

# Multi-Indication Cost-Effectiveness Analysis Framework and Pricing Strategy: A Case Study of Pembrolizumab

**EE158**

### INTRODUCTION

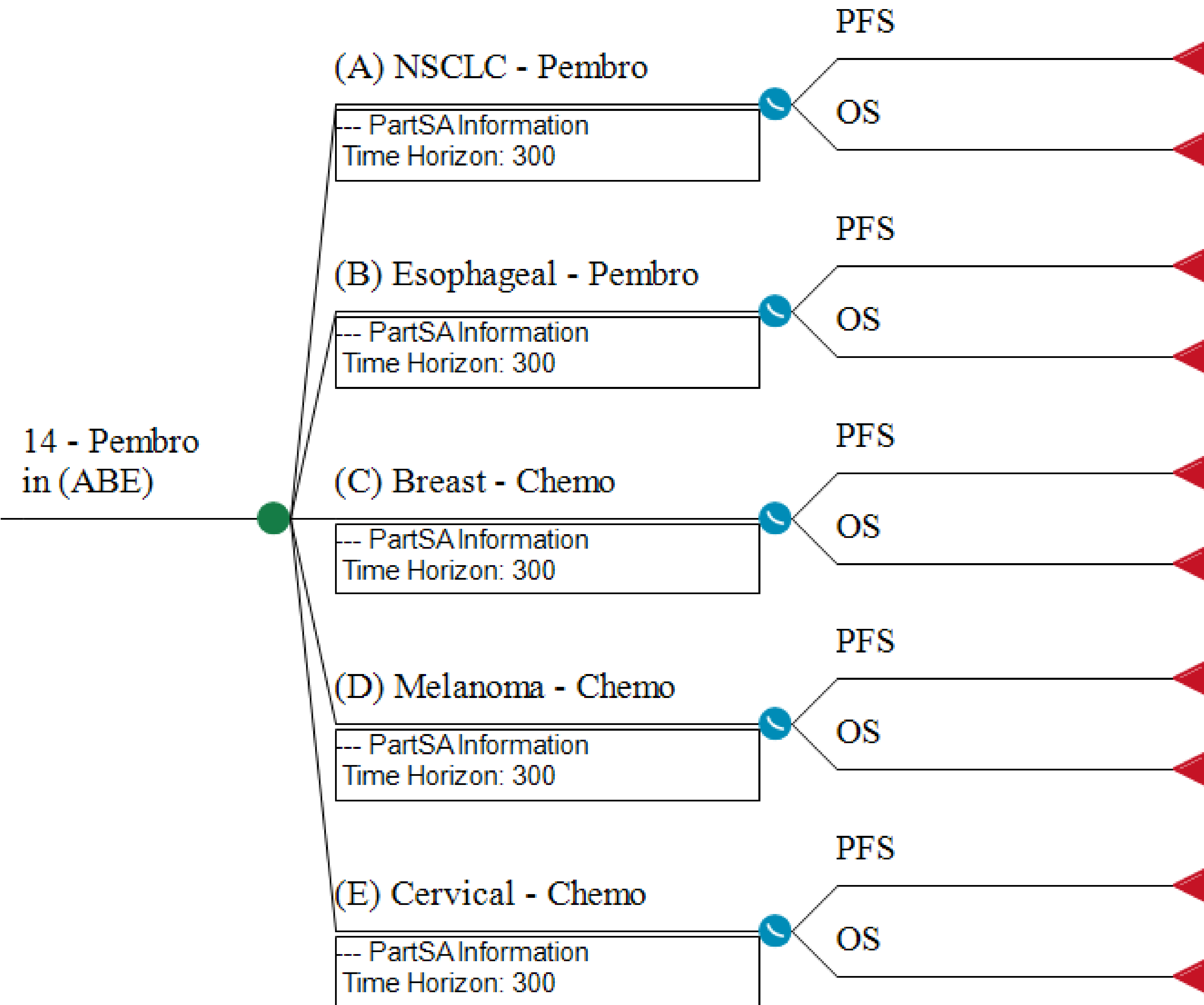
Pembrolizumab is an immune checkpoint inhibitor with more than 20 therapeutic indications in Brazil. To date, it has only been incorporated into the Brazilian public health system (SUS) for the treatment of melanoma, having been rejected for several other indications due to price and cost-effectiveness concerns.

### OBJECTIVE

This study aimed to evaluate the cost-effectiveness of pembrolizumab across five high-impact oncological indications and to propose pricing arrangements that improve SUS efficiency by maximizing the number of patients treated.

### METHODS

A partitioned survival analysis was conducted for pembrolizumab across five selected indications based on performance in the ESMO-MCBS: (A) non-small cell lung cancer (NSCLC), (B) esophageal cancer, (C) triple-negative breast cancer, (D) melanoma, and (E) cervical cancer. A total of 32 possible combinations of therapeutic strategies were evaluated, considering a base case scenario in which chemotherapy was used across all indications. The model adopted a lifetime horizon (300 months), with monthly cycles and a 5% discount rate. Supportive care costs were defined in consultation with oncologists from INCA and based on Brazilian Ministry of Health clinical guidelines (PCDTs). Chemotherapy costs were obtained from DATASUS and adjusted by a factor of 2.8, except for melanoma. Pembrolizumab dosing was set at 200 mg per cycle every three weeks, for up to 24 months or until disease progression. Overall survival and progression-free survival curves were extracted from published studies using WebPlotDigitizer and fitted to parametric survival functions based on visual inspection and AIC/BIC criteria. Hazard curves were derived for sensitivity analysis and calibrated to avoid cross-over. The prevalence of each indication was used to weight costs and effectiveness across the 32 treatment combinations, ensuring that each indication's impact on the model reflected its relative representation in the population.



Schematic representation of alternative 14 out of 32. In this scenario, NSCLC, esophageal, and cervical cancer indications use pembrolizumab, while breast cancer and melanoma use chemotherapy.

### RESULTS

At the price (BPS) of \$3,175.14 per vial (100 mg), none of the 32 alternatives was cost-effective (at a threshold of \$21,000 per life-year gained). Only five alternatives were non-dominated, and treating only breast cancer patients (indication C) was the dominated strategy with the lowest ICER (see table below).

A univariate deterministic sensitivity analysis on the price of pembrolizumab shows that reducing the vial price to \$761.20 changes the cost-effectiveness ranking, and treating only melanoma patients (indication D) becomes the only cost-effective strategy (ICER of \$21,000 per life-year gained).

Strategy	Cost (R\$)	Incr. Cost (R\$)	Life Years	Incr. Life Years	ICER R\$/life years
Strategy 0 (Chemo Only)	10.731,77		1,96		
Strategy 30 (C)	22.927,55	12.195,79	2,05	0,09	128.689,30
Strategy 16 (CD)	27.608,41	4.680,86	2,09	0,04	131.045,03
Strategy 24 (CDE)	70.994,39	43.385,98	2,4	0,31	139.450,36
Strategy 13 (BCDE)	77.714,56	6.720,17	2,44	0,04	163.911,96
Strategy 1 (ABCDE)	119.382,45	41.667,90	2,66	0,22	185.721,74

### Pricing Scenarios and Expansion of Cost-Effective Indications

**Threshold:** \$21,000 per life-year gained

Progressive price reductions enable **new indications to become cost-effective**, expanding patient access while maintaining efficiency.

### Key Findings:

**\$761 per vial** → Adds melanoma only (D) while remain cost-effective

**\$524.80 per vial** → Adds breast cancer (C) while remaining cost-effective

**\$450.60 per vial** → Adds cervical cancer (E)

**\$423 per vial** → Adds esophagus cancer (B)

**\$298.00 per vial** → All indications become cost-effective

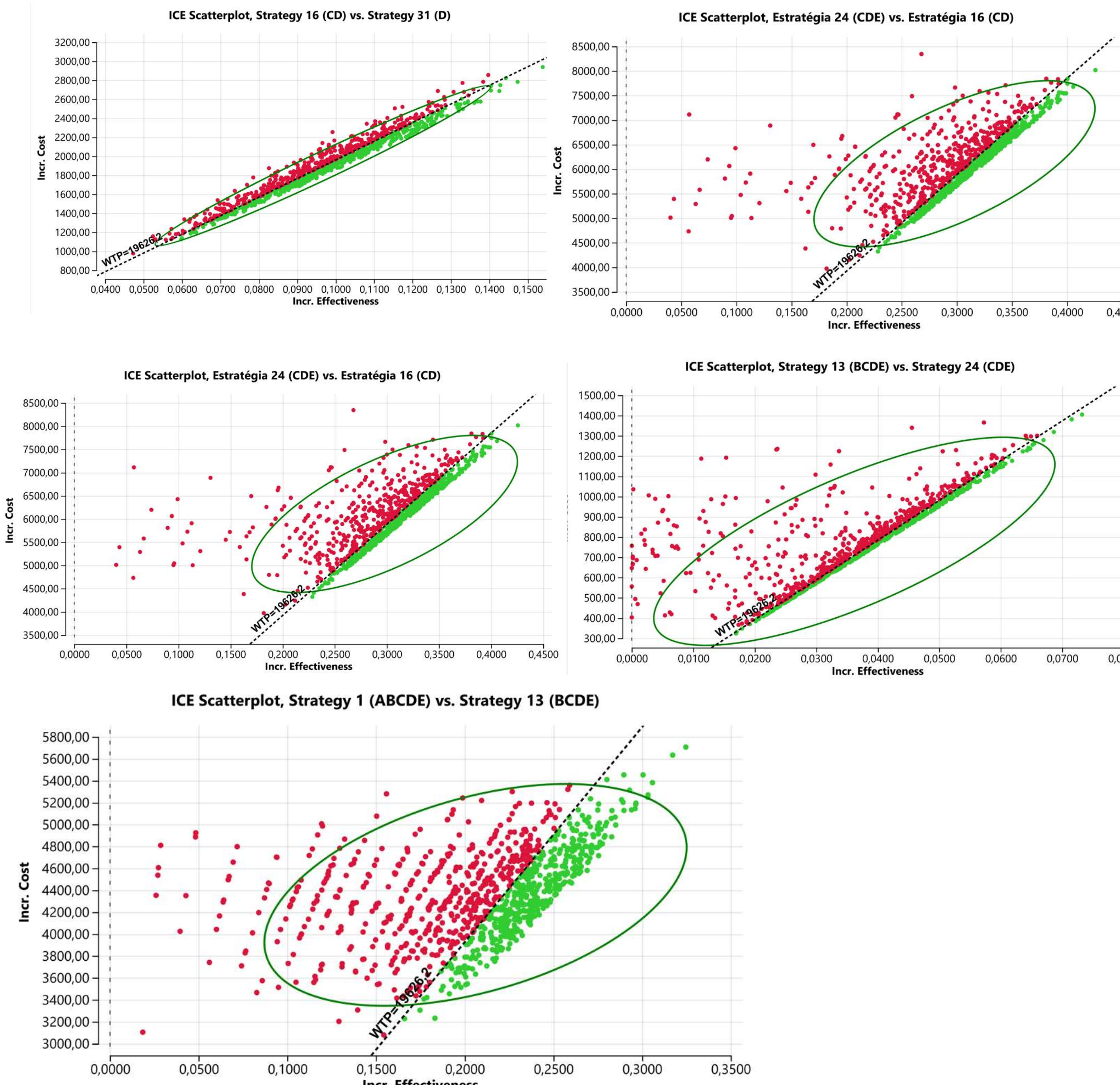
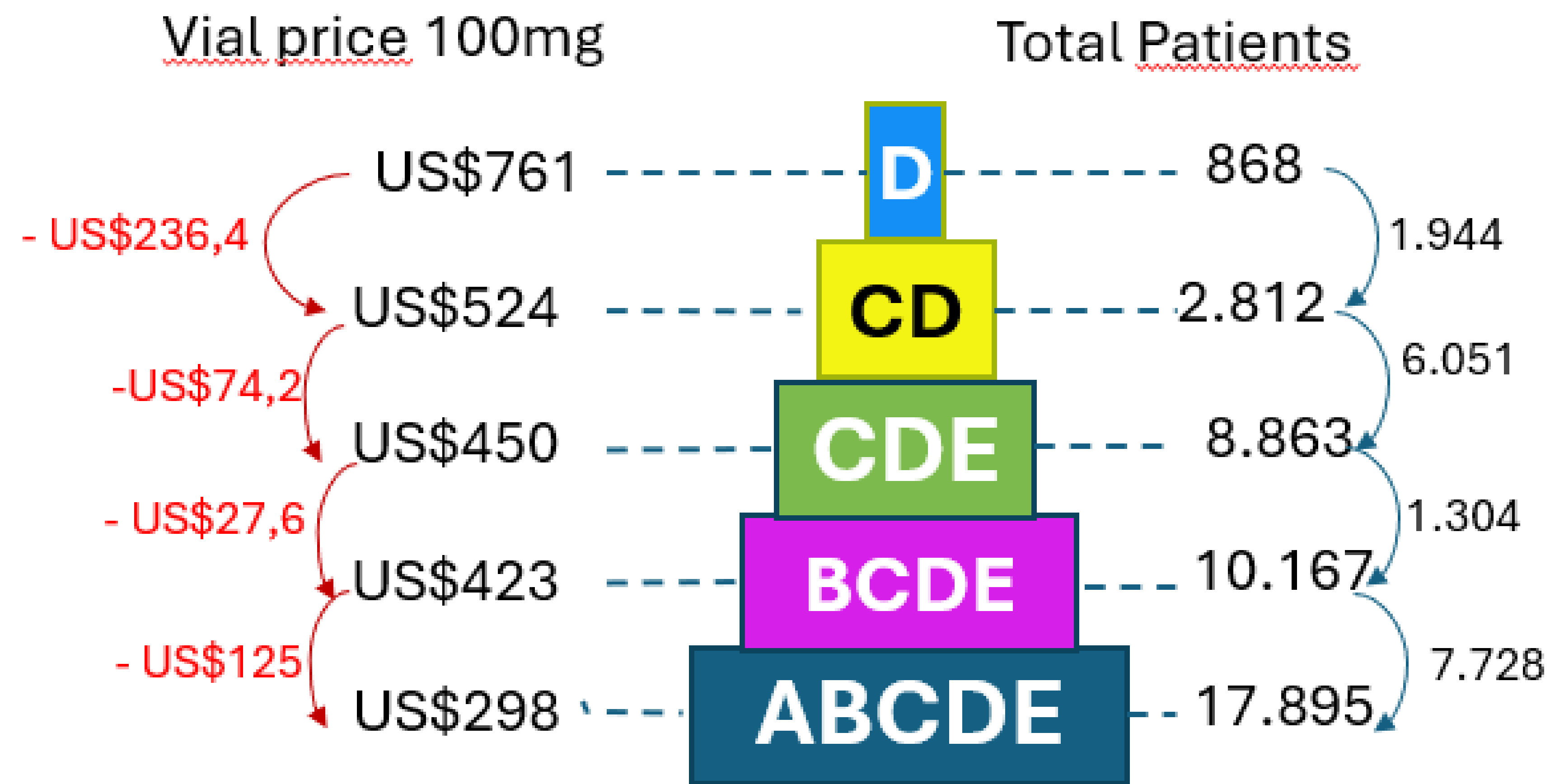
Total: **17,895 patients treated**

A sequence of discounts maintains the reimbursement of the drug efficient for the healthcare system as new indications are added.

Discounts of:

- **US\$2,413.8 (melanoma),**
- **US\$236.4 (breast),**
- **US\$74.2 (cervical),**
- **US\$27.6 (esophageal),**
- **US\$125 (lung).**

The Pyramid Figure in next column show this relationship.



Proposed prices and their respective discounts were validated using scatter plots in probabilistic sensitivity analyses. Across all plots, the proportion of simulations falling below the threshold of US\$21,000 per life-year was approximately 50%

### CONCLUSION

In conclusion, merging the insights from our results and the broader methodological literature, we advocate for robust frameworks that address price-indication interactions and conditional reimbursement strategies. This integration can facilitate sustainable access, informed negotiation, and the identification of true health value for pembrolizumab and other innovative therapies in the Brazilian public health system.