Cost effectiveness analysis of Pembrolizumab in combination with lenvatinib for the treatment of advanced second-line endometrial cancer

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BACKGROUND

- The incidence of endometrial cancer has increased by 30% in the last 30 years from 8.76 cases per 100,000 to 11.28 cases per 100,000.[1] This is especially relevant for countries with high Human Development Index (HDI) where the incidence of endometrial cancer increased by 37% from 1990 to 2019.[1]
- Mortality from endometrial cancer is higher in countries with high HDI.[1] The highest mortality percentage was noted in 2019 in Western Europe with 13,800 attributed deaths with 2.59 deaths per 100,000 life years.[2] The economic impact of premature mortality from endometrial cancer is significant.[3]
- Pembrolizumab is approved by the European Medicines Agency in combination with lenvatinib for the treatment of endometrial cancer patients, based on results from the KEYNOTE-775 (KN-775) clinical trial.[5] The combination has demonstrated statistically significant increase of overall survival with a hazard ratio (HR) of 0.62 (95% CI, 0.51 to 0.75; P<0.001) and a progression-free survival HR of 0.56 (95% CI, 0.47 to 0.66; P<0.001), compared to physician choice of chemotherapy.[4]
- Access to innovative combination treatments, such as pembrolizumab combined with lenvatinib, is essential for Greek patients and especially in an indication like endometrial cancer; because the 5-year survival under the previous therapeutic landscape was 17.8%, highlighting a significant unmet medical need for this patient population.[5]

AIM

The present study aims to estimate the cost-effectiveness of pembrolizumab in combination with lenvatinib for patients with patients with endometrial cancer in adults who have disease progression on or following prior treatment with a platinum-containing therapy in any setting and who are not candidates for curative surgery or radiation, in Greece.

METHODOLOGY

A partitioned survival model with three health states (Progression-free, Progressed Disease, Death), was adapted to a Greek payer perspective over a 35-year time horizon. The model schema is shown Figure 1. Efficacy and safety data applied in the model were extracted from the KN-775 clinical trial.[4] Utility values used in the model were retrieved from KN-775. 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-775. The EQ-5D-5L instrument was used to capture patients' utilities values within the KN-775 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.

Comparators within the model

The compared interventions in the model are pembrolizumab + lenvatinib (PEM+LEN) compared to physician's choice of chemotherapy between paclitaxel (pac) and doxorubicin (dx) which constituted the previous Standard of Care (SoC) before PEM+LEN combination. Lenvatinib was administered daily, orally at a dose of 20mg. Pembrolizumab was given at a fixed dose of 200 mg every three weeks, dx was also administered every 3 weeks at a dose of 60mg/m^2. Pac was administered at a dose of 80 mg/m^2 weekly for 3 weeks and 1 week off cycle.[6]

RESULTS

Description of the model base case results

The total cost of the PEM+LEN combination and the comparators was assessed. Table 1 shows the results of the cost-effectiveness analysis in detail. The costs were estimated at €99,172 for PEM+LEN ,€14,384 for pac, and €12,001 for dx. The PEM+LEN intervention arm was more effective than the comparators with 3.83 LY's gained which translated to 2.74 QALY's gained; compared to 1.53 life years gained and 1.06 QALY's gained for the other comparators. The incremental analysis showed that PEM+LEN resulted in an ICER of €50,248 per QALY gained compared to pac and €48,825 per QALY gained compared to dx. Thus, it fell within the Greek unofficial threshold of € 52,770 per QALY gained and was thus deemed cost-effective.[7] These results are shown in Table 1. 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.

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 the utility values of patients receiving treatment with pembrolizumab and other drugs within the model.

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 57.6% 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 PEM+LEN which provide cancer patients the opportunity to spend more time in the health-states with better quality of life, further away from the time of death.
- Based on the results of the model, we conclude that PEM+LEN is cost-effective intervention, which improves health outcomes and prolongs overall survival.

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Figure 1: Model Schema

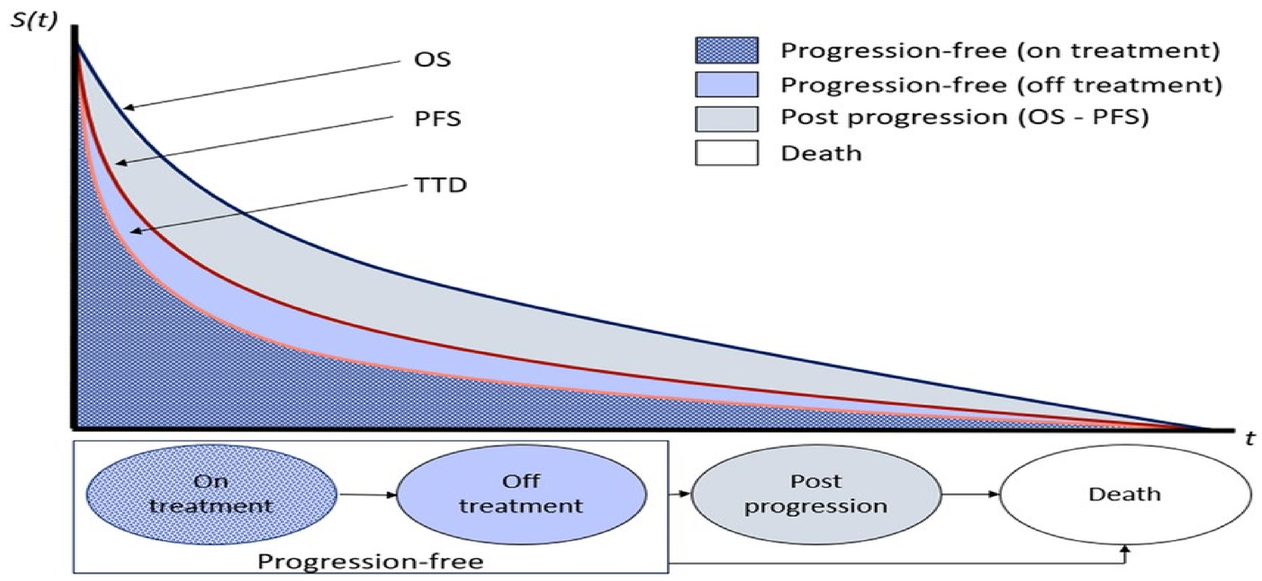

Table 1: Results of the Cost-Effectiveness Analysis-Base Case

	Total			Incremental				
	Costs	QALYs(€)	Life years	Costs (€)	QALYs	Life Years	Cost per QALY gained(€)	Cost per Life Year gained(€)
Pembrolizumab + Lenvatinib	96,172	2.74	3.83					
Paclitaxel	14,384	1.53	1.06	81,788	1.68	2.31	50,248	35,430
Doxorubicin	12,001	1.53	1.06	84,172	1.68	2.31	48,825	36,463

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

Disaggregated Life Years				
Category	Pembrolizumab + Lenvatinib	Paclitaxel / Doxorubicin	Incremental	
Pre-Progression	*1.17*	*0.52*	*0.64*	**+122%**
Post-Progression	*2.67*	*1.00*	*1.67*	*+167%*
Total ***QALYs***	**3.83**	**1.53**	**2.30**	*+**152**%*

Table 3: Comparison of modelled and reported PFS and OS

Comparison of modelled and reported median survival				
Health State	PEM+ LEN PFS	PEM+ LEN OS	Paclitaxel or Doxorubicin PFS	Paclitaxel or Doxorubicin OS
Modelled	*6.67*	*18.17*	*0.64*	11.27
Reported	*7.23*	*18.30*	*1.67*	*11.43*
Percentage difference between modelled and reported	**-8%**	**-1%**	**+3%**	*-**1**%*

Figure 2: Deterministic Sensitivity Analysis

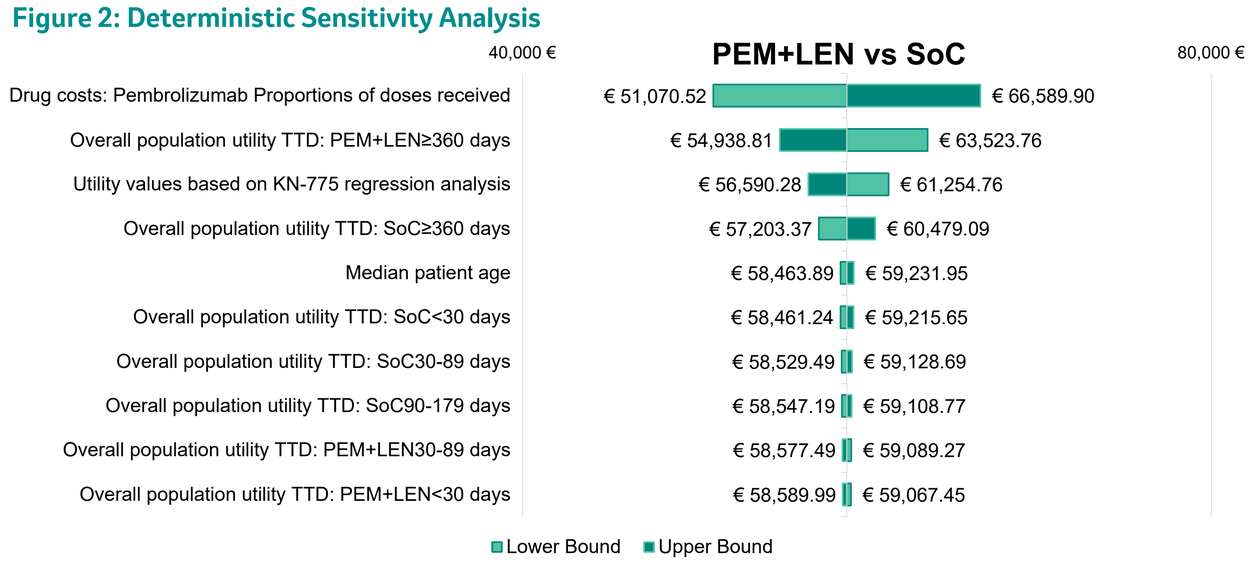

Figure 3: Probabilistic Sensitivity Analysis- Cost Effectiveness Plane