Cost-Effectiveness analysis of pembrolizumab as adjuvant treatment for resected stage IIB & IIC melanoma in Greece

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BACKGROUND

- **Since the early 1990s(1991-2019), there has been a significant decline, namely of 32%; in cancer death rates. A substantial portion, specifically 73%, of these advancements is attributed to medicine. [1]**
- **The incidence of cancer is expected to increase by 18,5% and cancer mortality by 25,2%, by 2040 in Greece.[2]**
- **In Greece melanoma has the 14th highest incidence among the different types of cancers; The estimated 5-year prevalence of melanoma in Greece is approximately 4,380 cases. Additionally, it is the 18th leading cause of cancer-related deaths in the country.[3]**
- Melanoma is the malignancy with the highest increase in incidence in males and the second highest increase in incidence in females, according to the Hellenic Society of Medical Oncology.[4]
- Pembrolizumab is indicated for adjuvant treatment of adults and adolescent patients aged 12 years and older with Stage IIB, IIC, melanoma who have undergone complete resection.[5]
- Given the anticipated significant increase in the burden of melanoma in the coming years, it becomes crucial for Greek patients to have access to innovative immunotherapies like pembrolizumab. This will aid in addressing the rising challenges associated with this disease and ensuring optimal patient outcomes.

AIM

The present study aims to estimate the cost-effectiveness of pembrolizumab for stage IIB & IIC melanoma patients who have undergone complete resection in Greece.

METHODOLOGY

Description of the model structure

A Markov model with four health states (recurrence free survival, Locoregional Recurrence, Distant metastasis, and death), was adapted from a Greek payer perspective over a 40-year time horizon. The model schema is shown Figure 1. Efficacy and safety data applied in the model were extracted from the KEYNOTE-716 (KN-716) clinical trial. [6] Utility values used in the model were retrieved from KN-716, as well. Utilities were calculated by health-state, based on patient reported data from KN-716. The EQ-5D-5L instrument was used to capture patients' utilities values within the KN-716 clinical trial. Greek inputs based on Greek DRG's and costs data, were used to populate the model, in order to have representative data of the day-to day clinical practice. The parametric extrapolations used in the model have been reviewed and validated by external clinical experts. Primary outcomes were quality-adjusted life-years (QALYs), total costs and incremental cost-effectiveness ratios (ICER)s per QALY gained. Both costs and outcomes were discounted at 3.0% per annum. One of the limitations of the model is that the indirect costs have not been included in the model and hence the value of the treatment is underestimated.

RESULTS

Description of the model base case results

The standard of care in stage II melanoma following complete resection- prior to pembrolizumab approval- was observation, hence this was used as a comparator in the model. The total cost of Pembrolizumab and simple observation were compared. Table 1 shows the results of the cost-effectiveness analysis in detail. The costs were estimated at €129,006 and €97,093, respectively. Pembrolizumab monotherapy was more effective than simple observation with 10.91 Life Years(LY's) gained which translated to 8.90 Quality Adjusted Life Years (QALY's) gained, compared to 9.79 Life Years gained and 7.94 QALY's respectively (for simple observation). Additionally, the subsequent treatment cost were € 58,358 in the pembrolizumab arm compared to 85,530 in the observation arm; which shows a decrease of 32% in subsequent treatment costs for pembrolizumab compared to observation. The incremental analysis showed that pembrolizumab resulted in an ICER of €28,395 per LY gained and €29,970 per QALY gained versus simple observation . Thus, it falls below the Greek unofficial threshold* of € 52,770 per QALY gained and was thus deemed cost-effective.[7]

Deterministic Sensitivity Analysis

A Deterministic Sensitivity Analysis was run to estimate the parameters with the biggest impact on the ICER. The results are presented in Figure 2. The parameters with the biggest impact on the ICER were, the parametric extrapolations which were used, changing the discount rate, including a different time horizon and excluding second line costs.

Probabilistic Sensitivity Analysis

A Probabilistic Sensitivity Analysis was run assess the sensitivity of the model outcomes to the parametric uncertainty. The analysis showed that pembrolizumab had a 70.5% probability of being cost effective at a threshold of 52,770 per QALY € (3x Greece 2021 GDP per capita).7 The results are shown in Figure 3.

RESULTS

- This analysis presents the value of Pembrolizumab and immunotherapies for cancer patients by allowing them to spend more time in the health-states with better quality of life-further away from the end-of-life health state.
- We conclude that Pembrolizumab is a highly cost effective and clinical effective intervention that optimizes health outcomes and resource allocation in cancer care in Greece ,especially in the adjuvant setting .

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Figure 1:. Model Schema

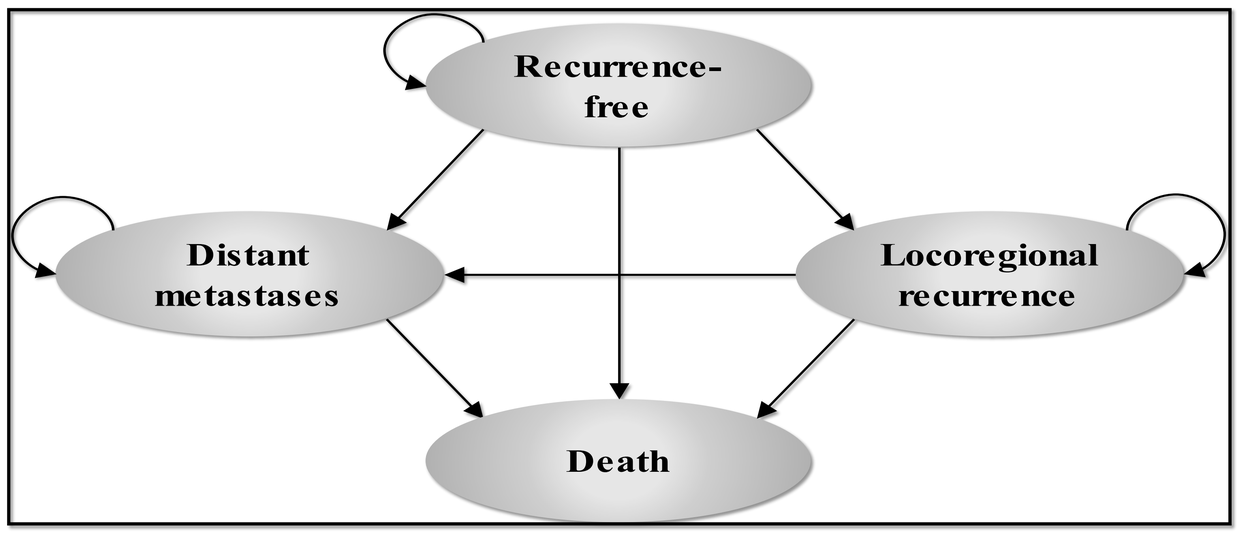

Table 1:. Results of the Cost-Effectiveness Analysis-Base Case

	Total			Incremental				
	Costs	**QALYs**	**Life years**	Costs (€)	**QALYs**	Life Years	Cost per QALY gained(€)	Cost per Life Year gained(€)
Pembrolizumab Monotherapy	120,006	8.90	10.91					
Observation	97,093	7.84	9.79	31,913	1.06	1.12	29,970	28,395

Table 2:. Time spent on each Health State per Treatment Arm

Health States	Pembrolizumab	Observation	Incremental
Quality-adjusted life years (QALYs)	**8.90**	**7.84**	**+14%**
Recurrence-free	*8.20*	*6.45*	*+27%*
Locoregional recurrence	*0.32*	*0.56*	*-43%*
Pre-progression distant metastases	*0.54*	*0.58*	*-8%*
Post-progression distant metastases	*0.33*	*0.64*	*-48%*
Life years (LYs)	**10.91**	**9.79**	**+11%**
Recurrence-free	*9.30*	*7.31*	*+27%*
Locoregional recurrence	*0.38*	*0.66*	*-43%*
Pre-progression distant metastases	*0.67*	*0.72*	*-8%*
Post-progression distant metastases	*0.57*	*1.09*	*-48%*

Figure 2:. Deterministic Sensitivity Analysis

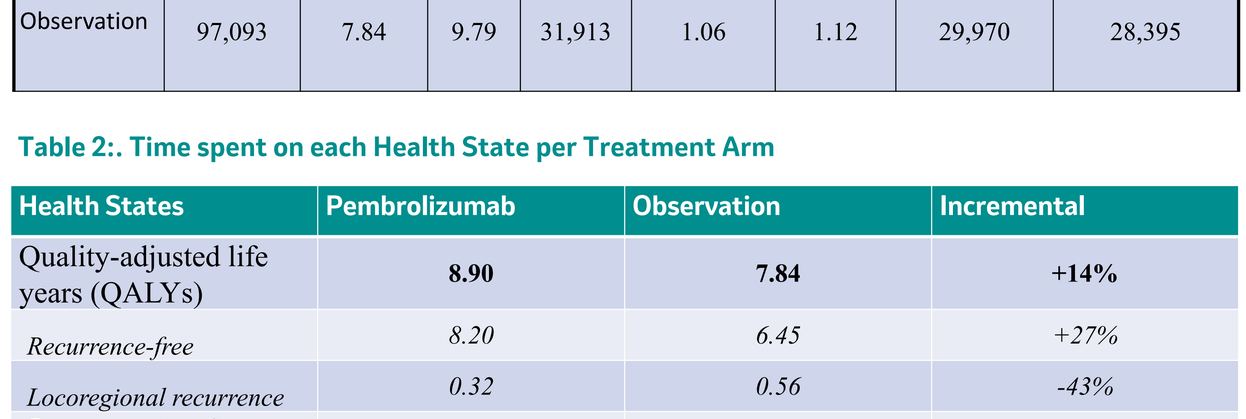

Figure 3:. Probabilistic Sensitivity Analysis