

Cost-effectiveness model for pembrolizumab for the adjuvant treatment of patients with renal cell carcinoma who have undergone nephrectomy 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 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 Kidney cancer has the 10th highest incidence among the different types of cancers; its 5-year prevalence is estimated around 5,190 cases and it also shows the 11th highest mortality.³
- Pembrolizumab demonstrated in the KEYNOTE 564 clinical trial statistically significant prolonged disease-free survival compared to placebo; with a hazard ratio for recurrence or death of 0.68(95% CI 0.53-0.87) .⁴
- In Greece, pembrolizumab is the only approved adjuvant treatment for adult patients with RCC at increased risk of recurrence following nephrectomy, or following nephrectomy and resection of metastatic lesions.⁵
- As a result, access to novel immunotherapies such as pembrolizumab, is essential for Greek patients and especially in an indication like RCC where the burden of illness is significant and no alternative adjuvant treatments are approved.

AIM

The present study aims to estimate the cost-effectiveness of pembrolizumab for adult patients will renal cell carcinoma at increased risk of recurrence following nephrectomy, or following nephrectomy and resection of metastatic lesions in Greece.

METHODOLOGY

Description of the model structure

A Markov model with four health states (Disease Free, Locoregional Recurrence, Distant metastasis, and death), was adapted from a Greek payer perspective over a 45-year time horizon. The model schema is shown Figure 1. Efficacy and safety data applied in the model were extracted from the KEYNOTE-564 (KN-564) clinical trial.⁴ Utility values used in the model were retrieved from KN-564 and KN-426 clinical trial. ^{4,6} Utilities were calculated based on each health-state provided by patient reported data from KN-564 and KN-426. The EQ-5D-5L instrument was used to capture patients' utilities values within the KN-564 clinical trial. Greek inputs based on Greek DRG's and costs data, which 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 evaluated is underestimated.

RESULTS

Description of the model base case results

The standard of care in RCC after surgery, has been observation, hence this was used as a comparator in the model. The total cost of Pembrolizumab and observation were compared. Table 1 shows the results of the cost-effectiveness analysis in detail. The costs were estimated at €92,715 and €47,469, respectively. Pembrolizumab monotherapy was more effective than observation with 13.02 LY's gained which translated to 10.52 QALYs gained, compared to 11.14 Life Years gained and 8.97 QALY's respectively (for observation). Additionally, the subsequent treatment cost were € 28,856 in the pembrolizumab arm compared to 42,444 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 €24,126 per LY gained and €29,088 per QALY gained versus observation. Thus, it fell below the Greek unofficial threshold* of € 52,770 per QALY gained and was 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 to assess the parametric uncertainty. The analysis showed that pembrolizumab had a 73.5% 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.

CONCLUSION

- This analysis presents the value of Pembrolizumab for patients at increased risk of recurrence following nephrectomy or following nephrectomy and resection of metastatic lesions. According to our analysis these patients are given the potentiality 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 cost-effective intervention from the payer's perspective in Greece, since the analysis falls within the cost effectiveness threshold.

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Figure 1:. Model schema

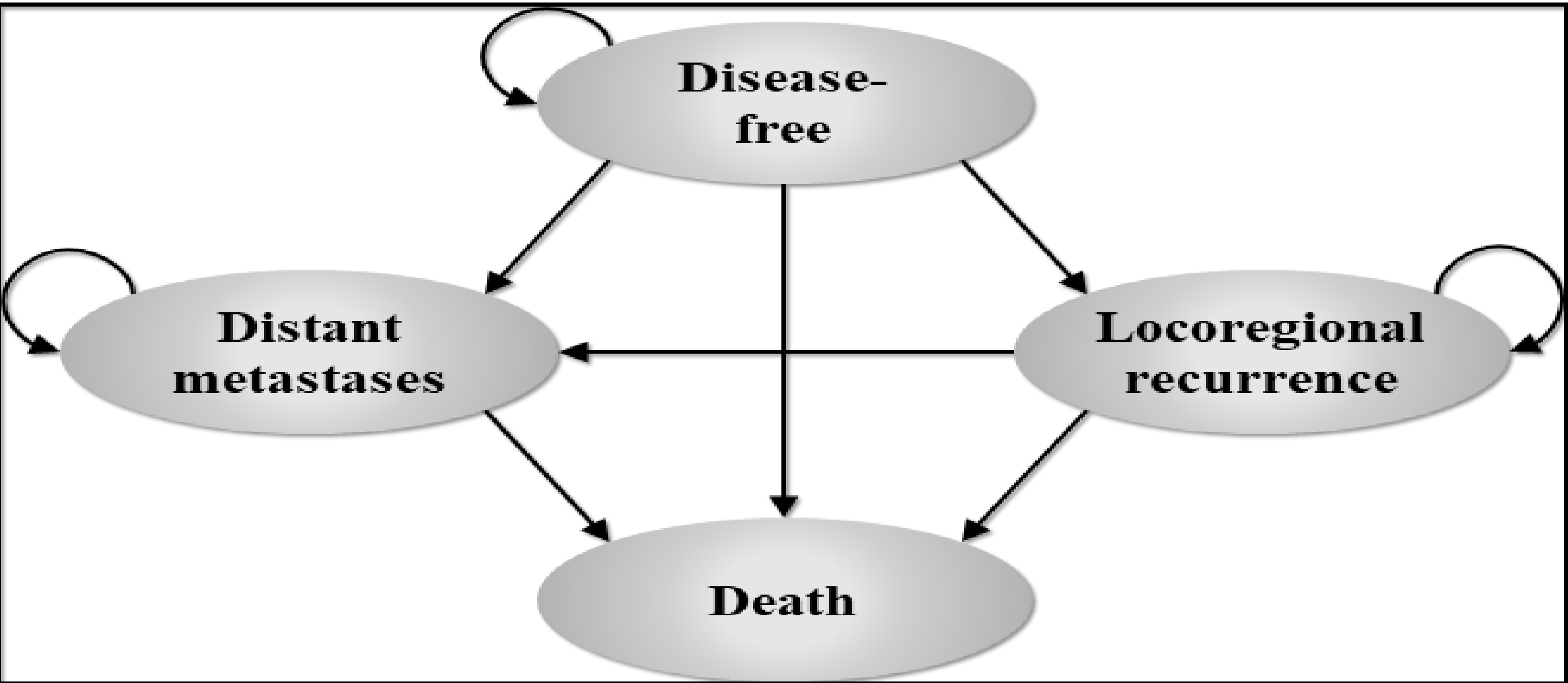


Table 1:. Results of the Cost-Effectiveness Analysis-Base Case

	Total			Incremental				
	Costs	QALYs	Life years	Costs (€)	QALYs	Life Years	Cost per QALY gained(€)	Cost per Life Year gained(€)
Pembrolizu mab Monotherap y	92,715	10.52	13.02					
Observation	47,469	8.97	11.14	45,246	1.56	1.88	29,088	24,126

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

Health States	Pembrolizumab	Observation	Incremental
Quality-adjusted life years (QALYs)	10.52	8.97	+17%
Disease-free	9.25	6.58	+41%
Locoregional recurrence	0.55	0.88	-38%
Distant metastasis	1.33	1.96	-32%
Life years (LYs)	13.02	11.14	+17%
Disease-free	10.66	7.59	+41%
Locoregional recurrence	0.65	1.05	-38%
Distant metastasis	1.70	2.51	-32%

Figure 2:. Deterministic Sensitivity Analysis

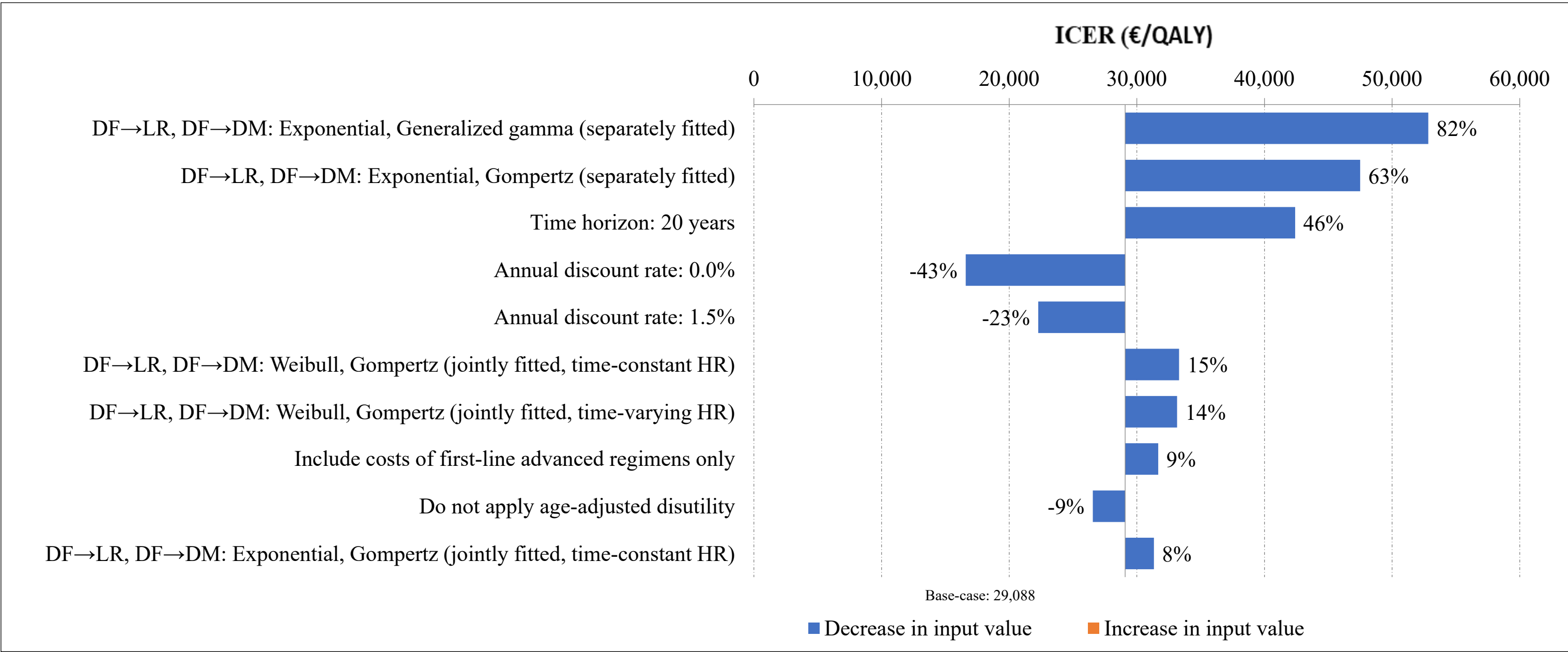


Figure 3:. Probabilistic Sensitivity Analysis

