Cost effectiveness analysis of Pembrolizumab as First-Line Treatment for Persistent, Recurrent, or Metastatic Cervical Cancer in Greece

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BACKGROUND

- **Since the early 1990s(1991-2019), cancer death rates have declined by 32%." A large proportion of these gains and namely 73% is estimated to be attributed to medicines.[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 cervical cancer has the 20th highest incidence among the different types of cancers; its 5-year prevalence is estimated around 2,060 cases, and it also shows the 19th highest mortality.[3]**
- Pembrolizumab has demonstrated statistically significant increase of Overall survival with a HR of 0.64(95% confidence interval[CI] 0.50 to 0.81; P<0.001) and a PFS hazard ratio of 0.58 (95% CI, 0.44 to 0.77; P<0.001) compared to placebo for the subgroup of patients with the PD-L1 combined score over 1.[4,6]
- As a result, access to novel immunotherapies such as pembrolizumab, is essential for Greek patients and especially in an indication like cervical cancer for which the World Health Organization has laid out a comprehensive strategy for countries to achieve cervical cancer elimination, where access to innovative treatment and treatment of women with cervical cancer is one of the three key pillars.[5]

AIM

The present study aims to estimate the cost-effectiveness of pembrolizumab in combination with the standard of care for patients with cervical cancer that had a recurrence after previous treatment or for patients whose tumor has spread and tested positive for PDL-1 protein, in Greece.

METHODOLOGY

A partitioned survival model with three health states (progression-free survival, Progressed Disease, 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-826 (KN-826) clinical trial.[6] Utility values used in the model were retrieved from KN-826. Utilities were calculated using the Time-to-Death approach to calculate the time spent on each health state, based on patient reported data from KN-826. The EQ-5D-5L instrument was used to capture patients' utilities values within the KN-826 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.

Comparators within the model

The compared interventions in the model are Pembrolizumab + standard of care compared to the combination of chemotherapies which constitute the current Standard of Care(SoC). All treatments were dosed in the trial once every three weeks. Pembrolizumab was given at a fixed dose of 200 mg, paclitaxel was 175 mg/m^2, cisplatin was 50 mg/m2, carboplatin was AUC5 (assumed to equal 750 mg), and bevacizumab was 15 mg/kg. The comparator arm included the same intervention excluding Pembrolizumab.

RESULTS

Description of the model base case results

The total cost of Pembrolizumab and the comparator arm were compared. Table 1 shows the results of the cost-effectiveness analysis in detail. The costs were estimated at €92,378 and €13,223, respectively. The Pembrolizumab intervention arm was more effective than the comparator arm with 6.06 LY's gained which is translated into 3.41 QALYs, compared to 2.94 Life Years gained and 1.80 QALY's respectively (for the comparator arm). The incremental analysis showed that pembrolizumab resulted in an ICER of €25,356 per LY gained and €49,073 per QALY gained versus the comparator arm. Thus, it fell within 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 number of cycles received from pembrolizumab and other drugs such as bevacizumab and paclitaxel, as well as the cost of several drugs within the model such as Bevacizumab and Gemcitabine .

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 46.9% 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.

CONCLUSION

- This analysis presents the value of Pembrolizumab and immunotherapy for cancer patients providing patients with the opportunity to spend more time in the health-states with better quality of life-further away from the time of death.
- We conclude that Pembrolizumab is a highly cost effective and clinical effective intervention that optimizes health outcomes and the efficient allocation of resources invested in cancer in Greece.

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Figure 1:. Model schema

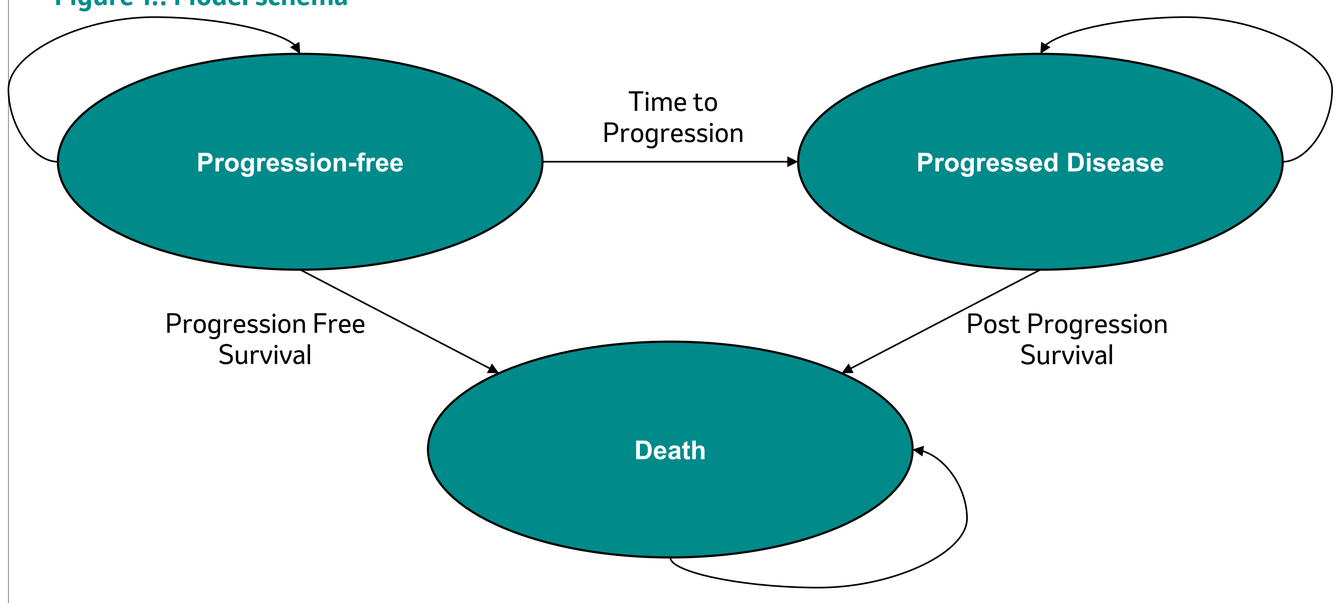

Table 1:. Results of the Cost-Effectiveness Analysis-Base Case

	Total			Incremental				
	Costs	**QALYs**	**Life years**	Costs (**€**)	**QALYs**	Life Years	Cost per QALY gained(**€**)	Cost per Life Year gained(**€**)
Pembrolizumab Treatment arm	92,378	3.41	6.06					
Standard of Care	13,223	1.80	2.94	79,156	1.61	3.12	49,073	25,356

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

Disaggregated QALY's				
Category	Standard of Care	Pembrolizumab Arm	Incremental	
Pre-Progression	*1.277*	*2.778*	*1.501*	**+118%**
Post-Progression	*0.460*	*0.414*	*-0.046*	*-10%*
QALY Loses from AEs	*-0.004*	*-0.005*	*-0.001*	*+24%*
Total ***QALYs***	**1.732**	**3.186**	**1.454**	*+84%*

Disaggregated Life Years				
Category	Standard of Care	Pembrolizumab Arm	Incremental	
Pre-Progression	*2.169*	*5.325*	*3.156*	**+145%**
Post-Progression	*0.773*	*0.739*	*-0.034*	*-4%*
Total Life Years	***2.942***	***6.064***	***3.122***	***-106%***

Figure 2:. Deterministic Sensitivity Analysis Results

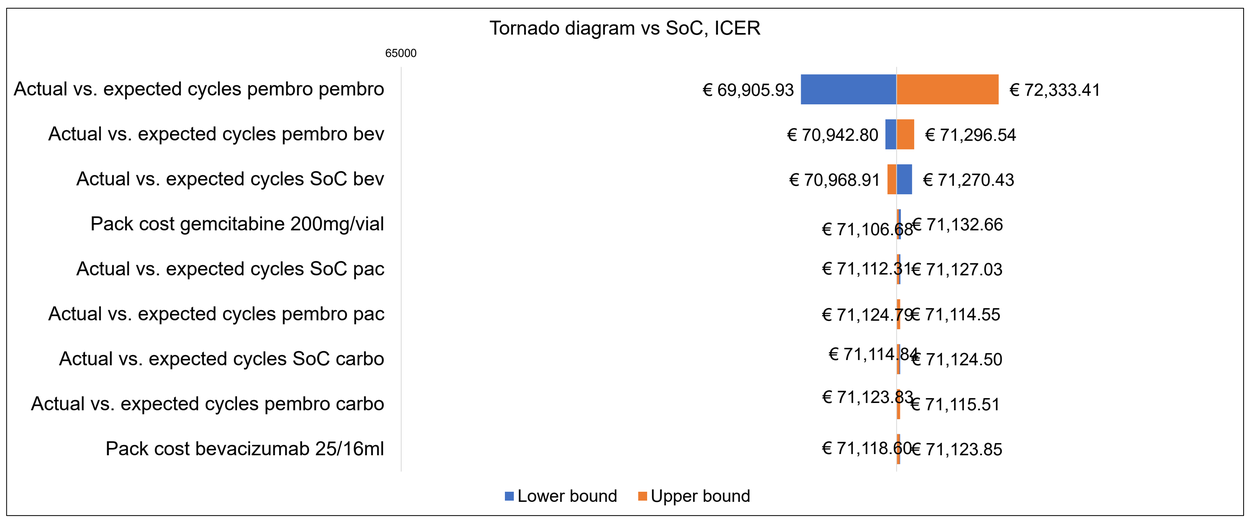

Figure 3:. Probabilistic Sensitivity Analysis Results