PCN102

COST-EFFECTIVENESS OF NIVOLUMAB VERSUS DACARBAZINE IN FIRST-LINE TREATMENT OF ADVANCED MELANOMA FROM THE BRAZILIAN PUBLIC HEALTHCARE SYSTEM PERSPECTIVE

Oliveira APCD[1], Miadaira S[1], Koloszuk A[1], Marinheiro P[1], Bernardino G[1]
[1]Bristol-Myers Squibb, Sao Paulo, Brazil

Introduction

- Nivolumab (NIVO) received authorization from the Brazilian National Health Surveillance Agency (ANVISA) in December 2016 for the treatment of advanced melanoma (unresectable or metastatic).[1]
- 6,260 new cases of melanoma in Brazil were estimated in 2018.[2]
- There is no official guideline for the treatment of advanced melanoma in the Brazilian Public Healthcare System, and the treatment most commonly prescribed is dacarbazine (DTIC).[3]
- The objective of this study was to evaluate the cost-effectiveness of NIVO therapy in relation to DTIC as first-line treatment in advanced metastatic melanoma, from the perspective of the Brazilian Public Healthcare System (SUS).

Methods

- A cost-effectiveness analysis was conducted to compare 1st line treatment with NIVO versus DTIC in patients with advanced melanoma regardless of BRAF mutation status attended by SUS. Effectiveness was assessed in terms of accrued life years while cost were focused on direct medical costs. The time horizon used in this study was 30 years.
- The three-state model employed a partitioned survival analysis approach in which progression-free and overall survival were modeled based on the data from the pivotal clinical studies CheckMate 066 (DTIC), 10.9 months median follow-up data, and CheckMate 067 (NIVO monotherapy), minimum 36 month minimum follow-up data **(Figure 1, 2 and 3)**. The best parametric function to extrapolate the overall survival and progression free survival was chosen assessing the fit criteria's AIC (Akaike Information Criterion) and BIC (Schwarz Bayesian Criterion) (**Table 1**) [4,6].

Figure 1. Three-state model with a partitioned survival approach adopted for cost-effectiveness analysis

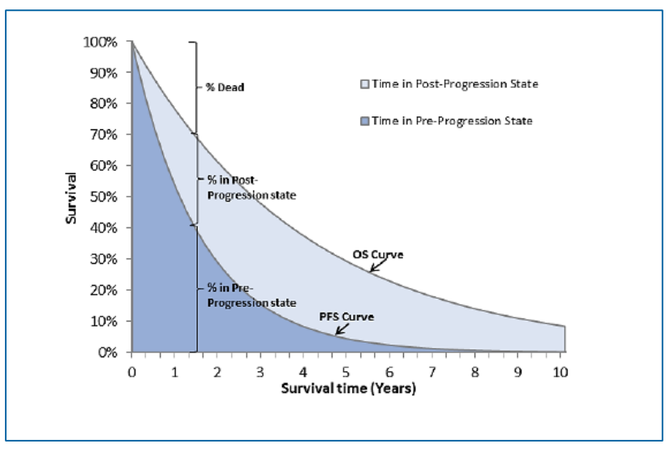


Table 1. Selection of extrapolation for the overall survival and progression-free survival curves

Extrapolation	AIC	BIC
Gompertz	3.919	3.931
Gamma	3.986	3.998
LogNormal	4.102	4.114
LogLogistic	4.109	4.120

- DTIC was selected as a comparator for this analysis because it is the most prescribed chemotherapy drug in the Brazilian Public Healthcare System.
- The Brazilian background mortality rates were considered.[5]
- A non-optimization of vials premise was assumed.
- Sensitivity analyses were performed to evaluate the overall robustness of the results.
- As the model takes the perspective of a Brazilian Public Healthcare System, Indirect costs were not taken into account. The costs considered in the model were: treatment (drug, administration costs), AE management (treatment of AE, laboratory and imaging tests) and disease management (follow-up procedures and medical visits).
- This analysis considered only grade 3-4 AEs. Their frequencies were derived from clinical trials for each comparator.[4,6]
- Disease management follow-up procedures and management of AEs were defined by published literature and validated by clinical experts opinion.
- Costs for administration, adverse events and procedures were estimated using a micro-costing approach, and prices were obtained from official Brazilian price lists – CMED (Drug Market Regulation Chamber) and SIGTAP (Management of Table of Procedures, Medicines, Orthoses, Prostheses and Materials Public Healthcare System) (**Table 2**).[7,8]
- Considering the budget restrictions of the Brazilian Government, a discount was considered in the cost of medications (**Table 3**).

Table 2. Adverse Event Management Costs

Adverse Event	Cost (BRL)
Fever	172.66
Myalgia / Pain	535.44
Skin reaction	50.39
Fatigue	35.99
Diarrhea	406.03
Nausea / Vomiting	383.67
Colitis	533.30
Dyspnea	109.50
Anemia	606.78
Thrombocytopenia	67.95
Neutropenia	304.85

Table 3. Product prices

Product	List Price (BRL)	Proposed price (BRL)
Nivolumab 40 mg	3,363.38[a]	2,018.03
Nivolumab 100mg	8,408.43[a]	5,045.06
Dacarbazine 200mg[c]	121.37[b]	12.14

[a] State taxes: 18%; [b] State taxes: 0%; [c] Eurofarma - 1 vial

Results

- Treatment with NIVO yielded 5.57 accrued Life Years Gained (LYG) and a total cost of BRL 334,571.14. While DTIC therapy was associated with 1.20 LYG and a total cost of BRL 8,902.24. As a result treatment with NIVO resulted in an incremental cost-effectiveness ratio of BRL 74,578.04 per LYG when compared to DTIC (**Table 4**).

Table 4. Results of the cost-effectiveness analysis of NIVO compared to DTIC

	NIVO	DTIC	Incremental	ICER (BRL/LYG)
LYG	5.57	1.20	4.37	**74,578.04**
Total cost (BRL)	334,571.14	8,902.24	325,668.90	

Figure 2. Modeled overall survival curves

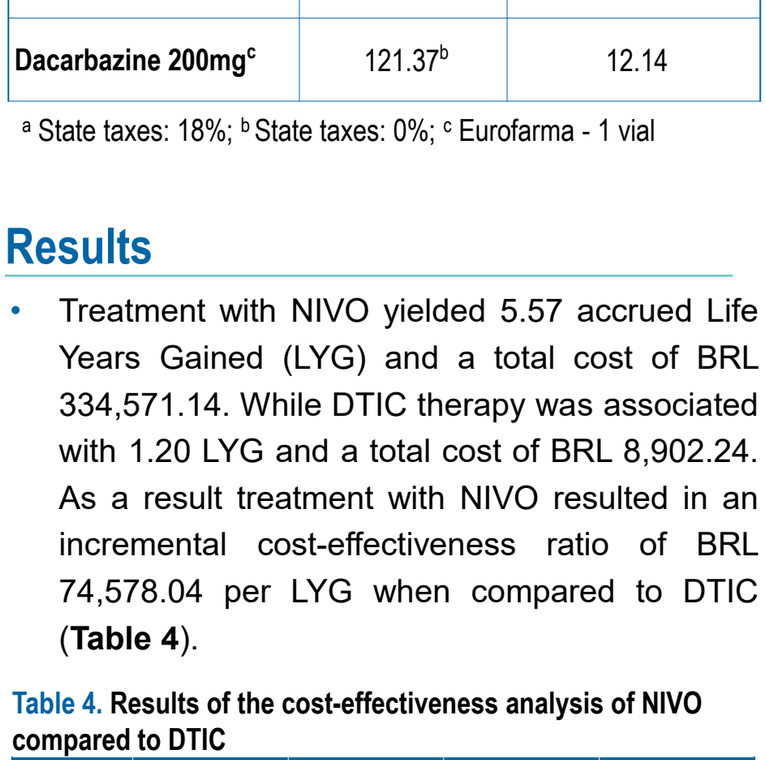
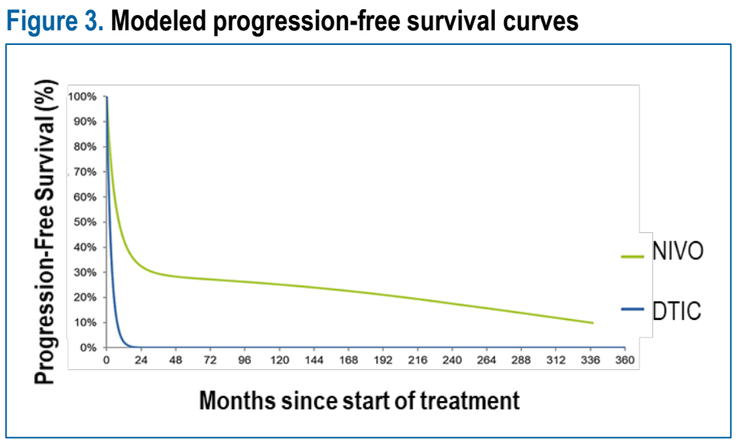


Figure 3. Modeled progression-free survival curves



- Univariate analysis demonstrated that discounts rates was the most important driver of cost-effectiveness results (**Figure 4**).
- The multivariate analysis shows that 95.9% of the simulations are below a cost-effectiveness threshold of 3 GDPs/capita and, therefore, treatment with NIVO can be considered as a cost-effective intervention for the Brazilian health care system (**Figure 5**).

Figure 4. Tornado Diagram - Univariate Sensitivity Analysis (BRL)

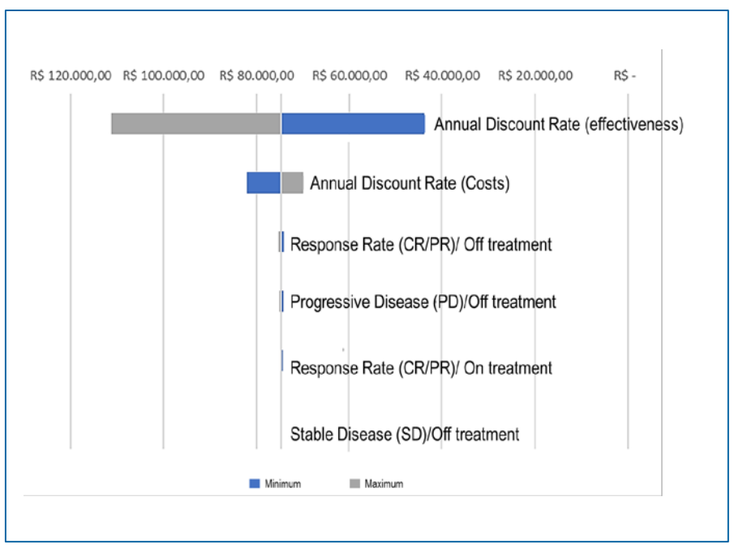
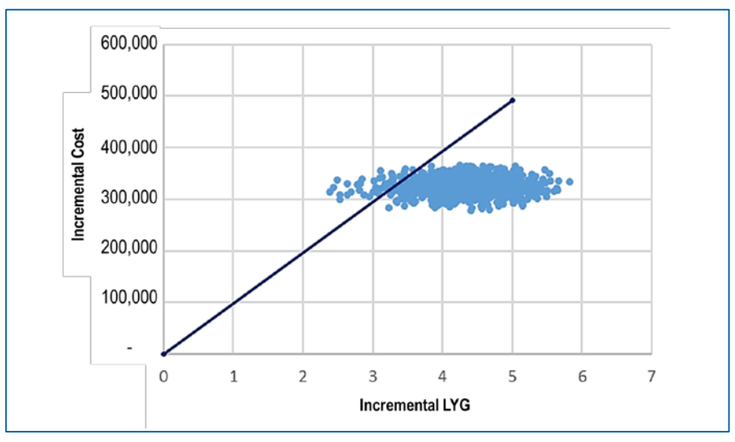


Figure 5. Dispersion Diagram - Probabilistic Sensitivity Analysis



Conclusions

Considering the Brazilian Ministry of Health's Economic Assessment Guideline, technologies with ICERs up to three times GDP (gross domestic product) per capita are considered cost-effective (3 x GDP = BRL 98,241.00).[9] To this end, the results show that NIVO is a cost-effective intervention. Sensitivity analyses show that NIVO has a 95.9% likelihood of being cost-effective, demonstrating the robustness of the obtained result. This study suggests that in patients diagnosed with melanoma treatment with nivolumab as a first line therapy is associated with clinically meaningful survival benefit versus DTIC and constitutes a cost-effective use of Brazilian Public healthcare resources.

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Acknowledgments

- Bristol Myers Squibb (Princeton, NJ) and ONO Pharmaceutical Company Ltd. (Osaka, Japan)
- This study was supported by Bristol Myers Squibb
- All authors contributed to and approved the presentation.

Presented at Virtual ISPOR 2020, the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) Annual International Meeting; May 18–20, 2020

Email: anapaula.oliveira@bms.com