



Cost effectiveness and estimate of economical impact of immune checkpoint inhibitors for NSCLC relative to PD-L1 expression



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Background

- Immune checkpoint inhibitors are active in the treatment of NSCLC.

- Some studies showed that immune checkpoint inhibitors are superior to docetaxel in the second-line setting of treatment.

- Programmed cell death-ligand 1 (PD-L1) receptor expression is related to the mechanism of action of immune checkpoint inhibitors.

- As a consequence, it is being studied as a predictive biomarker.

- PD-L1 receptor expression is predictive of a higher degree of responses and longer progression-free survival with the use of checkpoint inhibitors. However, these treatments are very expensive.

- Delivering high quality cancer care at an affordable cost is one of the main challenges for health care professionals and policy makers, especially in low- and middle-income countries.

- The objective of our study is to assess the economic impact of nivolumab and pembrolizumab with and without the use of PD-L1 as a biomarker in Brazil.

Material and Methods

- A decision-analytic model was developed to determine the cost-effectiveness of PD-L1 testing and second-line treatment with the two FDA-approved immune checkpoint inhibitors, nivolumab and pembrolizumab, versus docetaxel.

- The model used outcomes data from randomized clinical trials and drug acquisition costs from the United States, using a Medicare perspective.

- Published utility values were used. Health effects were expressed as quality-adjusted life-years (QALY) and incremental cost-effectiveness ratios (ICER) were calculated.

- Thereafter, we used epidemiologic data to estimate the economic impact of the treatment with and without the use of PD-L1 as a biomarker.

Results

- We included three RCTs (two with NIVO and one with PEMBRO).

- The estimated number of cases eligible for therapy with immune checkpoint inhibitors in Brazil is 4,733 each year in 2016 and 2017.

- Table 1 summarizes our findings for five different scenarios of treatment in Brazil.

SCENARIO	QALY GAIN	ICER (US\$)	Life-Years Saved	Years of Life not saved	% Not Treated	Total Cost (US\$)	Impact on total cancer drug expenditure	Cost/LYS (US\$)
NIVO ALL COMERS	0,148	129 K	885	0	0%	173 million	21,1%	196 K
NIVO PDL-1 > 1%	0,201	108 K	570	315	46%	93 million	11,3%	164 K
PEMBRO PD-L1 > 1%	0,138	137 K	666	NA	34%	100 million	12,1%	150 K
NIVO ALL SQ/> 1% NSQ	0,216	99 K	738	147	35%	116 million	14,0%	157 K
PEMBRO PD-L1 > 50%	0,164	116 K	285	NA	72%	43 million	5,2%	151 K

- Figure 1 shows the probabilistic sensitivity analysis

- Figure 2 shows the cost-effectiveness relative to PD-L1 expression.

- Figure 3 shows the economic impact estimate.

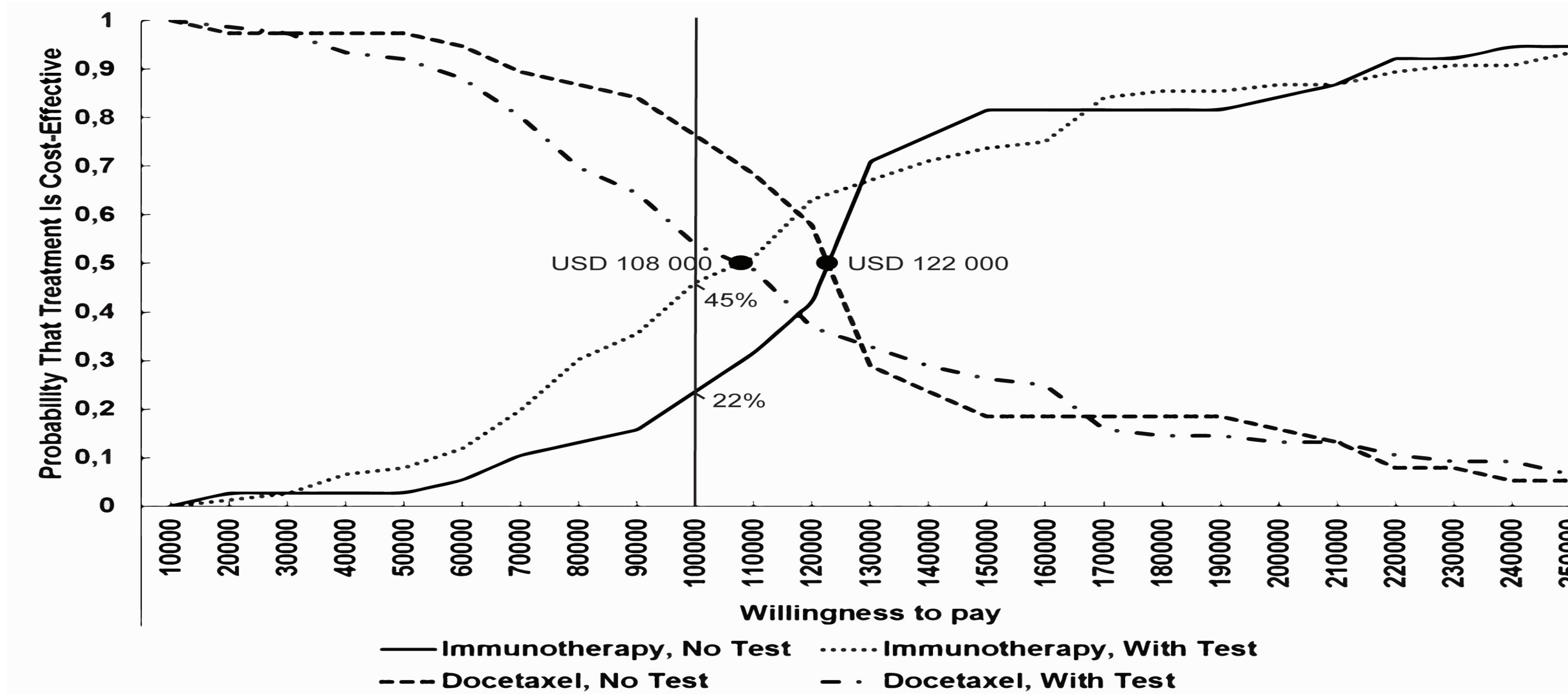


Figure 1. Probabilistic Sensitivity Analysis

Conclusions

- PD-L1 expression was associated with higher activity with immune checkpoint inhibitors.

- Using PD-L1 receptor expression as a biomarker also improved the cost-effectiveness of immune checkpoint inhibitors.

- Nevertheless, this effect was less robust among patients with squamous histology.

- A standard assessment and an optimal cut-off value remain unclear.

- Further biomarker development is warranted.

Figure 2. Cost-effectiveness of immune checkpoint inhibitors in NSCLC according to PD-L1 expression

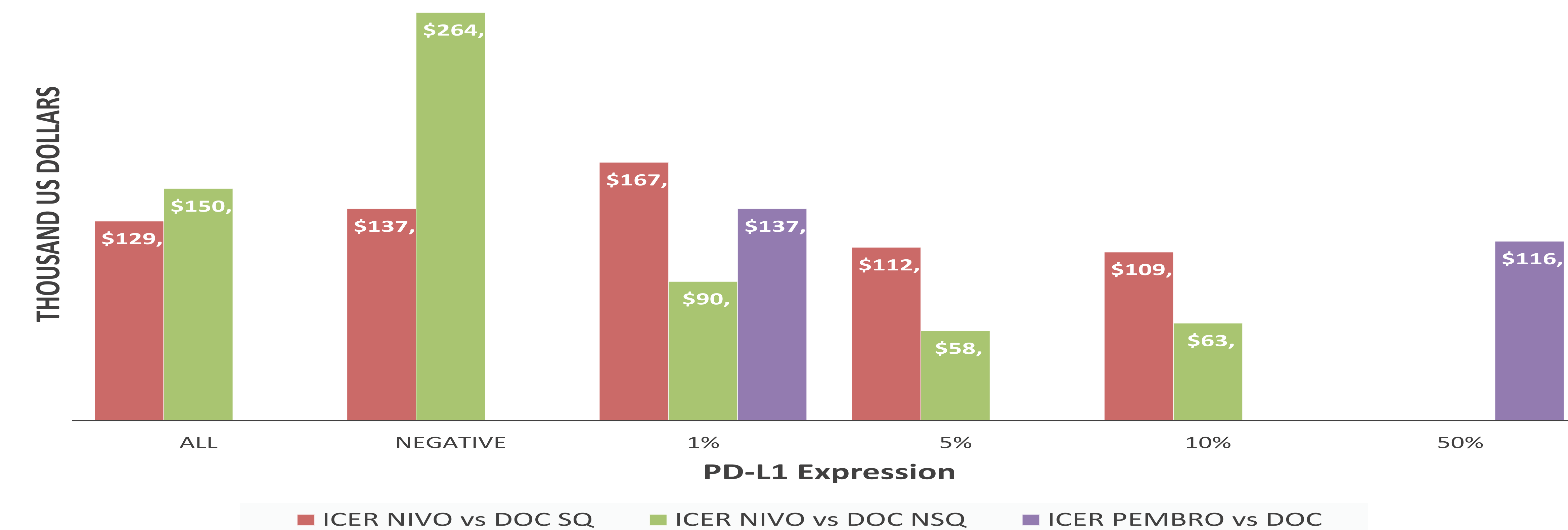
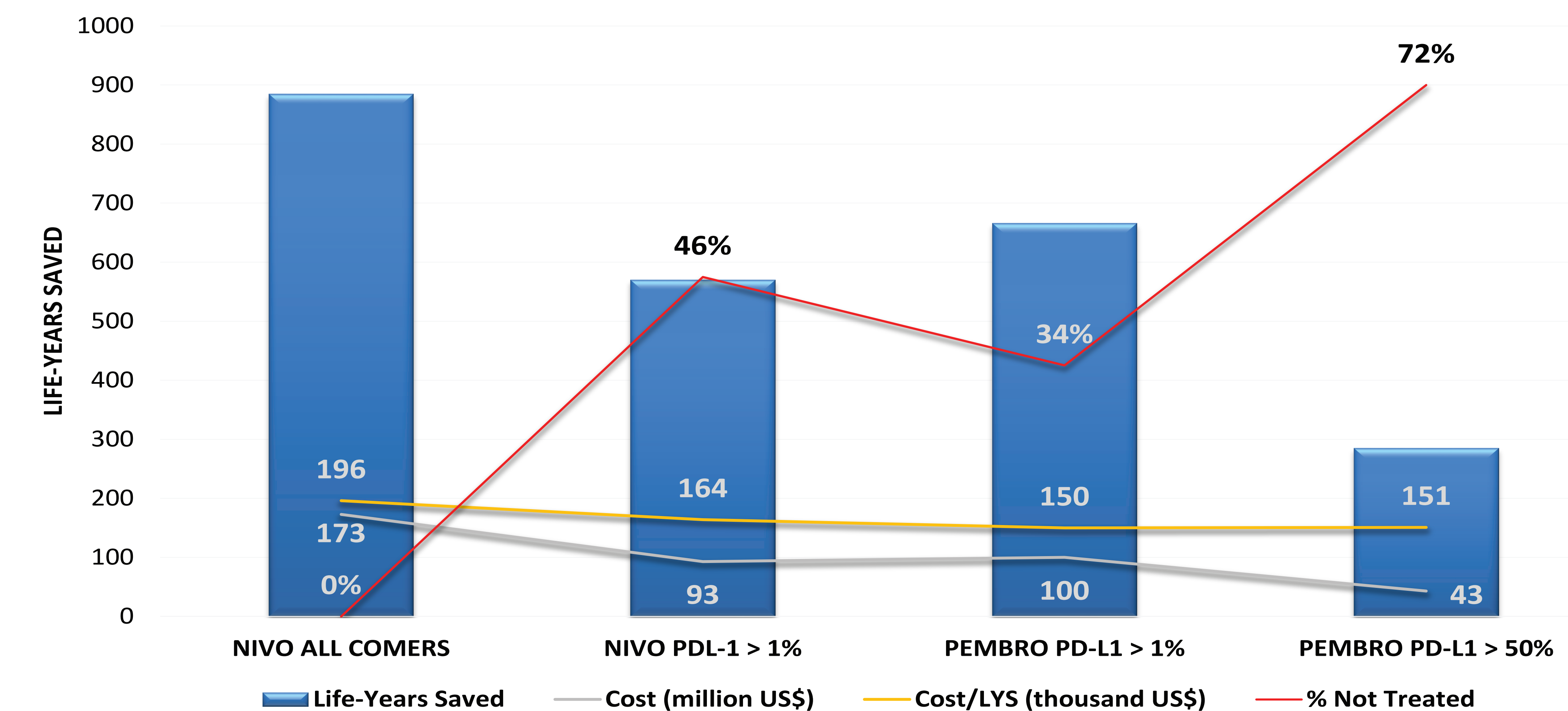


Figure 3. Economic impact estimate in Brazil



References

1. JPT H, S G. Cochrane Handbook for Systematic Reviews of Interventions: The Cochrane Collaboration; 2011. Available from: www.cochrane-handbook.org.
2. Rizvi NA, Mazières J, Planchard D, Stinchcombe TE, Dy GK, Antonia SJ, et al. Activity and safety of nivolumab, an anti-PD-1 immune checkpoint inhibitor, for patients with advanced, refractory squamous non-small-cell lung cancer (CheckMate 063): a phase 2, single-arm trial. Lancet Oncol. 2015;16(3):257-65.
3. Topalian SL, Hodi FS, Brahmer JR, Gettinger SN, Smith DC, McDermott DF, et al. Safety, activity, and immune correlates of anti-PD-1 antibody in cancer. N Engl J Med. 2012;366(26):2443-54.
4. Brahmer J, Reckamp KL, Baas P, Crinò L, Eberhardt WE, Poddubskaya E, et al. Nivolumab versus Docetaxel in Advanced Squamous-Cell Non-Small-Cell Lung Cancer. N Engl J Med. 2015. IL: J Clin Oncol; 2015. p. (suppl; abstr LBA109).
5. Paz-Ares L, Horn L, Borghaei H, Spigel D, Steins M, Ready N, et al. Phase III, randomized trial (CheckMate 057) of nivolumab (NIVO) versus docetaxel (DOC) in advanced non-squamous cell (non-SQ) non-small cell lung cancer (NSCLC). ASCO Annual Meeting; Chicago, IL: J Clin Oncol; 2015. p. (suppl; abstr 8025).
7. Antonia S, Gettinger S, Chow L, Juergens R, Borghaei H, Shen Y, et al. Nivolumab (anti-PD-1; BMS-936558, ONO-4538) and ipilimumab in first-line NSCLC: Interim phase I results. ASCO Annual Meeting; Chicago, IL: J Clin Oncol; 2014.
8. Rizvi N, Brahmer J, Ou S, Segal N, Khleif S, Hwu W, et al. Safety and clinical activity of MEDI4736, an anti-programmed cell death-ligand 1 (PD-L1) antibody, in patients with non-small cell lung cancer (NSCLC). ASCO Annual Meeting; Chicago, IL: J Clin Oncol; 2015. p. (suppl; abstr 8032).
9. Antonia S, Goldberg S, Balmanoukian A, Sanborn R, Steele K, Narwal R, et al. Phase Ib study of MEDI4736, a programmed cell death ligand-1 (PD-L1) antibody, in combination with tremelimumab, a cytotoxic T-lymphocyte-associated protein-4 (CTLA-4) antibody, in patients (pts) with advanced NSCLC. ASCO Annual Meeting; Chicago, IL: J Clin Oncol; 2015. p. (suppl; abstr 3014).
10. Garon EB, Rizvi NA, Hui R, Leigh N, Balmanoukian AS, Eder JP, et al. Pembrolizumab for the Treatment of Non-Small-Cell Lung Cancer. N Engl J Med. 2015.