Title: Cost-Effectiveness of metastatic melanoma treatments in Brazilian Health System perspective

Objective
The objective of this analysis was to evaluate the cost-effectiveness of the best alternative for metastatic melanoma treatment in National Health System (SUS), comparing all possible alternatives between target therapies and immunotherapy.

Methods
The target therapies evaluated were Dabrafenib, Cobimetinib, Vemurafenib and Trametinibe in combination with Dabrafenib. The immunotherapies were Ipilimumab, Nivolumab and Pembrolizumab. All were compared to Dacarbazine, which is the standard treatment in SUS. Targeted therapy treatments are only effective in patients with BRAF mutations that have an estimated incidence of 50% of patients. These strategies were combined with other immunotherapy in half the population without the mutation. A Markov model was constructed comparing treatment strategies from the SUS perspective with a 10-year time horizon. Randomized controlled trials provided progression-free survival and overall survival curves of patients on Dacarbazine treatment, along with Hazard Ratios for both outcomes, across all treatment strategies. Melanoma treatment guidelines and oncologists were consulted to estimate resource utilization, which were priced with procedure database consultation. The prices of the treatments were extracted from information contained in the respective leaflets, in the National Health Databank price (BPS) and in the CMED table. The main outcome of the model was quality-adjusted life years (QALY) and this information was extracted from the international literature. In the sensitivity analysis, a tornado diagram and an acceptability curve were constructed.

Results
Nivolumab was the only non-dominated technology and Ipilimumab underwent extended dominance. Their respective ICER for dacarbazine is R$ 131,879.09 and R$ 218,286.69. The tornado diagram showed that the cost of Nivolumab was the most sensitive variable, with the greatest ability to change model responses but not able to change ICER to acceptable willingness to pay thresholds.