EE210

Cost-Effectiveness analysis of Pembrolizumab plus chemotherapy as neoadjuvant therapy and continued as a single agent as adjuvant therapy for high-risk early-stage triple-negative breast cancer 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, breast cancer has the 2nd highest incidence among the different types of cancers; its 5-year prevalence is estimated around 30,879 cases, and it also shows the 3d highest mortality among the different types of cancers.[3]**
- Compared to other types such as HER2 negative, hormone receptor (HR) positive Breast Cancer, patients with Triple Negative Breast Cancer (TNBC) are at a 3-fold risk of worse overall survival (OS), and a 6-fold increase in risk of death within the first 2 years of diagnosis.[4]
- Pembrolizumab is currently the only therapy which is indicated as neo-adjuvant and adjuvant treatment for TNBC patients.[5]
- As a result, access to novel immunotherapies such as pembrolizumab, is essential for Greek patients and especially in an indication like TNBC where the burden of illness and mortality associated with the disease are significant .

AIM

The present study aims to estimate the cost-effectiveness of pembrolizumab in combination with chemotherapy as neoadjuvant treatment, and then continued as monotherapy as adjuvant treatment after surgery for the treatment of adults with locally advanced, or early-stage TNBC at high risk of recurrence in Greece.

METHODOLOGY

A Markov model with four health states (event-free, locoregional Recurrence, distant metastasis, and death), was adapted from a Greek healthcare payer perspective over a 51-year time horizon. The model Schema is shown in Figure 1. Efficacy and safety data applied in the model were extracted from the KEYNOTE-522 (KN-522) clinical trial.[6] Utility values used in the model were retrieved from KN-522. Utilities were calculated by health-state, based on patient reported EQ-5D-5L data from KN-522. 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 may have been underestimated.

Comparators within the model

The compared interventions in the model are neoadjuvant pembrolizumab + chemotherapy followed by adjuvant pembrolizumab (referred henceforth as 'pembrolizumab + chemotherapy') compared to neoadjuvant chemotherapy alone (referred henceforth as 'chemotherapy'). The pembrolizumab arm included four cycles of an intravenous infusion of pembrolizumab (200 mg) once every 3 weeks plus paclitaxel (80 mg/m2 once weekly) plus carboplatin (area under the curve [AUC])5 once every 3 weeks or AUC 1.5 once weekly in the first 12 weeks), followed by four cycles of pembrolizumab plus doxorubicin (60 mg per square meter) or epirubicin (90 mg/m2) plus cyclophosphamide (600 mg/m2 once every 3 weeks in the subsequent 12 weeks). After the last cycle of the neoadjuvant phase (2 to 6 weeks later) surgery followed. For the Adjuvant phase radiation therapy was administered, as indicated and pembrolizumab once every 3 weeks for up to 9 cycles. The comparator arm of chemotherapy included the same intervention both in the adjuvant and neo-adjuvant regimen, without pembrolizumab .

RESULTS

Description of the model base case results

Table 1 shows the results of the cost-effectiveness analysis in detail. The total costs associated with pembrolizumab + chemotherapy and chemotherapy were estimated at €162,314 and €107,767, respectively. Pembrolizumab+ chemotherapy yielded 17.75 Life Years gained which translated to 13.82 QALY's gained; whereas chemotherapy yielded 14.39 Life Years gained and 11.20 QALY's, making pembrolizumab+ chemotherapy more effective. Additionally, the subsequent treatment cost were €8,487 for pembrolizumab+ chemotherapy compared to €12,925 for chemotherapy. Thus, showing a decrease of 34% in subsequent treatment costs for pembrolizumab + chemotherapy arm. The incremental analysis showed that Pembrolizumab+ chemotherapy resulted in an ICER of €28,395 per LY gained and €29,970 per QALY gained compared to chemotherapy. 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 performed to assess the impact of each key parameter on the ICER. The results are presented in Figure 2. The parameters with the biggest impact on the ICER were, the parametric extrapolations, the utility values, the disease management costs and the metastatic treatment costs.

Probabilistic Sensitivity Analysis

A Probabilistic Sensitivity Analysis showed that pembrolizumab had a 97.5% 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.

CONCLUSIONS

Pembrolizumab is a highly cost effective and clinically effective intervention that optimizes health outcomes and the efficient allocation of resources for breast cancer treatment in Greece, in the adjuvant and neo-adjuvant setting.

REFERENCES

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Figure 1: Model Schema

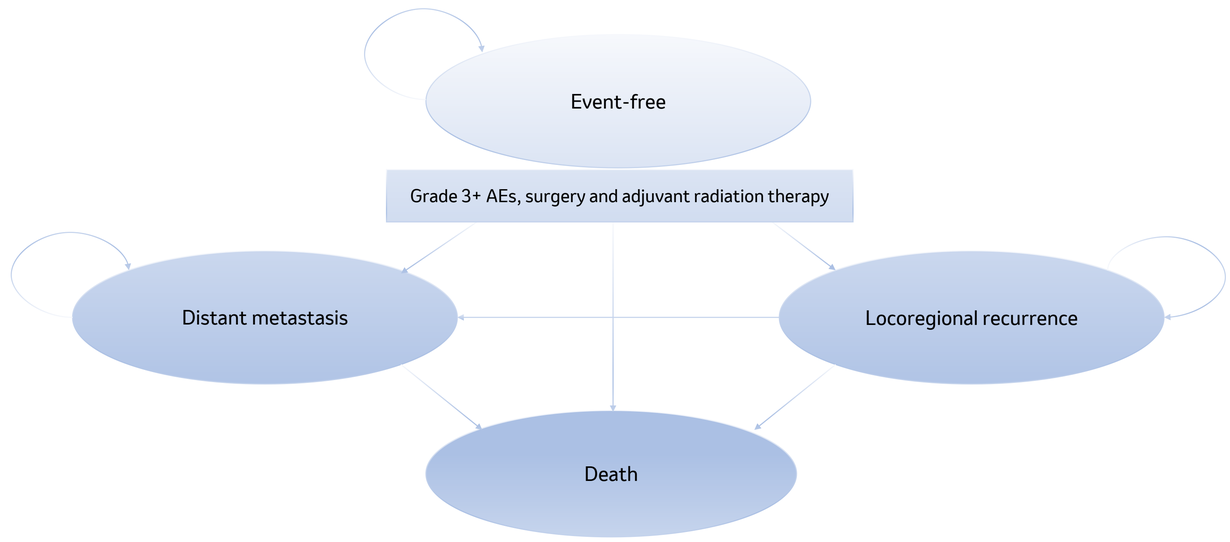

Table 1: Results of the Cost-Effectiveness Analysis-Base Case

	Total			Incremental				
	Costs	**QALYs**	**Life years**	Costs (€)	**QALYs**	Life Years	Cost per QALY gained(€)	Cost per Life Year gained(€)
Pembrolizumab+ Chemotherapy	162,314	13.82	17.75	54,547	2.62	3.37	20,830	16,209
Chemotherapy	107,767	11.20	14.39					

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

Health States	Pembrolizumab + Chemotherapy	Chemotherapy	Incremental
Quality-adjusted life years (QALYs)	**13.82**	**11.20**	**+23%**
Event-free	*14.68*	*11.53*	*+27%*
Locoregional recurrence	*0.32*	*0.56*	*-51%*
Distant Metastasis	*0.54*	*0.58*	*-57%*
Life years (LYs)	**10.91**	**9.79**	**+23%**
Event-free	*9.30*	*7.31*	*+27%*
Locoregional recurrence	*0.38*	*0.66*	*-51%*
Distant Metastasis	*0.67*	*0.72*	*-58%*

Figure 2: Deterministic Sensitivity Analysis Results

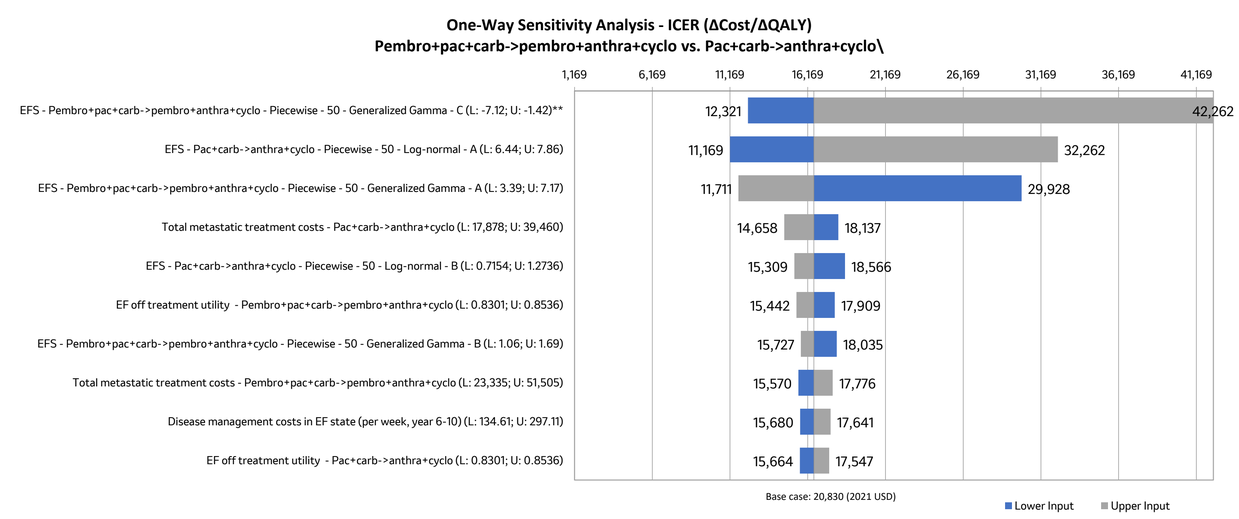

Figure 3: Probabilistic Sensitivity Analysis Results