



Budget projections and clinical impact of an immuno-oncology class of treatments: Experience in four EU markets

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ABSTRACT

Background: Immunotherapies have revolutionized oncology, but their rapid expansion may potentially put healthcare budgets under strain. We developed an approach to reduce demand uncertainty and inform decision makers and payers of the potential health outcomes and budget impact of the anti-PD-1/PD-L1 class of immuno-oncology (IO) treatments.

Methods: We used partitioned survival modelling and budget impact analysis to estimate overall survival, progression-free survival, life years gained (LYG), and number of adverse events (AEs), comparing “worlds with and without” anti-PD-1/PD-L1s over five years. The cancer types initially included melanoma, first and second line non-small cell lung cancer (NSCLC), bladder, head and neck, renal cell carcinoma, and triple negative breast cancer [1]. Inputs were based on publicly available data, literature, and expert advice.

Results: The model [2] estimated budget and health impact of the anti-PD-1/PD-L1s and projected that between 2018–2022 the class [3] would have a manageable economic impact per year, compared to the current standard of care (SOC).

The first country adaptations showed that for that period Belgium would save around 11,100 additional life years and avoid 6,100 AEs. Slovenia - 1,470 LYGs and 870 AEs avoided; Austria - respectively 4,200, 3,000; Italy - 19,800, 6,800. For Austria, the class had a projected share of about 4.5 % of the cancer care budget and 0.4 % of the total 2020 healthcare budget. For Belgium, Slovenia, and Italy - respectively 15.1 % and 1.1 %, 12.6 %, 0.6 %, and 6.5 %, 0.5 %.

Conclusion: The Health Impact Projection (HIP) is a horizon scanning model designed to estimate the potential budget and health impact of the PD-(L)1 inhibitor class at a country level for the next five years. It provides valuable data to payers which they can use to support their reimbursement plans.

Policy Summary: The model is a strategic tool which allows decisionmakers to assess the implications of policy decisions, such as additional investment, or accelerated access to IOs. It can drive tangible population health benefits by eliminating the questions around PD-(L)1 inhibitor spending and its related outcomes.

1. Introduction

Cancer care remains one of the most discussed global health policy issues. The number of people affected by cancer is rising, and health systems are pressed to plan for the costs associated with investment in

innovative drugs. According to the recently updated Comparator Report, published by the Swedish Institute for Health Economics, in the European Union “cancer medicines have accounted for a modest but growing share of total pharmaceutical expenditure” [4], reflecting increasing prices but also rapid development in cancer cures: in 1996, a physician

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had 4 treatment options in lung cancer, in 2016 she had 19 [5]. Ten years ago, only 5 out of 100 patients with skin cancer were alive 5 years after they were diagnosed - today, every second patient can expect to be alive [6]. Although in recent years significant advances in cancer diagnosis and treatment have resulted in declining cancer-related mortality rates, cancer is still the leading cause of death behind cardiovascular diseases: in 2016 5.2 million people died in Europe, 1.4 million of them from cancer - more than one in four deaths [4].

The growing array of treatment options and their potential use has led to concerns around the long-term affordability of IOs. For example, by 2025, the global cancer drug market's worth is estimated at \$176 billion, up from \$97 billion in 2017. Targeted and immuno-therapies are expected to contribute to that rise, with PD-1/PD-L1 inhibitors expecting the highest rate of growth [7]. Such rapid growth requires clarity and transparency of the costs and benefits of the anti-PD-1/PD-L1 class [3]. The funding decisions of governments, payers, and health authorities to finance ground-breaking cancer therapies need greater predictability, and a better understanding of the associated improvements in patient outcomes.

The HIP model [2] was conceptualized in 2017 with the first country adaptations based on 2017 and 2018 data. The model estimates key clinical and economic outcomes of PD-1/PD-L1 inhibitors across indications compared to SOC treatments over a 5-year period at a county level. It is based on a set of assumptions (see Appendix C) and draws on budget impact analysis for its structure and methods, while also projecting related health benefits. Given the stakeholder target audience – sick funds, healthcare ministries, budget planners, and patient organizations, we deemed appropriate to focus the model on obtaining a high-level estimate of the costs and benefits of the class.

2. Data and methodology

The inputs used in the HIP were sourced from available data on the products in the class (Fig. 1). When data were missing, comparable product figures were used instead.

Country-level (local) data define the context of the analysis, reflecting the characteristics of a country's population and market. Parameters such as size and growth of the population, proportion of patients who undergo PD-1/PD-L1 testing, and IO market share (See Appendix B), are also included.

For epidemiology data, the HIP model considers newly diagnosed patients with advanced stages of cancer (e.g., local advanced and metastatic).

The populations considered in the model are closely aligned with the subgroups approved within each indication in the respective clinical trials. No patients in these subgroups were assumed to be switching treatment. The model also restricted the eligible population based on PD-L1 testing. For example, included 1 L NSCLC patients would be those with the characteristics of the selected trial population in this indication, following the clinical trial protocol.¹

Market share inputs describe the projected uptake of treatments over the 5-year period. The HIP model relied on publicly available financial analysis reports [8] showing projections for the US market and the 'rest of the world' and regulatory approval timelines for each of the indications [9]. The market shares were then approved or adjusted, based on country expert opinions, to align with each country's reimbursement system (see Appendix B).

The HIP model projections are based on publicly available list prices for anti-PD-1/PD-L1s, as informed by the respective national formularies, and clinical evidence, based on key clinical trials (Table 2). Hernandez et al. (2020) investigate that although net prices for branded

products in the US have been growing between 2007–2018, they seem to have levelled in 2014, and decreased in 2017–18, while list prices continued rising [10]. To a lesser extent outside US, this trend could still mean that the HIP budget impact calculations using 2017–18 list prices may have overestimated anti-PD-1/PD-L1 budget projections.

The adopted selection criterion for clinical trials in the base case model was the use of the most conservative trial data from the approved treatment options. Where trials failed to show significant benefits the assumption was that the reimbursement would not be successful within that indication for the suggested treatment, hence the outcomes observed in the failed trials would not be relevant to those patients that would be treated with an anti-PD-1/PD-L1 therapy.

The model (Fig. 2) also used survival gains and outcomes associated with a particular anti-PD-1/PD-L1 treatment as representative of the whole class in that indication. Whenever more than one clinical trial was available, we used the trial with the smallest difference in median PFS between the anti-PD-1/PD-L1 drug and the SOC [22]. This condition was later relaxed - if there was more than one clinical trial per indication, the user could select the trial whose data were considered to be the best representation of clinical practice in a given country.

The modelling methodology used to estimate the key survival outcomes in each world was partitioned survival modelling (See Appendix A). The survival curves relating to SOC and anti-PD-1/PD-L1s were modelled using different approaches. As the model considers a five-year horizon, where trial data were only observable for a shorter time, SOC survival curves were fitted and then extrapolated into the future, assuming the survival data follows an exponential distribution [23]. Partitioned survival and Markov modelling have been shown to produce 'functionally equivalent' results, if survival data from clinical trials have been modelled correctly [24].

The hazard ratios of the anti-PD-1/PD-L1 treatment versus SOC were estimated from the relevant clinical trials (Table 2), applied to the SOC survival curves and used to derive the survival curves for the corresponding anti-PD-1/PD-L1 treatment in each indication. Goodness of fit was visually inspected and when the modeled curves did not show an accurate representation of the entire survival curve from a trial, or a realistic extrapolation of the latter into the future, changes were made to improve the fit.

The survival curves for anti-PD-1/PD-L1 products were observed to taper off or plateau in several indications. In the indications where the anti-PD-1/PD-L1 survival curve appeared to taper off, it was broken into two parts, each associated with its own hazard ratio and corresponding shape.

Only direct costs were included in the model adaptation (see Appendix B), in line with budget impact modeling (BIM) guidelines recommending that indirect costs are not included unless they have consequences for the budget holder [25–27]. Nevertheless, the model still allows for the inclusion of indirect costs, where the decision was left with the countries. Total costs were estimated by adding the costs of individual products and obtaining a weighted average using the market share for each product.

The five-year time horizon in the model fits BIM guidelines as well [25–27]. Health economics experts were involved with the validation of the model assumptions and their advice and feedback on the study was largely incorporated.

The longest, rather than the median, duration of treatment was used in the HIP model as a cap on the absolute maximum length of patient treatment (around two years for the class, but varying number of weeks per indication).

3. The increase of cancer incidence in Europe – the experience of Austria, Belgium, Slovenia, and Italy

The HIP adaptations for Austria, Belgium, Slovenia, and Italy [28] used the model to inform planning of immunotherapy funding and maintain a constructive dialogue with payers and healthcare authorities

¹ E.g., oncogene non-addiction, patients eligible are tested with PD-L1 and have an IHC>50%, and measurement of health gains was limited within the relevant patient subset.

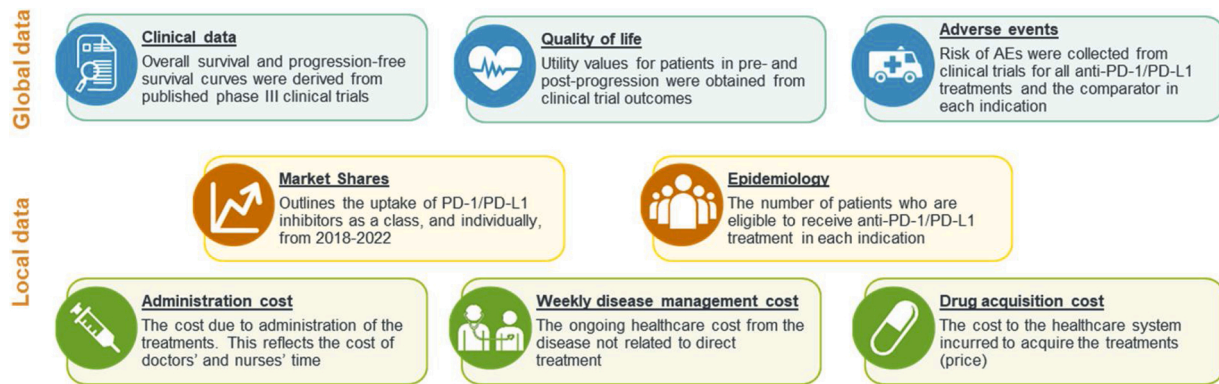


Fig. 1. Global and local data inputs.

Table 1
Indications and corresponding PD-1/PD-L1 treatments per country in the model (2018-22).

Country	Indications	PD-1/PD-L1s
Italy	Unresectable or metastatic melanoma (melanoma)	Pembrolizumab, Nivolumab, Atezolizumab
	Metastatic first-line non-small cell lung cancer (1 L NSCLC)	Pembrolizumab, Nivolumab, Atezolizumab, Durvalumab, Avelumab
	Metastatic triple negative breast cancer (TNBC)	Pembrolizumab, Atezolizumab
	Recurrent or metastatic head and neck cancer	Pembrolizumab, Nivolumab, Durvalumab
	Locally advanced or metastatic bladder cancer	Pembrolizumab, Nivolumab, Atezolizumab, Durvalumab, Avelumab
	Unresectable or metastatic melanoma (melanoma)	Atezolizumab, Pembrolizumab, Nivolumab
	Metastatic first-line non-small cell lung cancer (1 L NSCLC)	Pembrolizumab, Nivolumab, Atezolizumab, Durvalumab, Avelumab
Slovenia, Belgium, Austria	Locally advanced or metastatic 2L NSCLC	Pembrolizumab, Nivolumab, Atezolizumab, Durvalumab, Avelumab
	Metastatic triple negative breast cancer (TNBC)	Atezolizumab, Pembrolizumab
	Recurrent or metastatic head and neck cancer	Durvalumab, Nivolumab, Pembrolizumab (+Docetaxel in Austria)
Slovenia, Belgium, Austria	Locally advanced or metastatic bladder cancer	Avelumab, Atezolizumab, Durvalumab, Nivolumab, Pembrolizumab
	Locally advanced or metastatic renal cell carcinoma	Avelumab, Atezolizumab, Nivolumab, (+ Pembrolizumab for Slovenia)

Source: Cowen & Company Equity Research “PD-1/PD-L1 Market Model Update”, March 14, 2017. Data for products not expected to be on the market in this period are not presented. See also Reference [11] in the “References” section for Italy’s indications vs the rest.

about IO spending.

The project faced an increasing cancer disease burden - incidence increased by around 50 percent from 2.6 million to 3.9 million cases between 1995 and 2018 [4]. The main factors for this increase were population growth and population aging. Over the same period, however, fewer people have died of cancer as a result of advances in screening, diagnosis, and treatment, including PD-1/PD-L1 inhibitors [29].

The cancer care direct costs for the same period (1995–2018) increased by 89 percent from €52 billion to €99 billion (2018 prices), although spending on cancer as a share of total health expenditure has been relatively stable over time [4].

On this background, the first adopters of the HIP - Austria, Belgium,

Slovenia, and Italy have, overall, followed the common European trends.

According to the Belgian Cancer Registry, there were 67,087 new diagnoses of cancer in 2015. Due to ageing population, the incidence of cancer in Belgium was expected to increase by 17%–79,140 by 2025 [30]. This number, however, was surpassed in 2020 with the Belgian Cancer Registry reporting 83,267 new cases [31]. As part of the HIP, Belgium created two access scenarios – within a month and one year after EMA approval, highlighting the impact of accelerated access on health outcomes.

In Slovenia, new cases of cancer in 2015 reached 14,329. Within 20 years (1995–2015), the annual cancer incidence rate has increased by 0.6 %, resulting in an increase in the healthcare spend on cancer [32]. The World Health Organization indicated that cancer control will be one of the next major challenges for the Slovenian healthcare system due to the high concentration of cancer in older populations, as well as increased life expectancy [33]. According to the Slovenian Institute of Macroeconomic Analysis and Development, the country’s population is ageing more quickly than in other EU countries [34], indicating a need for more investment in innovative cancer therapies.

While cancer epidemiology in Italy has followed the common European trend, incidence has been higher (9.9 %) compared to the EU average [35]. In 2019 there were about 3.5 mln people living in Italy with a cancer diagnosis. Lung cancer represents still the most frequent cause of death, followed by colon cancer, breast, pancreas, and liver. Data collected by the network of Italian Cancer Registries (AIRTUM) which provides incidence, survival, and prevalence numbers for about 200 different cancer entities, projected that about 371,000 new cancer diagnoses were expected by the end of 2019 [36].

The cancer incidence in Austria (except non-melanoma skin cancer) has been lower than the EU incidence rate - 355.5 per 100,000 - around 23 per 100,000 lower than the EU average [37]. Decentralized planning and delegation of responsibilities reportedly lead to fragmentation and inadequate coordination - further investments in oncology are a recurring subject of discussion, as malignant neoplasms are currently the second largest cause of deaths in the country [4].

The results below show projected health outcomes data from HIP for these countries as a group, without making any country comparisons, but rather showing common trends despite country differences. For example, the targeted indications varied from country to country, e.g., Italy did not include 2 L NSCLC and TNBC in the model adaptation [1].

The projections in Fig. 3 and Table 3 show the impact of PD-1/PD-L1 inhibitors on life years gained based on the expected number of patients eligible for treatment and indication mortality. The 2 L NSCLC estimates assume that those who progress after the first year of 1 L NSCLC SOC treatment are eligible to receive anti-PD-1/PD-L1 agent in 2 L NSCLC in the following year, that patients on anti-PD-1/PD-L1s cannot be treated with another PD-1/PD-L1 in 2L, and that most patients progress one year after initiating 1 L treatment. This applies to all patient cohorts

Table 2
Overview of the SOC and trials used in Austria, Belgium, Italy, and Slovenia [11–21].

Indication	Country	SOC used in the modelled countries (Local input)	Trial used for survival analysis (Global input) ^a
Melanoma	Italy	Dabrafenib + trametinib	CheckMate 037
	Austria, Belgium, Slovenia	Ipilimumab	KEYNOTE 006
1 L NSCLC ^b	Italy	Pemetrexed + cisplatin	KEYNOTE 407 and KEYNOTE 189
	Austria, Belgium, Slovenia	Chemotherapy	KEYNOTE 024
2 L NSCLC	Austria, Belgium, Slovenia	Docetaxel	CheckMate 017
TNBC	Italy	Platinum-based chemotherapy ^x	Zhang et al. 2015 ⁱ
	Austria, Belgium	Gemcitabine	
Head and Neck	Italy	Chemo platinum + 5-FU ± cetuximab	KEYNOTE 048
	Austria, Slovenia, Belgium	Systemic therapy ^{††}	Checkmate 141
Bladder	Italy	Cetuximab	
	Slovenia, Austria, Belgium	Chemotherapy	KEYNOTE 045
Renal	Italy	Vinflunine	
	Slovenia, Austria, Belgium	Chemotherapy	KEYNOTE 045
		Paclitaxel	
		Sunitinib	
		Everolimus	Checkmate 025

NSCLC: Non-small cell lung cancer; SOC: Standard of care, TNBC: Triple-negative breast cancer.

ⁱ Zhang et al. (2015) was used to obtain progression-free survival (PFS) and overall survival (OS) Kaplan-Meier curves for extrapolation, prior to the publication of KEYNOTE and IMPassion trials in TNBC.

^{††} In the CHECKMATE 141 trial patients with recurrent or metastatic head and neck carcinoma were treated with investigators choice of Cetuximab, Methotrexate or Docetaxel as the standard of care. In the KEYNOTE 045 trial, patients with recurrent or metastatic urothelial cancer were treated with investigators' choice of paclitaxel, vinflunine or docetaxel as the standard of care. Data for docetaxel were used for the posology of the regimen.

[‡] In the KEYNOTE 045 trial, patients with recurrent or metastatic urothelial cancer were treated with investigator's choice of paclitaxel, vinflunine or docetaxel as the standard of care. Data for docetaxel were used for the posology of the regimen.

^a See also Table 1 for a full list of modelled treatments per indication.

^b The impact of 1 L NSCLC treatment on 2 L NSCLC treatment was incorporated through the selection of the 2 L input values. To achieve this, the eligible population size and uptake rates for the 2 L patient population were selected to reflect the expected utilization of anti-PD-1/PD-L1 products within the 1 L setting, e.g., in 2 L NSCLC, the use of anti PD-1/PD-L1 therapies was expected to decrease as a direct consequence of the increase in the uptake of the class in 1 L NSCLC.

entering the model annually for the whole 5-year period. The projections of life years gained for Austria, Belgium, Italy, and Slovenia show that the treatment of 1 L and 2 L NSCLC had the greatest LYG impact: for Belgium - 75 % of the total LYG, Austria - 72 %, Slovenia - 58 %, and Italy - 80 %.

In the adaptations for the four countries, the data was collated prior to the launch of the combination therapies in 1 L NSCLC (e.g., KN 189 and KN 407) and therefore only reflect monotherapy use (e.g., KN 024).

The anti-PD-1/PD-L1s come at a higher cost than the alternatives in cancer care but have allowed new patient groups to be treated. This trend is expected to bump up direct costs and is likely to continue in the foreseeable future (see Fig. 4, Table 4). The share of cancer medicine budget that PD-1/PD-L1 inhibitors require will be mainly dependent on

budget priorities, uptake, as well as approved indications. While for Austria (€108 cancer spend per capita) and Belgium (€90 per capita) the projected budget growth is expected to slightly decline after 2020–21, for Italy (€75 per capita) and Slovenia (€51 per capita) [36] it will continue growing into 2022.

4. Discussion

Using the HIP adaptations in Austria, Belgium, Italy, and Slovenia, the study shows that anti-PD-1/PD-L1 treatments are expected to provide improvements in health outcomes, with health gains gradually increasing between 2018–2022. Direct costs will continue to rise in parallel with the uptake increase of PD-1/PD-L1 inhibitors. First line NSCLC is the largest contributor to the class budget impact - it leads the other indications in health gains, and costs, due to the size of the affected population.

For all four countries the projections show that the additional expenditure on anti-PD-1/PD-L1 medicines in 2018 would be less than 7% of the total cancer care spend and less than half of a percent of the countries' total healthcare budget. These projections, however, are expected to double percentage wise in 2020 (with the exception of Austria). Several factors could be at play – according to the Comparator Report, cancer “has surpassed cardiovascular diseases and become the disease group causing the greatest burden...in mostly wealthier countries” [4], as well as the expected increase in anti-PD-1/PD-L1 uptake, population ageing and longevity, increased incidence, and the substitution effect with SOC treatments as anti-PD-1/PD-L1s become the standard of care themselves.

The HIP model enables policymakers to acquire a perspective on the impact of anti-PD-1/PD-L1s on health gains and budgets, exploring the implications of different policy decisions, such as updating oncology budgets with additional funds for immunotherapy.

Since immuno-oncology has seen rapid development, the model allows new data to be added when it becomes available for a continuous model update and to correct for changes in the market, such as the introduction of new combination therapies.

5. Key limitations

The HIP model was developed as a deterministic model, producing only point estimates, which can lead to uncertainty around many of the included parameter values. It is a horizon scanning tool with highly variable assumptions, across a spectrum of diverse cancer indications, and its base case did not include sensitivity analysis. The treatment landscape has changed since 2017 and a broader use of immunotherapy now and in the future may affect the projections and raise further questions. For example, the literature shows that to determine the optimum dose for monoclonal antibodies treatment is a challenge and speculates that the utilization of a flat-dose treatment could be a contributor to an increase in total costs [38].

The validity of the HIP model relies on a set of assumptions, which are central to ensuring the consistency of the study results (Appendix C). Several of them were made due to lack of data, which may underestimate the true impact of the therapies. One key limitation, for example, is the reliance on a single SOC and anti-PD-1/PD-L1 survival estimate to model the comparison between the SOC and the anti-PD-1/PD-L1 class in each country. Such comparison was used due to the complexity of the alternatives at that time.

Health outcomes are likely to be underestimated due to the relatively short time-horizon employed in the HIP model. For example, patients who start treatment in 2022 will accrue most of their costs of treatment, however, most of the health gains from anti-PD-1/PD-L1 treatment are not going to be realized until later stages as most benefits are only achieved beyond the time-horizon of this model.

The method used to model survival in the HIP model relies on visual inspection as the key criterion used to select the hazard ratios and the

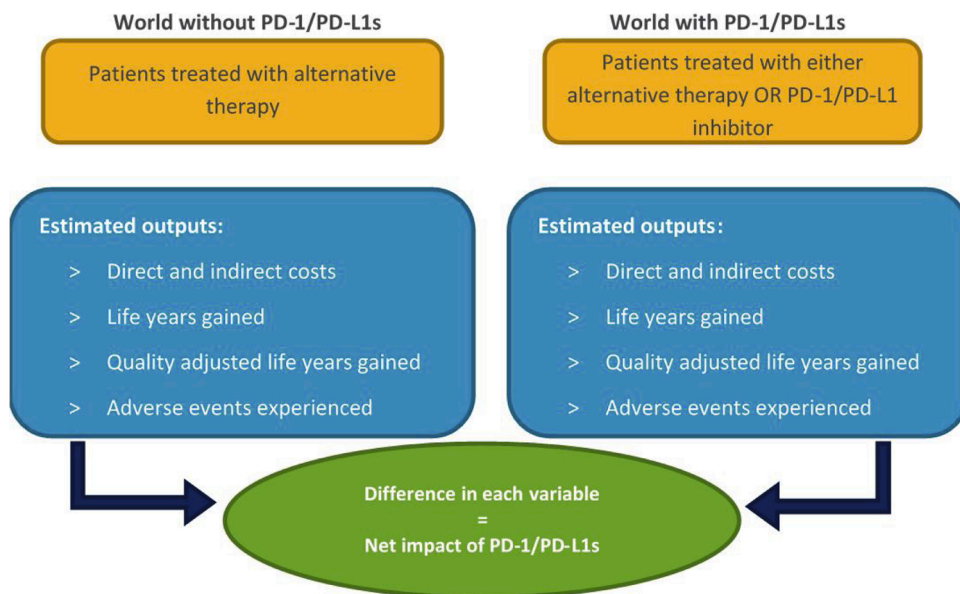


Fig. 2. Diagram of the model structure.



Fig. 3. Projected life years gained over a 5-year time horizon by country.

Note: Scale is different for different countries to capture trends, rather than differences. Austria and Slovenia assumed 100 % treatment rate for all eligible patients to project a “fully loaded” budget impact, while Belgium and Italy assumed more “realistic” ones - 80 % and 50 %, respectively. “N/A” in the case of Italy means that indications were not included in the adaptation, as clarified in Reference [1].

time period cut-off point along each survival curve. Such qualitative method is simple and intuitive but lacks the rigor of the more advanced statistical techniques as the extrapolated estimates are based on the shape of the curves.

A related limitation is that the interpretation of “plateau” could be somewhat subjective. The possibility of overestimating the plateau effect based on the “shape” of the curves, while not considering the number of events for which those plateaus persist, could possibly lead to debatable interpretations. Nonetheless, the updated analysis of Keynote-

024 confirmed the “plateau” effect for 1 L NSCLC in a subsequent long-term follow up study [39].

The lack of anti-PD-1/PD-L1 market share data in the four countries, and the reliance on proxy assumptions provided by global market reports (e.g., the Cowen Report [9]) could have potentially biased the budget projections in either direction. The uptake of anti-PD-1/PD-L1s was also expected to remain either constant or increase over the five modelled years, barring the impact of events such as the current COVID-19 pandemic.

Table 3

Total projected health gains by patient population in Austria, Belgium, Italy, and Slovenia (2018-2022).

Country	PD-1/PD-L1 Inhibitor vs SOC			
	Belgium	Slovenia	Austria	Italy
Life years gained	11,100	1,470	4,200	19,800
Quality adjusted life years gained	9,600	1,100	3,500	13,800
Progression free life years gained	13,600	1,400	3,800	14,100
High-grade AEs avoided ^a	6,100	870	3,000	6,800

^a Quality of life data was used in the form of utility measures, taken for patients in each health state for each of the treatment options. The high-grade adverse events were part of an additional analysis within the framework and therefore did not impact on the QoL assessment as the impact of adverse reactions was already captured within the sourced utility measures.

6. Summary

The model offers a flexible tool to project the budget and health impact of anti-PD-1/PD-L1s over five years and help decisionmakers acquire the insight needed to support their budget plans. The HIP model results for Austria, Belgium, Italy and Slovenia show that the introduction of the PD-1/PD-L1 inhibitor class in 2017 could lead to more than 36,570 life years gained and 16,770 high-grade AEs avoided, just in the following five years.

The horizon scanning approach has the potential to facilitate a more

targeted discussion about investment in immune-oncology treatments and innovative healthcare technologies in general.

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Transparency document

The [Transparency document](#) associated with this article can be found in the online version.

Declaration of Competing Interest

Boris Rachev, Alexander Roediger, and Raphaël Normand are employees of Merck Sharp & Dohme Corp. or MSD, a subsidiary of Merck & Co., Inc., Kenilworth, NJ USA, who may own stock and/or hold stock options in the Company.

Frederico Spandonaro, professor at Università di Roma Tor Vergata, Italy, and Nils Wilking, professor at Department of Oncology-Pathology, Karolinska Institutet, Stockholm and Dr. Gisela Kobelt, of European Health Economics were hired by Merck & Co., Inc., Kenilworth, NJ USA, to provide methodological support for the HIP project.

Christoph Zielinski, an employee at Vienna Cancer Center (VCC),

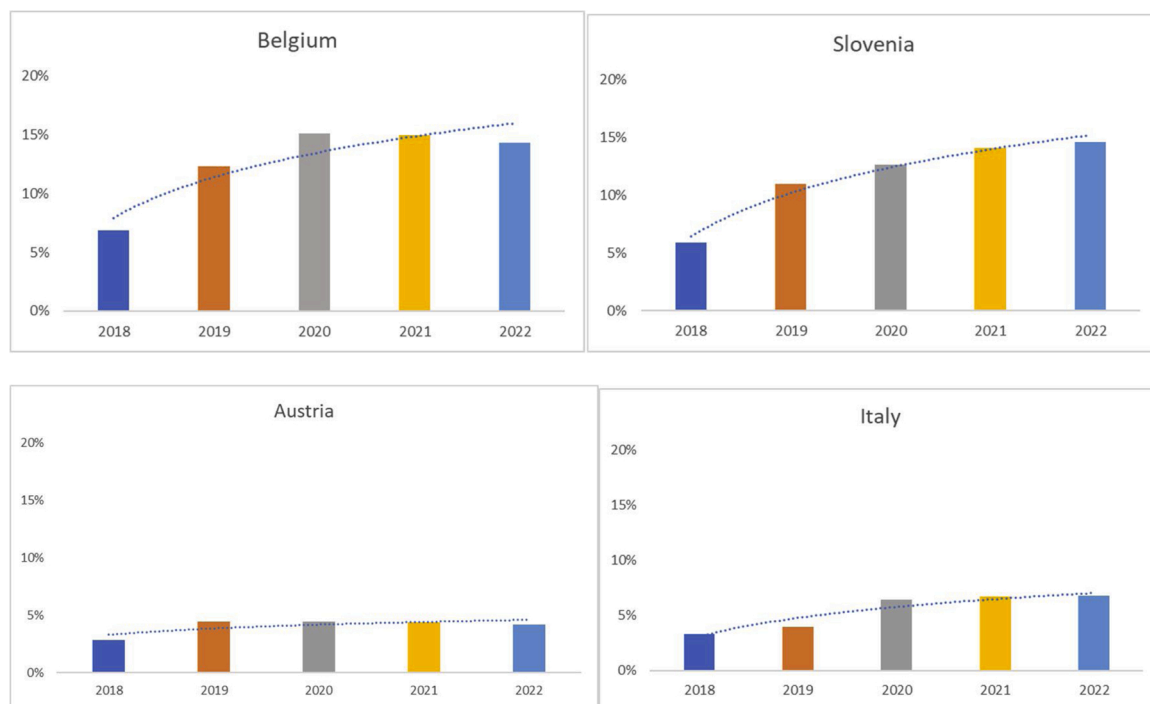


Fig. 4. Projected PD-1/PD-L1 budget impact as a percentage of total cancer expenditures (2018-2022).

Table 4

Projected health and budget impact of introducing anti-PD-1/PD-L1s in Austria, Belgium, Slovenia, and Italy and their share as percentage of cancer and total care in 2018 and 2020.

Country	LYG, average (2018–2022)	AEs avoided, average (2018–2022)	% of the total cancer care expenditure in 2018	% of the total healthcare expenditure in 2018	% of the total cancer care expenditure in 2020	% of the total healthcare expenditure in 2020
Austria	4,200	3,000	3.0	0.2	4.5	0.4
Belgium	11,100	6,100	7.0	0.5	15.1	1.1
Slovenia	1,470	870	6.0	0.5	12.6	0.6
Italy	19,800	6,800	3.3	0.2	6.5	0.5

Source: OECD Health Statistics were used for the calculation of the last four columns. The projections assume average annual growth of 8% for cancer care expenditure and 3% for total healthcare expenditure.

Vienna Medical University, owns stock in MSD.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.jcpo.2021.100279>.

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- [1] Italy used 5 indications in the adaptation: melanoma, 1L NSCLC, head and neck, bladder cancer, and renal cell carcinoma. This was due to the differences in the marketing authorization (EMA) and reimbursement approval (AIFA) timelines.
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