Assessing the impact of anti-PD-1/ PD-L1 inhibitors on cancer care health and budget in Greece

D. Ktena[1], E. Dalakaki[1], Y. Dimitriadis[1], G. Mountain[2], R. Hughes[2], S. Clarke-Melville[3], A. Roediger[4], P. Naoum[5], K. Athanasakis[6]

[1] MSD Greece; [2] PROVE, Adelphi Values, UK; [3] Merck & Co. Inc., Rahway, NJ, USA; [4] MSD International Business GmbH, Switzerland; [5] Institute for Health Economics, Greece; [6] Laboratory for Health Technology Assessment (LabHTA), University of West Attica, Greece

BACKGROUND – OBJECTIVE

- The burden of cancer in Greece is significant, with 64,530 new diagnosed cases and 33,166 deaths recorded in 2020. Lung cancer ranks first (among neoplasms) in both incidence and mortality rates[1].
- Cancer has been identified as among the 3 top causes of DALYs (Disability-Adjusted Life Years) globally[2] and in Greece[3]. The increasing burden of cancer in the ageing Greek population will create additional health and pharmaceutical care demand, and challenge health system financing.
- Immunotherapies such as the anti-PD-1/PD-L1 class, are being established as the new standard of care (SoC) across a wide range of tumours (e.g., metastatic melanoma, lung cancer[4], triple-negative breast cancer[5], etc.)
- The objective of this study was to highlight the health and economic impact of the uptake of anti-PD-1/PD-L1 therapies in Greece across:
  1) Early stage, high-risk (adjuvant melanoma)
  2) Metastatic melanoma
  3) First-line metastatic non-small cell lung cancer (1L met NSCLC)
  4) Locally advanced, unresectable NSCLC (Stage III NSCLC)
  5) Second-line metastatic Urothelial Carcinoma after platinum-containing chemotherapy (2L met UC)
  6) First-line advanced Renal Cell Carcinoma (1L adv RCC)
  7) First-line/Second-line metastatic Head & Neck Squamous Cell Carcinoma (1L/2L met HNSCC)

METHODOLOGY

- The Health Impact Projection (HIP) model was developed to compare, the economic impact and health outcomes between a world with and without anti-PD-1/PD-L1 inhibitors, drawing heavily on budget impact analysis (BIA) for its structure and methods.[6]
- HIP estimates the economic and clinical outcomes of the anti-PD-1/PD-L1 class compared with various SoC treatments over a 5-year period (2021-2025). SoC includes chemotherapy, targeted treatments, as well as the "watch & wait" option in the adjuvant settings. The difference between the two worlds represents the impact of anti-PD-1/PD-L1s (Fig. 1).

Figure 1. Structure of the Health Impact Projection model
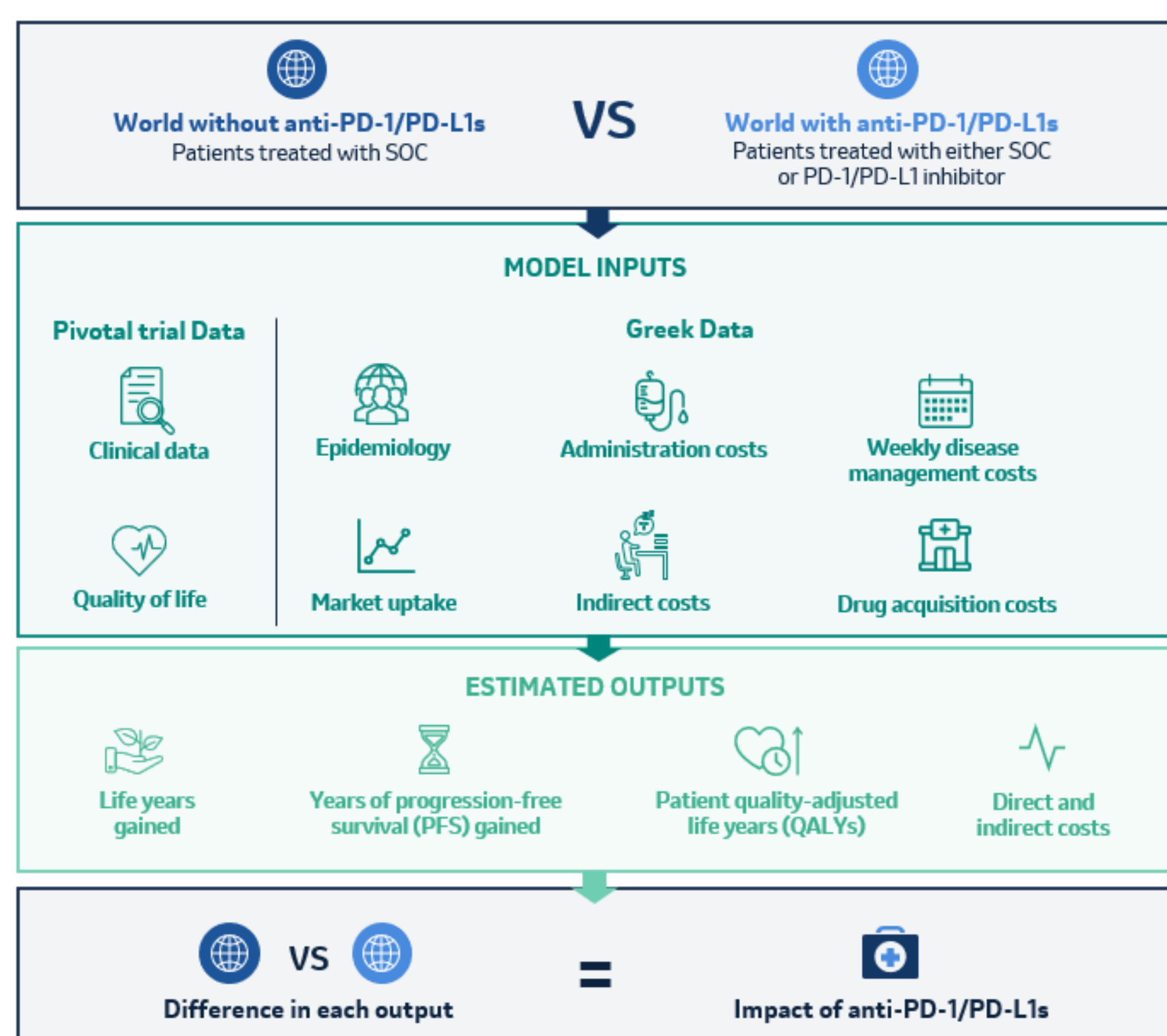
- Local data was used for deriving cost[7], epidemiology[1] and market uptake, to most accurately reflect the Greek context. In lack of publically available local data, HIP relied on primary research insights provided by "i-hecon" (the Greek Institute for Health Economics), ensuring data validation and robustness.
- Health outcomes were based on inputs from pivotal clinical trials[8-21], selected to represent conservative survival gains. Survival outcomes attained with anti-PD-1/PD-L1 treatments were modelled for the entire class, and not for each product individually.

- A limitation of the analysis is the lack of modelling all assets' available pivotal and/or longest follow-up trials, thus health benefits of the anti-PD-1/PD-L1 class are likely to be underestimated.
- Partitioned survival models were used to estimate health outcomes, due to consistency with literature and less stringent data requirements, allowing for programming simplicity.[22]
- Total costs include direct, indirect and adverse event costs. Direct costs included monitoring, administration & visit to physician, drug acquisition, testing, end-of-life and disease management costs.
- An advanced indirect cost analysis was constructed using the predicted hours of work lost due to cancer to estimate patient productivity loss. Mortality cost[23] and caregiver productivity loss[24] were also modelled.
- In order to estimate the hours that a cancer patient in Greece "gains back" per year by receiving anti-PD-1/PD-L1 treatment –and which would have been lost due to cancer– the following formula was used :

$$\text{Number of patients treated with anti-PD-1/PD-L1s in Greece*} \times \text{Working days lost due to cancer per year**} \times \text{Hours worked per day (in full health)***}$$

* 21,067 based on assumptions of the Greek HIP model
** Average calculated across indications (proxy country data) = 1 full workday/ week → 52 days/ year
*** 8 hours/ day based on EURES data (Living and working conditions: Greece (europa.eu))

RESULTS

- The uptake of the anti-PD-1/PD-L1 class within the 5-year model horizon (2021-2025) would result in 21,067 cancer patients in Greece gaining an additional 9,848 life years (+34% vs SoC).
- Furthermore, looking into the additional 9,632 progression-free survival life years gained (+70%), as well as the additional 8,409 quality-adjusted life years gained (+40%), it is observed that anti-PD-1/PD-L1s improve quality of life, as patients live longer in a disease-free state (Figure 2).

Figure 2. Health outcomes from HIP Greece

	Life years gained:	PFS life years gained:	QALYs gained:
Total gains considering treatment with IO, as well as SoC	38,602	23,379	29,345
Additional gains due to use of anti-PD-1/PD-L1 therapies	+ 9,848 +34%	+9,632 +70%	+ 8,409 +40%
	• Total gain	• Absolute gain	• Relative gain

Total gains refer to the total number of cancer patients (25,851) treated with anti-PD-1/PD-L1s as well as SoC across the 7 indications modelled for Greece, while additional gains are derived from the estimated use of anti-PD-1/PD-L1s among 21,067 of the total (25,851) cancer patients in Greece.

Table 1. Additional Life years, PFS years and QALYs gained over 5 years (2021-2025)

	2021	2022	2023	2024	2025	Total across years
Additional Life years	375	1,072	1,903	2,796	3,701	9,848
Additional PFS years	537	1,222	1,924	2,636	3,313	9,632
Additional QALYs	403	981	1,641	2,342	3,042	8,409

- While additional life years gained continue growing, the economic impact of the anti-PD-1/PD-L1 class reaches a plateau by the end of 5-year model horizon. (Figure 3 & Table 2)
- Health gains are underestimated in the model, as most health benefits gained from patients entering in 2025 will be realized beyond the model time horizon.

Figure 3. Additional Life years gained trend and economic impact of the introduction of anti-PD-1/PD-L1s in Greece (2021-2025)
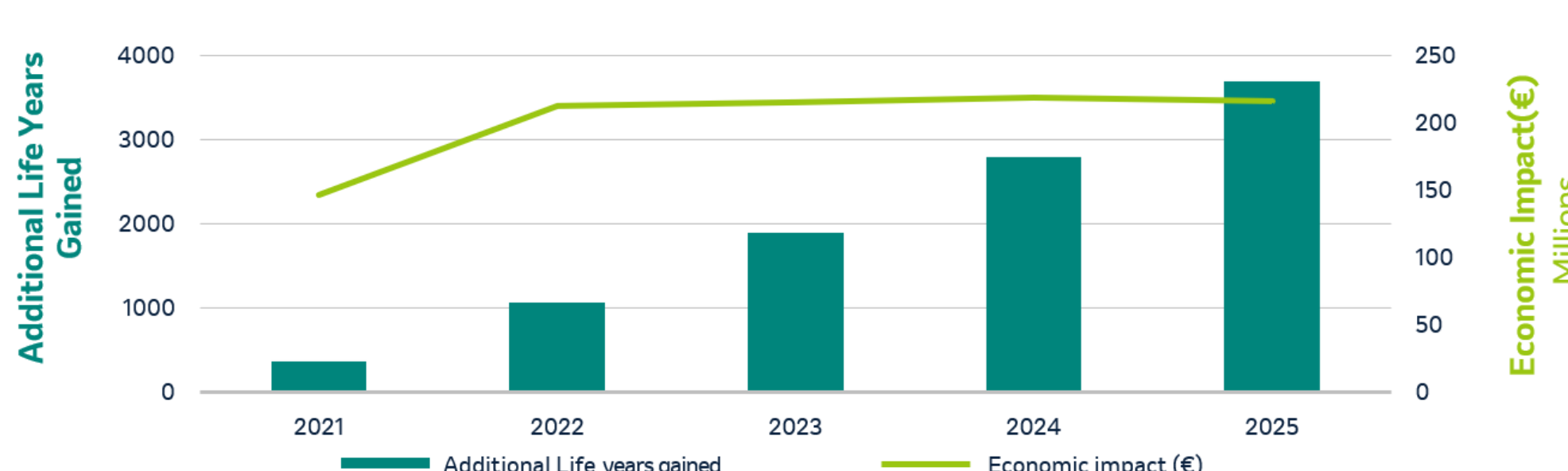

Table 2. Economic impact of the introduction of anti-PD-1/PD-L1 treatments in Greece over 5 years

	2021	2022	2023	2024	2025	Average / year
Economic impact	147,277	213,116	214,765	219,238	215,630	**202,005**

Please note that no inference should be made regarding the cost-effectiveness of the anti-PD-1/PD-L1 class based on the results above. The methodology used to calculate the above data does not allow for accurate estimations of cost-effectiveness.

- 2021 results suggest that investing in this class would require a minor amount of 1.2% of the country's total health care expenditure (Figure 4).

Figure 4. The economic impact of the anti PD-1/PD-L1 class in the Greek context (2021)
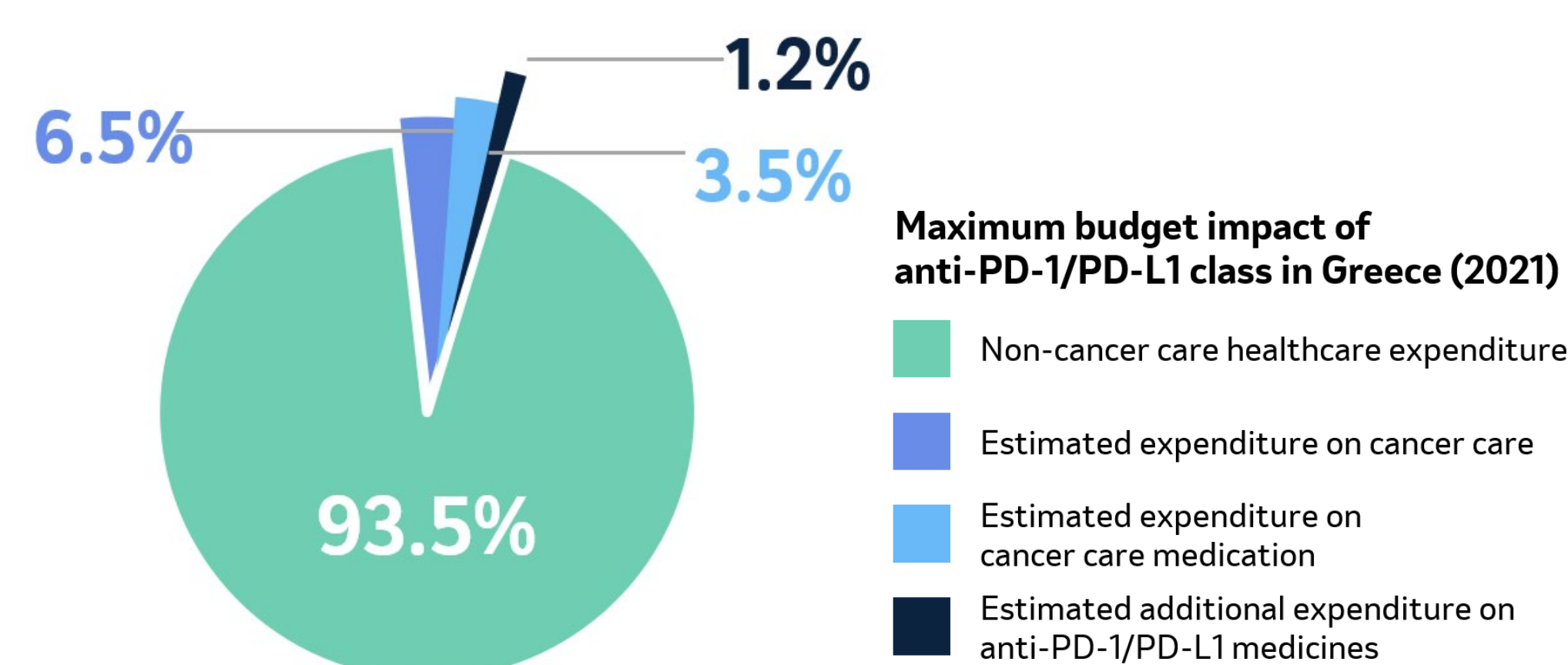
- Uptake of anti-PD-1/PD-L1s can also lead to a significant reduction (~€260mil.) in terms of indirect costs across the 5-year model horizon, helping patients work an additional day per week, or in total an additional ~9million hours per year for the 21,067 cancer patients that are assumed to be treated with this treatment class in the Greek HIP.

DISCUSSION AND CONCLUSION

- The uptake of the anti-PD-1/PD-L1 class across 7 indications is expected to allow cancer patients in Greece to gain ~10,000 life years across 5 years.
- Moreover, cancer patients receiving these innovative immunotherapy treatments are benefited from improved quality of life (+40% in QALYs), as they live longer in a disease-free state (+70% of PFS years).
- Investment in anti-PD-1/PD-L1 medicines, requires a manageable amount (1.2%) of Greece's total healthcare budget in 2021.
- Use of anti-PD-1/PD-L1s could also lead to a significant reduction (~€260 million) in terms of indirect costs across the 5-year model horizon, allowing patients to remain healthy and productive, gaining ~9mil.hours per year.
- HIP provides an estimate of the budget and health impact of immunotherapies, allowing more informed decision-making about investing in novel cancer treatments in Greece and ensuring sustainable patient access to them.

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