

Cost-Effectiveness of Pembrolizumab in First-Line Recurrent/Metastatic Head and Neck Squamous Cell Cancer in Brazil

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Introduction

- Head and neck cancer (HNC) includes tumors in areas like the oral cavity, larynx, oropharynx, and hypopharynx, with head and neck squamous cell carcinoma (HNSCC) making up about 90% of cases¹
- HNC is the seventh most common cancer globally, with more than 660,000 new cases and 325,000 deaths reported annually.² In Brazil, 2022 statistics showed approximately 61,504 new HNSCC cases and 16,505 associated deaths³
- Stage IVC metastatic HNSCC is rare at diagnosis (3.7% of cases), while most patients present with stage III-IVB, facing a 30%-45% recurrence risk. The 5-year survival rate for stage IVC is only 14.2%⁴
- The KEYNOTE-048 trial found that pembrolizumab, used alone or with chemotherapy, significantly improved overall survival for patients with recurrent or metastatic (R/M) HNSCC⁵

Objective

This study evaluated the cost-effectiveness of pembrolizumab either as monotherapy or in combination with platinum + 5-fluorouracil (5-FU) vs cetuximab + platinum + 5-FU for the first-line treatment of R/M HNSCC from a public health care system perspective in Brazil.

Methods

Model structure

A 3-state cohort-based partitioned survival model was developed to predict the lifetime costs and health outcomes of treatment with pembrolizumab, either as monotherapy or in combination with platinum-based therapies (cisplatin or carboplatin) plus 5-FU vs cetuximab + platinum + 5-FU and platinum + 5-FU. The model structure consists of 2 health states; ie, progression-free (PF) and progressed disease (PD), and a single state for death (all-causes). The time horizon was 40 years, using weekly intervals and a piecewise approach. It incorporated Kaplan-Meier (KM) curves for progression-free survival (PFS) up to 52 weeks and overall survival (OS) up to 80 weeks, with parametric curves for extrapolation beyond these points. Time on treatment was based on KM data, with a maximum treatment duration of 24 months for pembrolizumab.

Clinical data

Clinical data for pembrolizumab monotherapy and combination therapy came from the KEYNOTE-048 study for CPS≥1 (combined positive score) and the overall population, while data for platinum + 5-FU were obtained through network meta-analysis (NMA). Parametric distributions for PFS, time on treatment, and OS were developed from regression survival models based on the trial data, with model selection based on goodness of fit metrics like Akaike information criterion (AIC) and Bayesian information criterion (BIC). The 2-stage method to adjust for treatment switching was used in the base case analysis to account for the bias in the estimation of OS in the comparators arm, attributable to patients switching to immunotherapies.

Costs data

The health care costs included the costs of treatment (drug acquisition, administration, and subsequent therapy), disease management, and management of treatment-related adverse events (TRAEs). Resource use was based on published literature sources, and the resource use cost inputs were sourced from Brazil specific sources⁶.

Utility data

Utility inputs were derived from the EQ-5D-3L data collected in KEYNOTE-048 using Brazilian algorithm. Costs and health outcomes were discounted based on an annual discount rate of 5%, following Brazilian Ministry of Health guidelines.

Results

Monotherapy CPS ≥1

Over a lifetime horizon, pembrolizumab monotherapy demonstrated an incremental gain of 0.772 quality-adjusted life-years (QALYs) compared to cetuximab plus chemotherapy in the CPS ≥ 1 population, with an additional cost of R\$65,303. The incremental cost-effectiveness ratio (ICER) per QALY was R\$84,557 (**Table 1**)

Table 1. Results pembrolizumab monotherapy vs cetuximab + platinum + 5-FU

Interventions	Total LYs	Total QALYs	Total costs (R\$)	ICER (R\$/QALY)
Pembrolizumab monotherapy	2.344	1.664	177,333	84,557
Cetuximab + platinum + 5-FU	1.269	0.891	112,030	

ICER, incremental cost-effectiveness ratio; LY, life year; QALY, quality-adjusted life year; FU, Fluorouracil.

Combination therapy all patients

Considering the all- comers population, there was an incremental gain of 0.911 QALYs at an additional cost of R\$78,176 resulting in an ICER per QALY of R\$85,828 for pembrolizumab combination therapy compared to cetuximab + platinum + 5-FU (**Table 2**).

Table 2. Results pembrolizumab combination therapy vs cetuximab + platinum + 5-FU

Interventions	Total LYs	Total QALYs	Total costs (R\$)	ICER (R\$/QALY)
Pembrolizumab combination therapy	2.567	1.794	193,639	85,828
Platinum + 5-FU + Cetuximab	1.272	0.884	115,464	

ICER, incremental cost-effectiveness ratio; LY, life year; QALY, quality-adjusted life year; FU, Fluorouracil. These results were lower than the willingness-to-pay threshold of R\$120,000, which is 3 times the gross domestic product per capita of Brazil.⁷

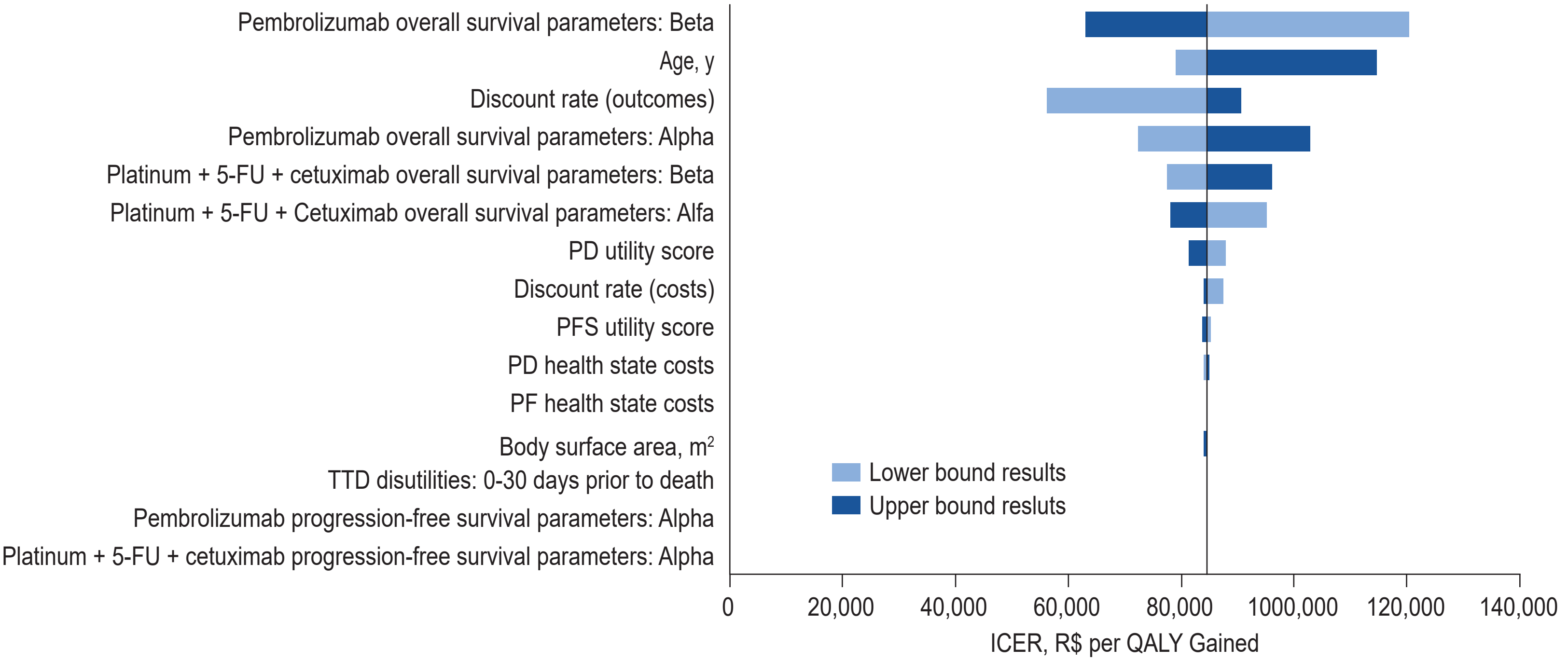
Sensitivity analysis

- The probabilistic sensitivity results indicated an 86.50% acceptance probability for pembrolizumab monotherapy at the R\$120,000 per QALY threshold vs cetuximab + platinum + 5-FU, and 84.00% for pembrolizumab combination therapy against cetuximab + platinum-based therapies + 5-FU
- In the monotherapy scenario, the incremental cost per QALY ranged between R\$56,245 per QALY and R\$120,163 per QALY in the one-way sensitivity analyses (OWSAs). Survival parameters associated with pembrolizumab were key model drivers; survival parameters for cetuximab and platinum + 5-FU also had a substantial influence on the ICER. The OWSAs are summarized in a tornado diagram in **Figure 1** that illustrates the other key factors of influence

References

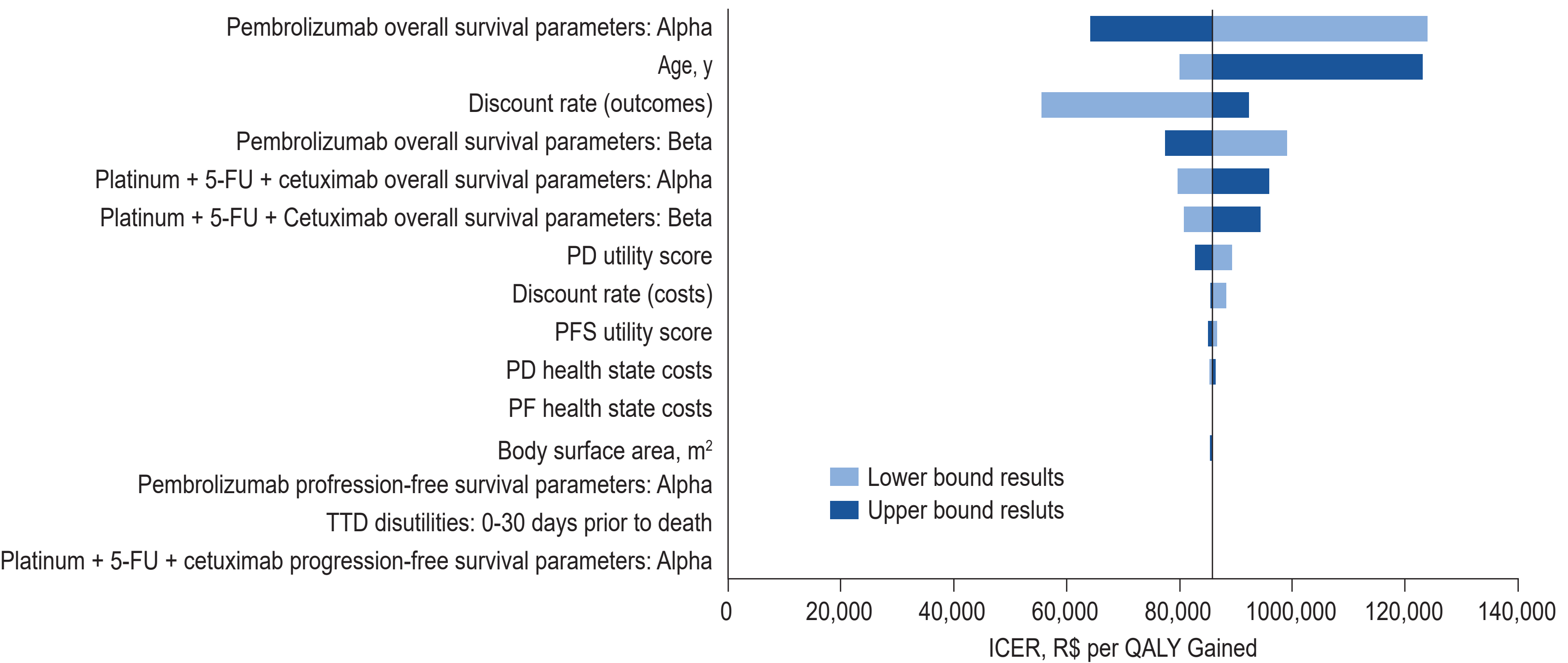
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Figure 1. OWSA. Tornado. Pembrolizumab monotherapy vs cetuximab + platinum + 5-FU



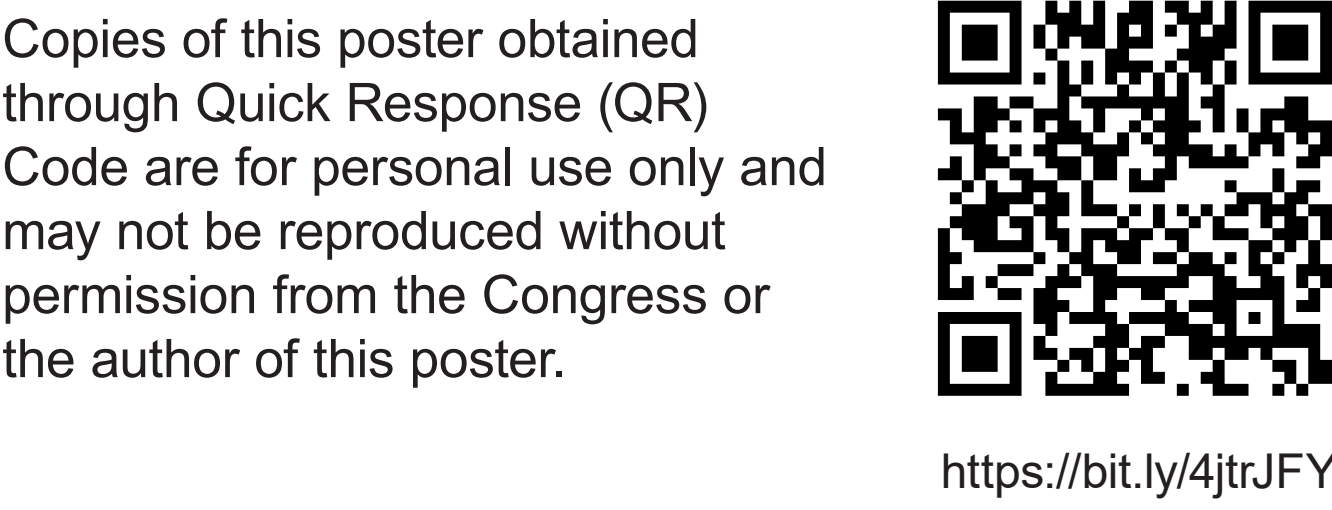
- In the combination scenario, the incremental cost per QALY ranged between R\$55,571/QALY and R\$123,876/QALY in the OWSAs. The primary model driver identified was the survival parameters associated with pembrolizumab. The tornado diagram in **Figure 2** illustrates the other key factors of influence

Figure 2. OWSA Tornado. Pembrolizumab combination therapy vs cetuximab + platinum + 5-FU



Conclusions

- Whether used as a monotherapy or in combination with platinum and 5-FU, pembrolizumab demonstrated greater clinical benefits and cost-effectiveness compared to the KEYNOTE-048 trial comparator of cetuximab combined with platinum and 5-FU over a 40-year time horizon
- Health state utility values and survival parameters were the primary drivers of these results, as evidenced by both deterministic and probabilistic sensitivity analyses
- Pembrolizumab, in either scenario, provided significant QALY gains for patients with R/M HNSCC at only a modest increase in costs, making it a cost-effective treatment option compared to the combination of cetuximab, platinum, and 5-FU in Brazil



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