The Health Impact Projection Model of the PD-1/PD-L1 Inhibitor Class in Cancer Care in Turkey

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BACKGROUND

- In Turkey 233,834 new cases of cancer were diagnosed in 2020, with the age-standardized incidence rate (231.5 per 100,000 person years) of cancer being higher for males (291.5 per 100.000 person years) than for females (188 per 100,000 person years).[1] The overall mortality from cancer in Turkey is among the lowest in the Organization for Economic Co-operation and Development (OECD).[1]
- A combined healthcare infrastructure comprises public and private services in Turkey.[2] The Health Transformation Program reformed Turkish healthcare between 2003 and 2013, allowing for a shift towards improving access to free healthcare for the majority of the population.[3] The universal health insurance, called the General Health Insurance Scheme exists to provide the public with free healthcare in hospitals and also covers access to chemotherapy drugs and oncology care.[2] These reforms have improved Turkey's healthcare services, increasing average life expectancy.[4] As such, it is expected there will be an increased demand for oncology services as this population ages.[5,6]
- Combining the aim of the Turkish government to ensure an effective fight against cancer with the growing number of innovative anti-cancer drugs coming to the market results in concerns regarding the affordability of anti-cancer drugs. Considering Turkish healthcare expenditure in 2017 was 4.22% of GDP, lower than the European Union average of 9.6% the same year, affordability for the healthcare system for any new oncology products entering the market will be a major consideration in pursuing fiscal sustainability for healthcare expenditure.[7,8]
- Treatment options in the Turkish healthcare system vary extensively depending on the cancer type, location, and disease stage. A range of treatments is currently prescribed to cancer patients, with chemotherapy still being commonly used in various cancers. Other treatment options include targeted therapies and radiotherapy.
- Cancer care has changed dramatically over the last five years, with the introduction of numerous new treatment options for various cancer indications. In the last few years in particular, important developments in oncology have led to numerous immunotherapy treatments being approved across several oncology disease areas.[9]
- The PD-1/PD-L1 inhibitor class of immunotherapies has demonstrated significant clinical efficacy in a wide range of malignancies[10-11] and includes agents such as Atezolizumab, Avelumab, Durvalumab, Nivolumab, Pembrolizumab. Additional combinations of anti–PD-1/PD-L1 products and other agents are expected to change the future immuno-oncology landscape.[12]
- The introduction of immunotherapy treatments in oncology offers new opportunities and the hope to turn cancer into a chronic disease. However, there is widespread uncertainty regarding the ability of existing budgets to accommodate these costs.

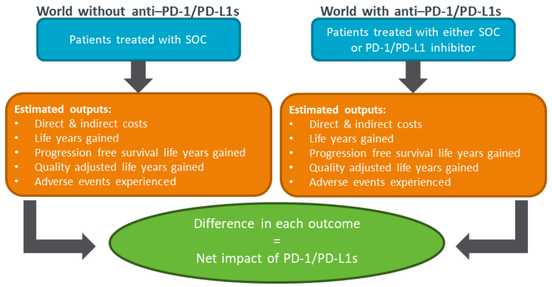
OBJECTIVE

- The overall objective of this policy-focused model is to estimate the potential health and economic impact of introducing the PD-1/PD-L1 inhibitors in Turkey.
- This is implemented through estimating the health and economic impact of the anti–PD-1/PD-L1 class over a 5-year period among below listed indications:
  - Adjuvant Melanoma
  - Metastatic Melanoma
  - First-line Non-Small Cell Lung Cancer (1L NSCLC)
  - Second-line Non-Small Cell Lung Cancer (2L NSCLC)
  - Neo-adjuvant Triple-Negative Breast Cancer (nTNBC)
  - Metastatic Triple-Negative Breast Cancer (mTNBC)
  - Recurrent or Metastatic Head and Neck Cancer
  - Second-Line Advanced Urothelial Carcinoma
  - Advanced Renal Cell Carcinoma (RCC)
  - Extensive-Stage Small Cell Lung Cancer (SCLC)
- These indications were chosen due to the availability of treatment options within Turkey for these indications within the financial arrangement time-period (2021–2025).
- Given the level of uncertainty around the anti–PD-1/PD-L1 class of products, it was deemed appropriate to focus on obtaining a high-level estimate of mean costs and benefits rather than focusing on precision and estimating uncertainty in the estimates.
- This was achieved by:
  - Estimating the health impact of introducing the anti–PD-1/PD-L1 class.
  - Estimating the economic impact of introducing the anti–PD-1/PD-L1 class.
- The study focused on simulating the relationship between the number of patients treated, health benefits gained, and healthcare costs accrued by the introduction of anti–PD-1/PD-L1 treatment to the Turkish oncology clinical practice between 2021–2025.

METHODOLOGY

- The Health Impact Projection (HIP) was developed as a Microsoft® Excel workbook to achieve the outlined objectives. The HIP is a macro-oriented tool that estimates the key economic and health outcomes of the anti–PD-1/PD-L1 class compared with various Standard of Care (SOC) treatments over a five-year period (2021-2025). The HIP draws heavily on Budget Impact Analysis (BIA) for its structure and methods, while also incorporating a broader assessment of value encompassing the health benefits achieved by patients undergoing treatment.[13]
- The model compared the economic and health outcomes obtained in a world without anti–PD-1/PD-L1 treatments, where patients were treated with SOC, to those obtained in a world where patients were treated with a mix of SOC and anti–PD-1/PD-L1 treatments. The difference in outcomes between these two scenarios over a five-year period (2021-2025) was used to estimate the impact of introducing the anti–PD-1/PD-L1 class in a specific healthcare system (Figure 1). The term SOC refers to all treatments routinely used in clinical practice that are not anti–PD-1/PD-L1 therapies.

Figure 1. Schematic of the model structure



- Costs and outcomes were compared across the two scenarios, including: the costs incurred from treatment, indirect costs, number of patient life years gained, number of quality adjusted life years gained, and the number of AEs expected to occur in both scenarios.
- Partitioned survival modelling was preferred to Markov modelling due to several factors including: the recommendations from the external experts involved with this project, the consistency it provided with the literature and its less stringent data requirements and programming simplicity.[14]
- Survival outcomes attained with anti–PD-1/PD-L1 treatments were modelled for the entire class, rather than for each product individually. Due to the lack of available data for some products within indications, the model assumed that the survival outcomes associated with the anti–PD-1/PD-L1 product, for which data were available, were representative of the whole anti–PD-1/PD-L1 class (although, in reality, health benefits may vary considerably from molecule to molecule). In indications where data on multiple anti–PD-1/PD-L1 products were available, a conservative approach was taken whereby only data on the product which achieved the lowest gain in median time to progression, versus the comparator in a trial, was used as an estimate for the entire class in that indication. Consequently, the health impact of the anti–PD-1/PD-L1 class is likely to be underestimated.
- All clinical data inputs used in the HIP were sourced from the published literature.
- Direct and indirect costs included factors such as: the cost of administering the drugs, drug procurement, disease management, PD-L1 testing, palliative care, missed hours of work due to illness, and the cost of any AEs associated with the treatment.
- The total costs of the anti–PD-1/PD-L1 class were estimated using costs for each individual product within each class and combining these to calculate a weighted average total cost, weighted using the market share of each product.
- Acquisition costs of all drugs within the HIP were based on list prices which were likely to be upper estimates as actual acquisition costs incurred by healthcare providers are often lower than the list prices, due to confidential rebates often agreed between the payer and the company. Consequently, the economic impact of the anti–PD-1/PD-L1 class is likely to also be an upper estimate.
- The model adopted a one to five-year time horizon and was structured in weekly cycles. This is consistent with the identified literature and common approaches to health economic modelling.[13,15] Future costs and health gains were discounted at a rate of 5% to account for the opportunity cost of investment.
- When data for the model could not be sourced from the relevant literature, assumptions were made and validated based on feedback from experts involved in this research.

RESULTS

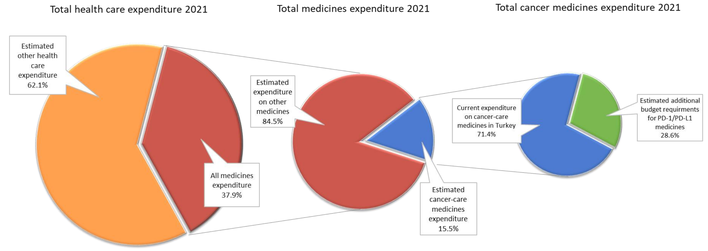
- Results show that over the next five years, the number of total eligible patients is expected to be 118,128 in Turkey and of these incident patients, 87,837 are expected to be treated with anti–PD-1/PD-L1s, whereas the rest are treated with SOC.
- The class of PD-1/PD-L1 inhibitors is expected to deliver a gain of 23,345 additional life years whilst simultaneously preventing over 14,586 adverse events (AEs) with a budget impact of approximately €1,871 million versus SOC treatments.

Figure 2. Total health outcomes over 5 years

Absolute gains	Gains with anti-PD-1/PD-L1s	Relative gains
23,345	Life years gained	+19%
18,221	PFS life years gained	+27%
18,899	QALYs gained	+21%
14,586	AEs avoided*	+25%

*14,586 AEs will be avoided, a 25% decrease compared to using SOC alone.

Figure 3. The economic impact of the anti PD-1/PD-L1 class in the Turkish context



DISCUSSION

- This model was not intended to provide cost-effectiveness results and built on a budgetary perspective with a time-horizon of five-years. The majority of health benefits from patients entering the model in later years (e.g., 2024-2025) will be realized beyond the time-horizon of the model, resulting in the model underestimating health gains.
- The HIP model is not intended to make comparisons across PD-1/PD-L1 inhibitors and is also not designed to calculate the budget of anti–PD-1/PD-L1 treatments alone.

CONCLUSION

- The HIP model is a policy-focused model to estimate the "world with" and "world without" anti–PD-1/PD-L1 class to inform future policy considerations. The PD-1/PD-L1 inhibitors can deliver considerable benefits to the Turkish population in terms of survival and life years gained. The 5-year economic impact of these drugs represents 1.67% of the expected total healthcare expenditure.
- The model might help to reduce the uncertainty and inform the decision-makers on the health and economic impact of PD-1/PD-L1 inhibitors in Turkey to facilitate continued access to these innovative treatments over time.

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