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Assessing the health outcomes and additional budget impact of PD-(L)1 inhibitors in the early stages of cancer treatment in Greece

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Background

- Cancer has been a significant issue globally; one in six deaths was attributed to cancer in 2015, making it the 2nd leading cause of mortality.[1]
- The incidence and mortality of cancer globally have been increasing and are expected to continue to increase. Projections of the International Agency for Research on Cancer, of the World Health Organization show that from 2022 to 2045, a 63% increase is expected in the incidence of cancer and a 73% in the mortality of cancer.[2]
- The cost of cancer in the European Union was €199 billion in 2018. Given the expected increase in the incidence and mortality of cancer, the cost of cancer is expected to further increase.[3]
- In similar fashion, the burden of cancer in Greece is significant, with 64,530 new cancer cases and 33,166 deaths attributed to cancer annually.[4] The incidence of cancer in Greece is projected to increase by 16.5%, whereas mortality is anticipated to increase by 23.8%; from 2022 until 2045.[2]
- In 2018 the total cost of cancer in Greece was more than 2 billion, of which 37% was attributed to productivity loses from premature mortality and cancer related morbidity.[5]
- Decision makers are called forth to make important decisions around budget allocation. Hence, payers are required to manage the upfront cost of innovative treatments, compared to the impact in outcomes and patients lives.

Objectives

This study aims to assess and quantify the health benefits of including PD-(L)1 inhibitors in four early-stage cancer indications which have a meaningful burden both in incidence and mortality in Greece: melanoma (stage IIB/C and stage III), renal cell carcinoma, and triple-negative breast cancer.

Methodology

A Markov model was employed to forecast clinical outcomes and financial implications over a time horizon of 10 years. The model compared two scenarios: 1) the use of PD-(L)1 inhibitors for patients with both early-stage and metastatic disease, and 2) SoC treatment before PD(L)1 inhibitors became available in the early stage; with PD-(L)1 inhibitors used only in advanced and metastatic stages. The projected outcomes included life-years (LY), quality-adjusted life-years (QALY), events or recurrences, active treatment for metastatic disease, adverse events (AE), and deaths as well as total costs and costs per health state in disaggregated categories. The model incorporated efficacy data from clinical trials, market share data from Greece as well as projected eligible patient numbers. Lastly the cost inputs were obtained from country specific sources such as local DRG's, scientific manuscripts and the local legislation.

Results

Figure 1 illustrates the outcomes of the analysis conducted. Introducing PD-(L)1 inhibitors in the early stages could result in 2,556 additional life years (+4%), 5,556 additional life years in the recurrence-free state (+11%), and 2,363 additional quality-adjusted life years (QALYs) (+4%) compared to the use of PD-(L)1 inhibitors only in the metastatic setting. Furthermore, there is a notable reduction in the number of recurrences (-25%) , while maintaining a comparable safety profile in terms of drug-related adverse events. Most significantly, the early introduction of anti-PD(L)1 treatments over a 10-year period could prevent 881 deaths (-24%) and 1,782 active treatments in the metastatic disease stage (-27%).

Figure 2 presents the healthcare costs associated with these outcomes. All cost categories have been included in this analysis including Drug acquisition, Drug administration, Adverse events management, Salvage Surgery, Terminal Care and Societal cost. On average, the model predicts an overall cost increase of €35,042 per patient receiving treatment with PD-(L)1 inhibitors annually over the 10-year analysis period, compared to a scenario without early-stage PD-(L)1 inhibitors.

It is important to note that the incremental disease management costs of introducing PD-(L)1 inhibitors rise from year 1 to year 3, peaking at year 3, and subsequently decline steadily until year 10. The incremental cost per patient receiving active treatment with PD-L1 inhibitors from year 3 to year 10 shows a 35% decrease, primarily due to savings from societal costs and prevented metastatic disease treatment costs. These cost-saving results are depicted in Figure 3, which showcases the cumulative savings within the model from Year 1 to Year 10.

The incremental budget impact of the model amounts to €35,042 on average, per patient per year receiving treatment with PD-(L)1 inhibitors, throughout the 10 year time horizon. However, cost-offsets arise specifically within some cost categories within the model which are important to be highlighted. The primary sources of cost-offsets originate from the prevention of metastatic disease treatment costs, followed by reduced indirect costs, disease management costs, and savings in terminal care costs. These data are shown in Figure 3.

Sensitivity analyses were conducted to assess the parameters with the biggest impact on key outcomes of the model. The most sensitive parameter in the OWSA was the uptake of anti-PD(L)1s, which when increased to 100% would result up to 1,177 potential deaths prevented. Other influential parameters in the model include the population which receives treatment, delaying the launch of PD(L)1 inhibitors in the early stage setting and not accounting for relative dose intensity within the model. Another important finding is that an increase of 20% of the eligible population would result in 1,057 deaths averted and an equivalence of 17% increase in cost. Table 2 shows the economic results associated to the increase in outcomes presented in Table 1.

Strengths-Limitations & Conclusion

- The models used to make projection about the estimated benefits and budget impact of neoadjuvant/adjuvant treatments, have been submitted to and assessed by international HTA agencies such as NICE.[6-8]
- A limitation of the model is that the time horizon of 10 years might not accurately capture the full value of early-stage treatments. The reason for that being that events or recurrences prevented, for patients entering the model's cohort at the 8th, 9th and 10th year of the analysis, might occur at a later point than the time horizon examined. Hence the predicted outcomes might be underestimated.
- Lastly, the economic analysis included list prices, which do not take into account the confidential price discounts provided by the marketing authorization holder during negotiations. As a result, the incremental economic cost is overestimated.

1. From the perspective of the healthcare payer, benefits arise by avoiding metastatic disease cost with a manageable additional investment of €35,042 per patient per year receiving treatment with PD-(L)1 inhibitors, whereas the benefits in patient outcomes amount to avoiding 24% of deaths and 25% of recurrences.
2. Thus, continuing these interventions moving forward is expected to further improve cancer mortality, health outcomes for patients and societal gains from productivity costs for the economy from healthier cancer patients.

Figure 1: Incremental Outcomes for the introduction of PD(L)1 inhibitors to the early stage in the 10-year time horizon per key category

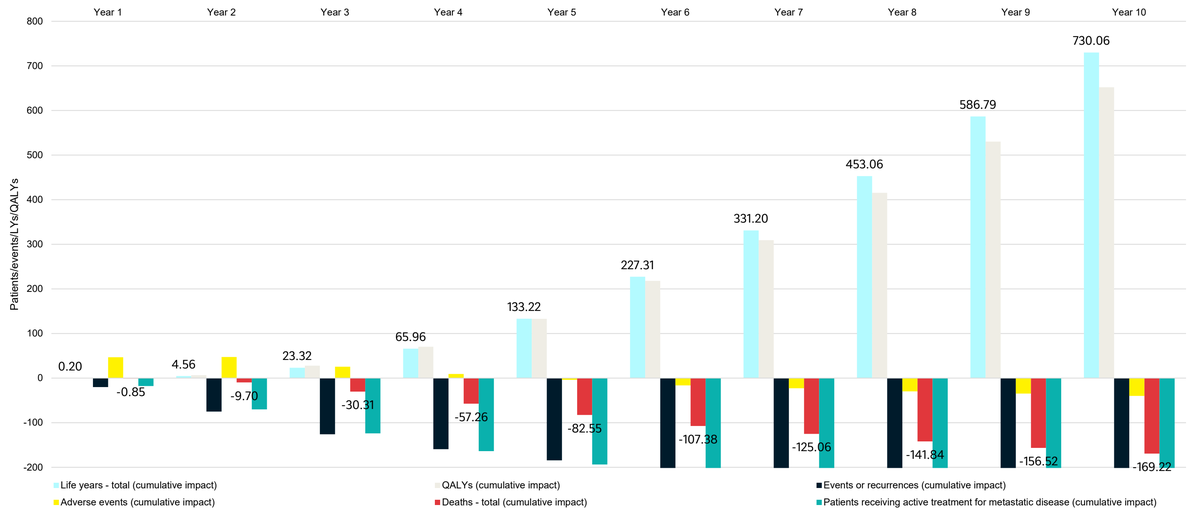
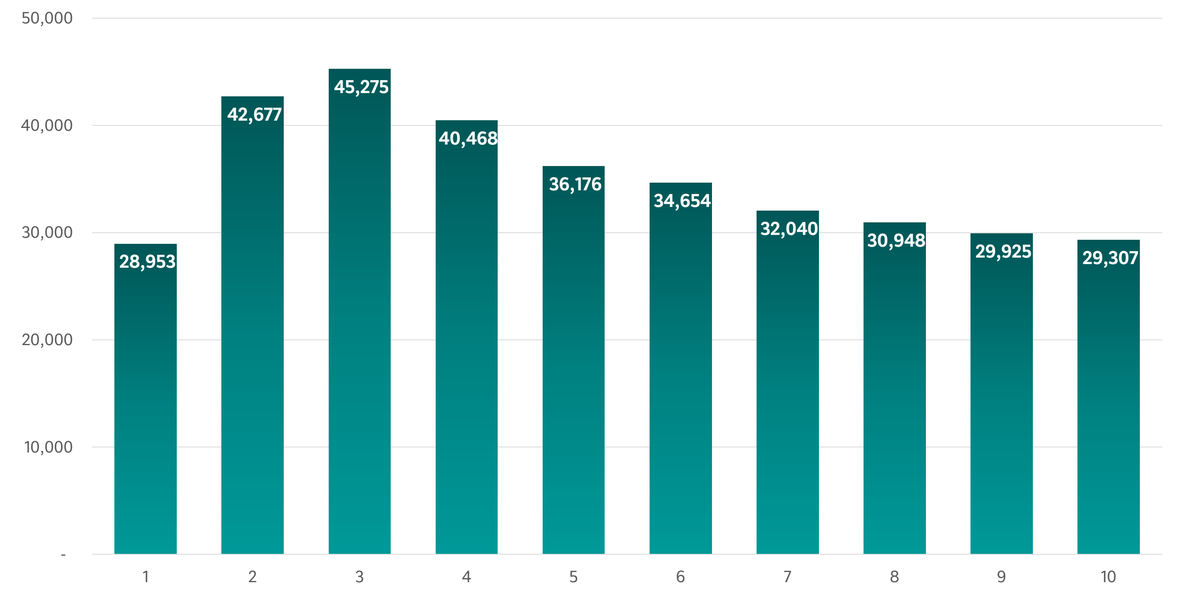


Figure 2: Incremental disease management (direct and indirect) cost* per patient receiving PD-(L)1 inhibitors in the early-stage treatment in the 10-year horizon



*Cost categories included in this analysis: Drug acquisition, Drug administration, Adverse events management, Salvage Surgery, Terminal Care, Productivity Loses

Figure 3: Cost categories resulting in cost-offsets within the model of PD-(L)1 inhibitors agents additional to the early stage in the 10-year time horizon per key category

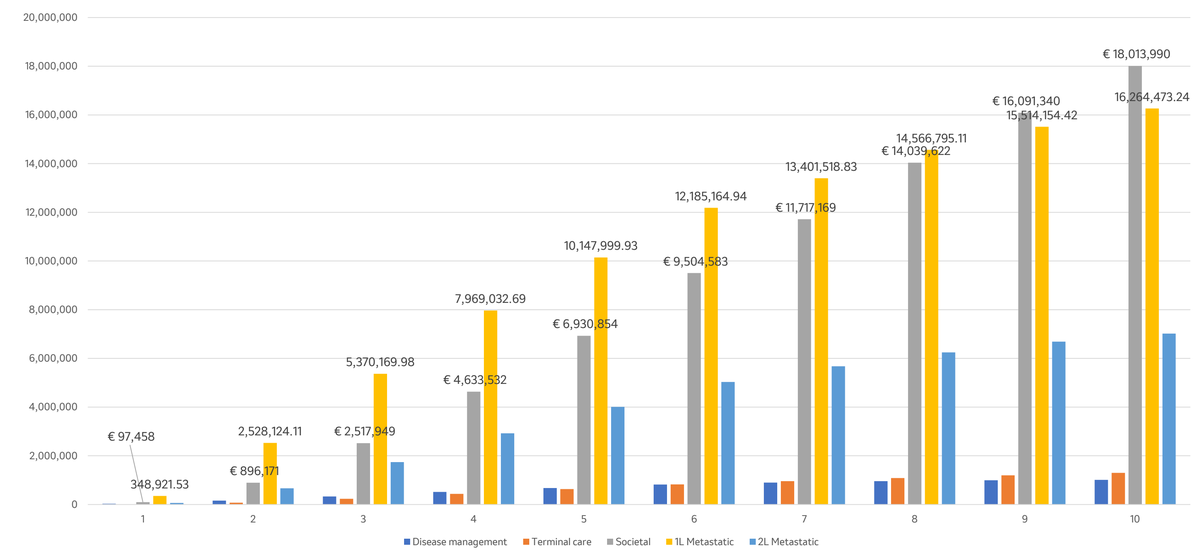


Table 1: Sensitivity Analysis of the Incremental Impact of PD(L)1 inhibitors agents additional to the early stage on deaths

Scenario tested	Number of deaths Avoided over 10 years	Percentage change from base case
Base scenario	881	
100% uptake of anti-PD-1/PD-L1 agents in future environment	1,177	+34%
20% increase of target population for all years	1,057	+20%
20% decrease of target population for all years	730	-17%
Delayed time to launch of anti-PD-1/PD-L1 agents in future environment	776	-9%
Do not account for relative dose intensity	881	No change

Table 2: Sensitivity Analysis impact of the Incremental Impact of PD(L)1 inhibitors agents additional to the early stage on costs

Scenario tested	Cost Variation
100% uptake of anti-PD-1/PD-L1 agents in future environment	+19%
20% increase of target population for all years	+17%
20% decrease of target population for all years	-4%
Delayed time to launch of anti-PD-1/PD-L1 agents in future environment	-10%
Do not account for relative dose intensity	+2%

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