Cost-effectiveness of pembrolizumab combined with chemotherapy vs chemotherapy as first-line treatment for metastatic TNBC that expresses PD-L1 in the United States

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Introduction

- Accounting for nearly 10%-20% of breast cancer diagnoses, triple-negative breast cancer (TNBC) is associated with a high risk of relapse, poor prognosis, and a considerable economic burden on health-care payers
- KEYTRUDA® (pembrolizumab) is a humanized monoclonal antibody against programmed death 1 (PD-1) that has durable antitumor activity and manageable safety in TNBC. In patients with previously untreated, locally recurrent unresectable or metastatic TNBC (mTNBC), whose tumors express programmed death ligand 1 (PD-L1) (with the combined positive score [CPS] at the cutoff of ≥10), pembrolizumab plus chemotherapy has demonstrated significantly longer progression-free survival (PFS) and overall survival (OS) compared to chemotherapy alone[1]

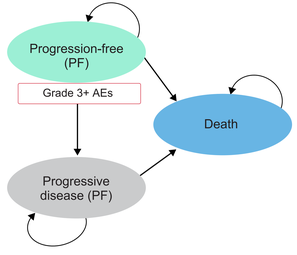
Objective

- To evaluate the cost-effectiveness of pembrolizumab plus chemotherapy compared with chemotherapy alone in patients with previously untreated PD-L1 positive (CPS ≥10) mTNBC. The analysis was conducted from a US third-party payer perspective

Methods

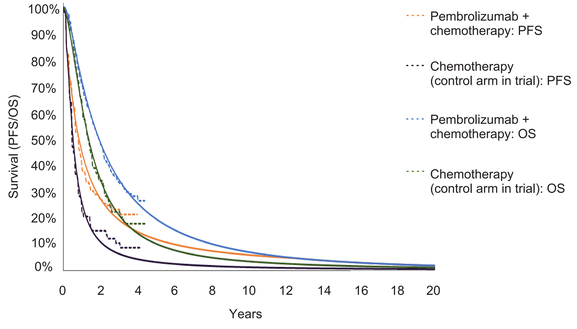
- A three-state partitioned survival model was developed to estimate the clinical effectiveness and expected medical costs associated with the first-line treatment strategies for mTNBC over a 20-year time horizon
- Movement between health states was determined by PFS and OS data for patients treated with pembrolizumab plus chemotherapy and chemotherapy alone from a randomized phase 3 study, KEYNOTE-355 (KN355), with extrapolation based on fitted parametric functions[1]
- Statistical tests based on the Akaike information criterion (AIC) and the Bayesian information criterion (BIC), combined with visual inspection, were used to select the best-fitted parametric functions. In addition, the clinical plausibility of the extrapolated results was considered in selecting the final parametric functions for the model[2]

Figure 1. Model diagram



- PFS: A piecewise modeling approach was used for both treatment arms
  - KN355 Kaplan Meier (KM) estimates were used until week 9, around which point the first radiologic tumor response assessment was performed
  - The best-fitting parametric function, log-logistic distribution was used for both treatment arms thereafter
- OS: A standard parametric modeling approach was used for both treatment arms
  - Log-normal distribution was selected as the best fit for pembrolizumab plus chemotherapy arm
  - Log-logistic distribution was considered as the best fit for chemotherapy arm

Figure 2. Modeled PFS and OS



- Treatment duration: Time-on-treatment data from KN355 were used to model treatment duration
  - The best-fitting parametric function was used for each treatment (gamma for pembrolizumab plus chemotherapy and log-logistic for chemotherapy)
  - Maximum of 35 cycles (2 years) of pembrolizumab treatment was assumed per protocol of KN355 and US label[3]
- EQ-5D-3L health-related quality of life utility data were collected in KN355
- Utility by time to death[4] was used in the model as base case analysis
- Utility decrements associated with adverse events (AE) have been already captured in the EQ-5D utility estimates. No further utility decrements were applied

Table 1. Utility values by time-to-death

Time to death (days)	Mean utility	95% CI
≥360[a]	0.833	(0.817, 0.850)
(180, 360)	0.778	(0.757, 0.799)
(90, 180)	0.712	(0.684, 0.739)
(30, 90)	0.634	(0.590, 0.677)
<30	0.540	(0.442, 0.638)

[a]This time-to-death category includes the records of the patients whose death dates were observed or censored ≥360 days after the report of EQ-5D scores. Other categories only include the records of patients with an observed death date.

- Drug acquisition costs were based on US list prices
  - Pembrolizumab: $5,134 per 100 mg vial
- Drug administration costs were based on 2021 Medicare hospital outpatient payment
- Other cost elements included were AE management, disease management, subsequent therapy, and end-of-life care costs
- All costs prior to 2021 were updated to 2021 US dollars (USD) based on the Medical Care component of the Consumer Price Index
- 80% of medical costs were assumed to be paid by health-care payers

Results

- The base-case analysis projected a longer PFS (1.62 years) and OS (1.31 years) and greater quality-adjusted life-years (QALY, 1.05) in patients receiving pembrolizumab plus chemotherapy compared to those who received chemotherapy alone
- The incremental cost per QALY gained with pembrolizumab vs SoC is $182,732, which is cost-effective per the WHO criteria[5] of three times GDP per capita (which is $209,000 based on 2021 US GDP)

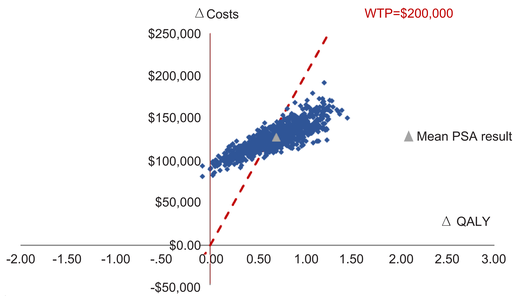
Table 2. Cost-effectiveness results

	Pembrolizumab plus chemotherapy	Chemotherapy	Incremental pembrolizumab plus chemotherapy vs chemotherapy
Life-years (LY)	2.40	1.70	0.70
Quality-adjusted life-years (QALY)	2.99	2.16	0.84
Total cost	$284,122	$156,416	$127,706
Incremental cost-effectiveness ratio (ICER)			
Cost per QALY			**$182,732**
Cost per LY			**$152,289**

Sensitivity analysis result

- One-way sensitivity analyses showed the results were most sensitive to the extrapolation of OS and ToT, and disease management costs
- The cost-effectiveness acceptability curve from the probabilistic sensitivity analysis showed a 65% probability that the ICER will be below $200,000/QALY

Figure 3. Incremental cost-effectiveness plane



Conclusions

- Pembrolizumab plus chemotherapy improves the expected QALYs and is projected to be a cost-effective option compared to chemotherapy alone in PD-L1 positive (CPS ≥10), previously untreated mTNBC patients in the US, based on the WHO willing-to-pay threshold of 3 times GDP per capita

References

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