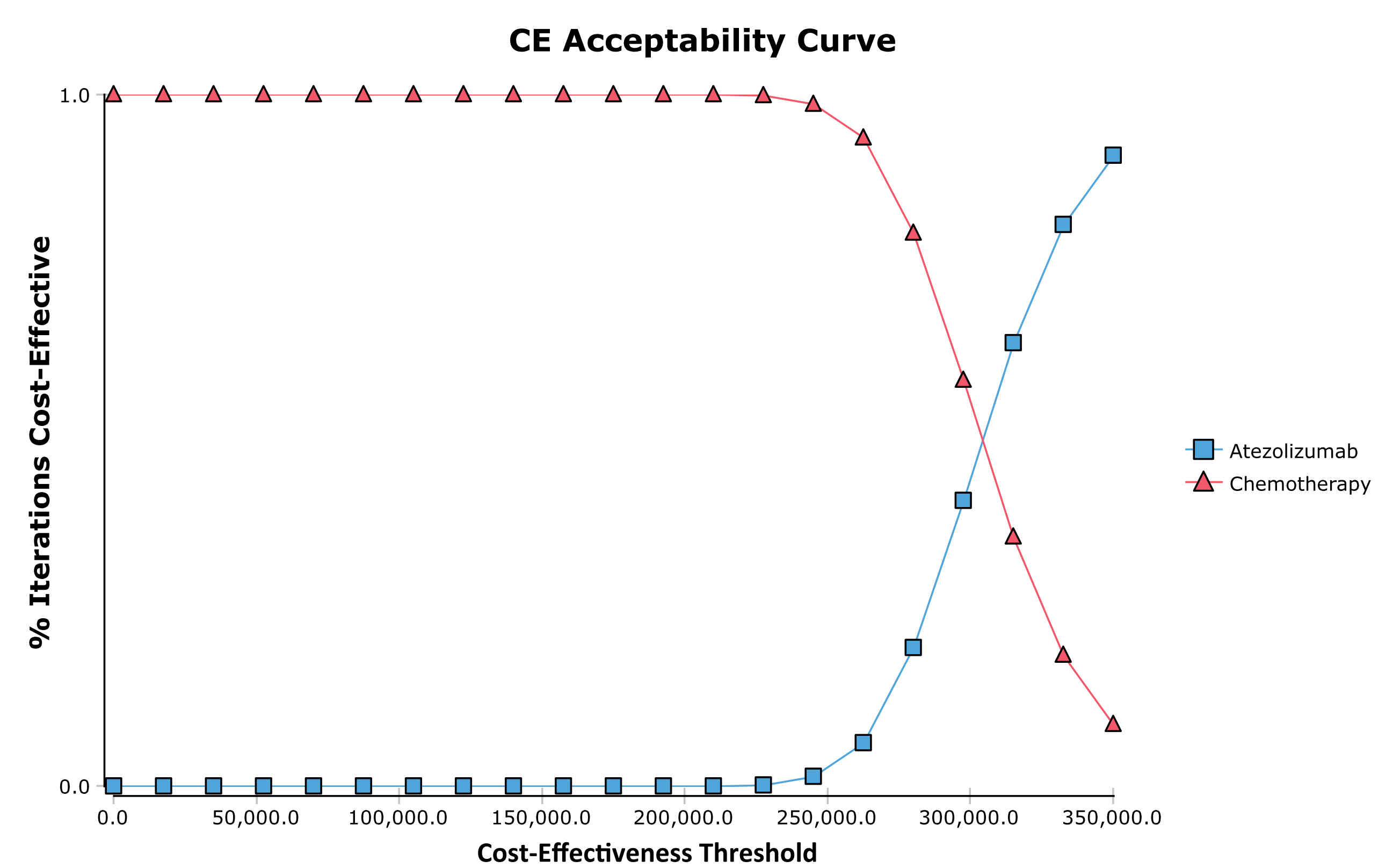


Figure Legend. Cost-effectiveness acceptability curve demonstrates that atezolizumab is cost-effective in 50% of cases at a cost-effectiveness threshold of \$300,000/QALY. CE: cost-effectiveness.

FIGURE 2. Cost-Effectiveness Acceptability Curve

Cost of Atezolizumab

Price Reduction	Cycle Cost (\$)	Annual Cost (\$)	ICER
100% of List Price	9,187	119,432	\$294,888/QALY
25% of List Price	6,890	89,574	\$237,312/QALY
50% of List Price	4,594	59,716	\$150,951/QALY
75% of List Price	2,297	29,855	\$79,983/QALY

Figure Legend. Scenario analysis with various price reductions of atezolizumab demonstrating cost-effectiveness at price reductions of 75% using a cost-effectiveness threshold of \$100,000/QALY.

FIGURE 3. Scenario Analysis for Cost of Atezolizumab

TABLE 2. Scenario Analyses

Variable	Atezolizumab	Chemotherapy	ICER
PD-L1 ≥ 1%			
Cost (CAD\$)	64,167	11,472	\$263,475/QALY
QALY	0.87	0.67	
PD-L1 ≥ 5%			
Cost (CAD\$)	94,422	12,052	\$137,283/QALY
QALY	1.04	0.64	
Within Trial Time Horizon for Intention-to-Treat Population			
Cost (CAD\$)	54,237	10,381	\$877,120/QALY
QALY	0.55	0.50	

CONCLUSIONS

- At cost-effectiveness thresholds of \$50,000-100,000/QALY, atezolizumab is not cost-effective for the second-line treatment of MUC.
- Cost-effectiveness of atezolizumab may be demonstrated with reduction in pricing to ≤ 25% of current list prices.
- Variation in ICER as per PD-L1 status highlights potential role for biomarker-driven patient selection for investment decisions.
- Adopted time horizon generated a notable difference in ICER with 88% of cost derived within trial but only 69% of effectiveness, as compared to life-time horizon. Thus, extrapolated effectiveness must be carefully interpreted, particularly in the era of immunotherapy, given the unique potential for durable responses.

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