Cost-effectiveness analysis of pembrolizumab monotherapy treatment for previously treated advanced microsatellite instability high (MSI-H) or mismatch repair deficient (dMMR) solid tumors in Greece

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BACKGROUND

- The prevalence of MSI-H varies depending on the type of cancer and the stage of the disease. Several tumors, including endometrial, colorectal, and gastric cancers, consistently show the highest prevalence of MSI-H, generally above 5%[1]
- Patients with MSI-H/dMMR metastatic disease had a poor prognosis and a very low chance of survival at 24 months, with a life expectancy of less than one year[2]
- It is clear that there is an unmet medical need for patients with MSI-H tumors whose options are limited to successive lines of chemotherapy, given the limited survival prognosis of these advanced cancers[2] and evidence suggesting that these patients may have even worse outcomes under the current standard of care compared to MSS patients[3,4]
- Pembrolizumab was approved by the European Commission on April 25, 2022 for the treatment of pre-treated patients with MSI-H solid tumors
- This technology would represent a "step change" in the management of the condition, providing an alternative treatment that may be more effective for patients with microsatellite instability, thereby improving survival outcomes.

AIM

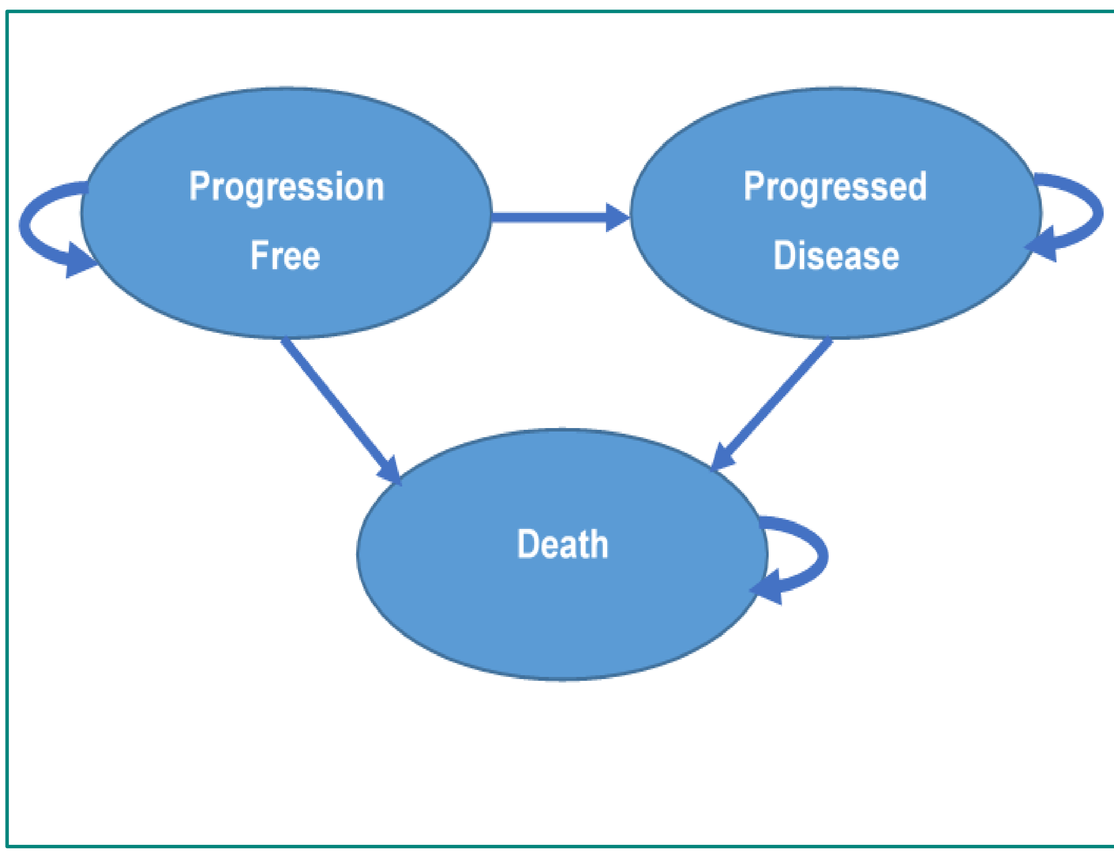
Patients with MSI-H/dMMR solid tumors have limited therapeutic options at their disposal. Pembrolizumab is indicated for pre-treated MSI-H/dMMR tumors, including colorectal, endometrial, gastric, small intestine and biliary cancers, based on **KEYNOTE-158** and **KEYNOTE-164** clinical trials. This study aimed to estimate the **cost-effectiveness** of pembrolizumab for patients with previously treated **MSI-H/dMMR solid tumors** in Greece.

METHODOLOGY

Model Structure

A partitioned survival model with three **health states** (progression-free, progressed disease, and death) was developed using the **Greek payer** perspective over a **lifetime** horizon.

Figure 1. Model Structure



Model Inputs and settings

Efficacy and safety data for pembrolizumab were obtained from **KEYNOTE-158** and **KEYNOTE-164** trials, whereas comparator outcomes were derived from the literature. For each tumor site a weighted average of the available comparators based on market share constituted the standard of care (SoC). Drug acquisition costs and healthcare resource utilization data were extracted from the literature and public sources. An **annual discount** of **3.5%** was applied to both costs and outcomes. Tumor sites were modelled separately and then pooled, weighted by tumor site distribution. Model robustness and uncertainty were assessed through one-way sensitivity (OWSA) and probabilistic sensitivity analyses (PSA).

RESULTS

Base-case Results

A pairwise comparison between pembrolizumab and a weighted SoC was conducted. Pembrolizumab was associated with **€78,746.77** incremental costs, **7.405** life years gained and **3.488** additional quality-adjusted life years (QALYs), yielding an incremental cost-effectiveness ratio of **€22,573/QALY** when compared with the weighted SoC, which is significantly lower than the country's willingness to pay threshold of **€52,770**.

Sensitivity analyses

Both **OWSA** (See **Figure 2**) and **PSA** (See **Figure 3**) confirmed the robustness of the results.

Table 1. Disaggregated Pairwise Results: QALY breakdown by health state

Health state	Pembrolizumab	SoC	Increment	Absolute increment	% absolute increment
Progression-free	2,259	0,348	1,911	1,911	54,79%
Progressed	1,960	0,383	1,577	1,577	45,21%
Total	**4,219**	**0,730**	**3,488**	**3,488**	**100,00%**

Key: QALY, quality-adjusted life year

Notes: Adapted from Pharmaceutical Benefits Advisory Committee (2008) Guidelines for preparing submissions to the Pharmaceutical Benefits Advisory Committee (Version 4.3). Canberra: Pharmaceutical Benefits Advisory Committee.

Figure 2. Tornado Diagram-Top 10 Parameters (ICER) - Pembrolizumab vs. SoC (Incremental) in Weighted average

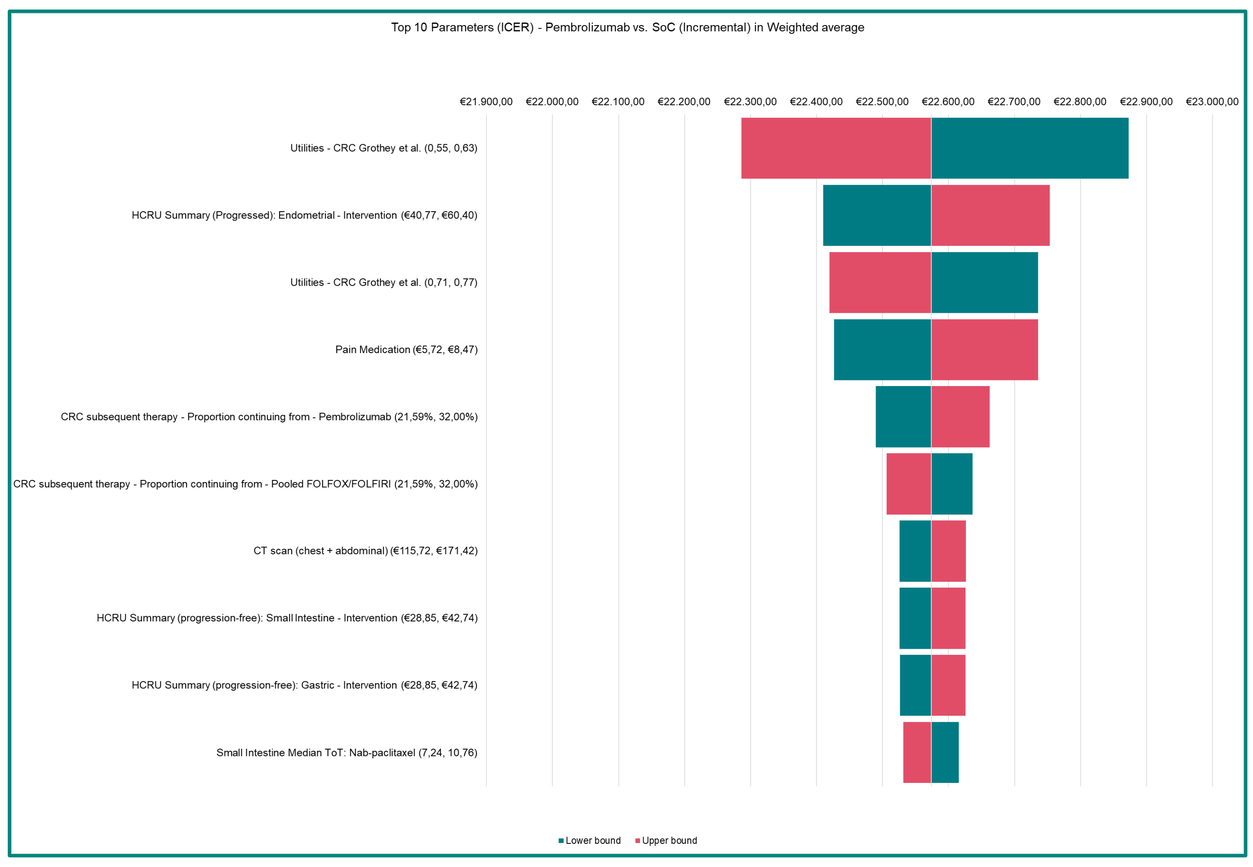
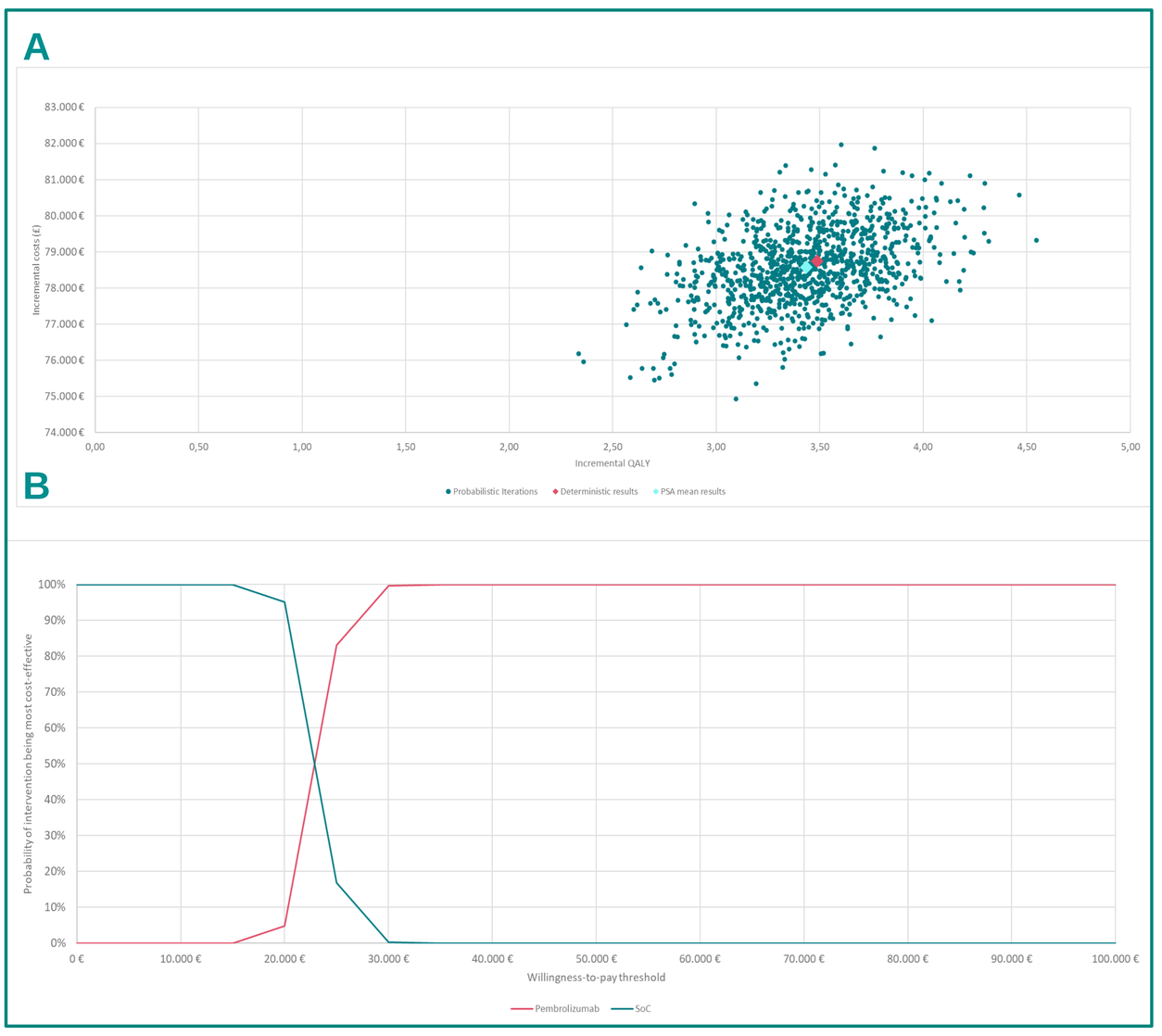


Figure 3. Probabilistic Sensitivity Analysis – A. Pairwise cost-effectiveness plane B. Pairwise cost-effectiveness acceptability curve



CONCLUSIONS

In conclusion, this analysis suggests that pembrolizumab monotherapy for the treatment of previously treated MSI-H/dMMR solid tumors is cost-effective compared to SoC from a payer perspective in Greece. Pembrolizumab substantially improved health outcomes at an increased cost. The analysis was informed by the best available clinical, HRQOL and cost data available for both pembrolizumab and relevant comparators.

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