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Budget-Impact Analysis of Encorafenib with Binimetinib for Unresectable or Metastatic Melanoma in BRAFV600-Mutated Patients in an Argentinian Social Security Payer Setting

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INTRODUCTION

Melanoma stands out as the most aggressive and lethal form of skin cancer. Over the past few decades, it´s incidence rate has consistently increased, consequently melanoma-related mortality has also risen[1].

Several key molecular pathways are involved in the onset, proliferation, survival, progression, and invasion[2]. The treatment landscape for unresectable stage III and IV melanoma has undergone a revolutionary transformation, thanks to the introduction of immunotherapies and targeted therapies. Both approaches have demonstrated significantly enhanced survival rates when compared to traditional chemotherapy regimens. The most frequent mutation in melanoma is the BRAF V600 mutation, occurring in 40% to 60% of cutaneous melanoma[3,4]. The BRAF gene encodes a kinase that is part of the mitogen-activated protein kinase (MAPK) signaling pathway. The V600 mutation of BRAF leads to a constitutively active BRAF kinase, stimulates activity of the downstream effector proteins: mitogen-activated protein kinase (MAPK) kinase (MEK) and extracellular signal-regulated kinase (ERK). This leads to tumor growth and disease progression[5].

Melanoma is associated with a substantial direct and indirect economic burden, with the highest costs accrued in the metastatic setting. The introduction of the latest generation treatment options, such as targeted therapies, has led to increased melanoma direct costs, primarily driven by the drug costs incurred by patients with advanced disease and the management of treatment-related adverse events (AE). Encorafenib in combination with binimetinib demonstrated clinical benefits in a large Phase III randomized clinical trial, mainly based on progression free survival[6]. The combination of encorafenib plus binimetinib provides dual inhibition of the MAPK pathway, as encorafenib inhibits BRAF V600E kinase and binimetinib inhibits MEK1 and MEK2 activity[7].

The current scenario highlights the significant challenge into which melanoma is becoming for the worldwide healthcare system.

OBJECTIVES

This study aimed to describe the impact of incorporating encorafenib with binimetinib (a BRAF-MEK inhibitor approach) for the treatment of irresectable or metastatic melanoma in BRAFV600 mutated adult patients from a Social Security perspective in Argentina.

MATERIALS AND METHODS

We developed and adapted the budget-impact model to the local context in accordance with the good practices guidelines of the International Society for Pharmacoeconomics and Outcomes Research (ISPOR). The model estimates the number of patients eligible for treatment with Encorafenib in combination with Binimetinib from the social-security health subsystem perspective, and the budget impact for three years after its adoption. The social-security health subsystem in Argentina includes 26 million people (56% of total population), including the Union HMOs *(Obras Sociales Sindicales)* that cover around 14 million people (30% of the total Argentinean population). For the current analysis, we considered the adult population covered by the Union HMOs (~10 million people). The model compared two scenarios:

- a reference scenario including all the currently available systemic treatments, such as anti-PD-1 and anti-CTL4 monoclonal antibodies and other BRAF-MEK inhibitors;
- a new scenario reflecting the availability of encorafenib+binimetinib.

Healthcare cost parameters were expressed in 2023 US dollars (average exchange rate: $185, Jan 2023). The treatments included were:

Treatment schemes included	Combo or Monotherapy	Mean treatment duration (months)
Encorafenib+Binimetinib	Combo	11.80
Dabrafenib+Trametinib	Combo	11.80
Nivolumab	Mono	6.10
Pembrolizumab	Mono	6.64
Ipilimumab+Nivolumab	Combo	6.64
Cobimetinib+Vemurafenib	Combo	11.80

The model considered drugs´ acquisition costs as well as medical resources associated to patient monitoring, AE management and post-progression management.

Disclosures: *Lucila Rey Ares, Celina Guadalupe Vega, Gustavo Zeballos and María Paula Ascárate are employees of Pfizer Argentina. Pablo Macadam and Natalia Jorgensen received consulting fees from Pfizer Inc for the model adaptation and analysis.*

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RESULTS

We estimated the total number of patients based on the total number of adult female and male affiliates from the social-security health subsystem, using epidemiological data from Argentinian health system and the market shares assumed for encorafenib+binimetinib (Table 1).

TABLE 1	2023	2024	2025	TOTAL
N° adult affiliates (>20 years)	10,893,079	10,893,079	10,893,079	
N° adult patients with newly diagnosed cutaneous melanoma (incidence 0.0048% females/0.0065% males)	618	627	636	1,881
A- N° patients diagnosed at unresectable or metastatic stage (43%) with BRAF mutation (38.5%) at 1L treatment (90%)	92	93	95	280
B- N° patients diagnosed at early stages (57%) progressing to unresectable or metastatic (17%) with BRAF mutation (38.5%) at 1L treatment (90%)	20	21	21	62
Total N° candidate patients (all 1L, A+B)	**112**	**114**	**116**	**342**
Total N° candidate patients to be treated with encorafenib+binimetinib	**8**	**17**	**35**	**60**

Based on this assumptions, Table 2 shows the budget impact of incorporating encorafenib+binimetinib for the treatment of adult patients with unresectable or metastatic melanoma presenting BRAFV600 mutation (in USD):

TABLE 2	2023	2024	2025	TOTAL
Total costs with encorafenib+binimetinib	$17,173,956	$18,503,807	$17,902,580	$53,580,344
Total costs without encorafenib+binimetinib	$17,611,614	$19,374,711	$19,658,013	$56,644338
Net budget impact	**-$437,657**	**-$870,904**	**-$1,755,433**	**-$3,063,994**
Net budget impact per treated patient/year	**-$3,908**	**-$7,640**	**-$15,133**	**-$8,959**
Net budget impact per affiliate/year	**-$0.029**	**-$0.058**	**-$0.118**	**-$0.205**

Lower acquisition costs of encorafenib+binimetinib compared to other available treatments (82% of savings) and post disease progression costs in the new scenario (18% of savings; Figure 1) mainly explain the savings observed.

Figure 1- Distribution of costs (in USD) in the two scenarios considered.

In the deterministic sensitivity analysis, the difference in treatment prices between encorafenib and the other options was the most sensitive variable affecting the budget impact, followed by the treatment duration of encorafenib+binimetinib and the target population to treat.

CONCLUSIONS

In the Union HMOs setting, reimbursement of encorafenib+binimetinib would result in savings for the treatment of irresectable or metastatic melanoma in adult patients with BRAFV600 mutation.

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