Cost-Effectiveness of Neoadjuvant and Adjuvant Pembrolizumab in Locally Advanced Head and Neck Cancer

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Background

- Head and neck squamous cell carcinoma (HNSCC) ranks as the sixth most common cancer, with an estimated 900,000 new cases and more than 400,000 deaths annually[1]
- A substantial proportion of patients continue to present with locally advanced HNSCC (stage III–IVA/B), which is associated with a high risk of recurrence and mortality[2,3]
- Pembrolizumab was recently approved as a neoadjuvant and adjuvant therapy in resectable locally advanced HNSCC (LA-HNSCC) based on interim results from the phase III KEYNOTE-689 trial[4]

Objective

To estimate the cost-effectiveness of pembrolizumab as a neoadjuvant and adjuvant therapy in addition to standard of care for resectable LA-HNSCC using a US payer perspective.

Methods

- **Target Population**
  - Patients presenting with resectable LA-HNSCC at time of diagnosis (target population for KEYNOTE-689)
- **Intervention**
  - Neoadjuvant and adjuvant pembrolizumab in addition to standard of care (surgery and adjuvant radiotherapy ± concomitant cisplatin)
- **Comparator**
  - Standard of care alone (surgery and adjuvant radiotherapy ± concomitant cisplatin)
- **Model Approach**
  - Partitioned-survival model with 3-weeks cycles and a 25-year time horizon
- **Perspective**
  - United States payer
- **Health States**
  - Event-free survival (EFS), progressed disease (PD), death
- **Clinical Data**
  - Overall survival (OS) and EFS data were extracted from interim results from KEYNOTE-689 trial, with individual patient data reconstructed using the Guyot algorithm[5]
  - Curve fits were selected based on the lowest Akaike information criterion, visual inspection, and clinical plausibility to project data for a 25-year time horizon
  - Generalized gamma distribution were selected for pembrolizumab OS and standard of care EFS, and lognormal distribution were selected for pembrolizumab EFS and standard of care OS in the base case
  - Background mortality was incorporated from a life table beginning at the baseline age of 60 at cycle 1

Methods (cont.)

- **Costs and Utilities**
  - Costs and utilities were sourced from published literature, the CMS Drug Payment Table, and the CMS Physician and Laboratory Fee Schedules.
  - An annual discount rate of 3% was applied to both costs and health outcomes
- **Analyses**
  - ICERs were calculated for pembrolizumab in addition to standard of care versus stand of care alone
  - One-way and probabilistic scenario analyses were performed for the base case
  - Two scenario analysis in which plausible curves that maximized and minimized pembrolizumab QALYs and were selected ("best case" and "worst case" scenarios)

Figure 1. Parametric Distributions for OS and EFS Curves

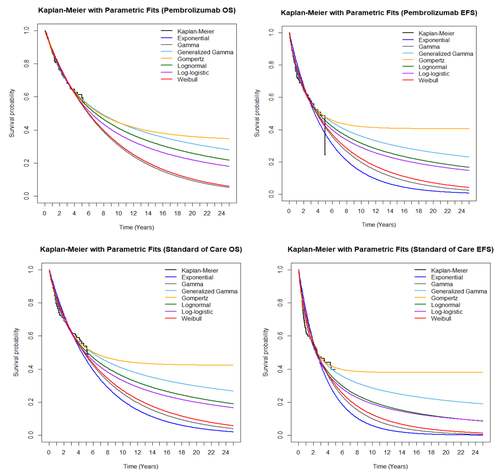


Table 1. Model Inputs

Parameter	Base Case	Lower[b]	Upper[b]
Drug Costs[6-8,a]			
Pembrolizumab[c]	$12,781	$11,503	$14,060
Cisplatin	$44	$39	$48
Health State Utilities[8]			
Event-free survival (EFS)	0.82	0.80	0.90
Progressed disease (PD)	0.77	0.69	0.80
Death	0	N/A	

Table 1. Model Inputs (cont.)

Parameter	Base Case	Lower[b]	Upper[b]
Costs of Adverse Event Management[10]			
Neutropenia	$11,431	$10,288	$12,574
Stomatitis	$20,195	$18,176	$22,215
Adverse Event Disutility[d]			
Neutropenia[11]	-0.14	-0.15	-0.13
Stomatitis[12]	-0.15	-0.17	-0.14

[a] Costs of supportive drugs, drug administration, and laboratory fees also included, assumed body surface area of 1.8 m²; [b] Based on 95% confidence interval where available, otherwise ±10% of the base case value; [c] Patients received 2 cycles of neoadjuvant pembrolizumab and 15 cycles of adjuvant pembrolizumab per the KEYNOTE-689 trial protocol; [d] Adverse events occurring in KEYNOTE-689 with a prevalence of ≥5% in either arm with a ≥2% difference between arms; constant hazard was calculated for median time on treatment in each arm and then adjusted for cycle length

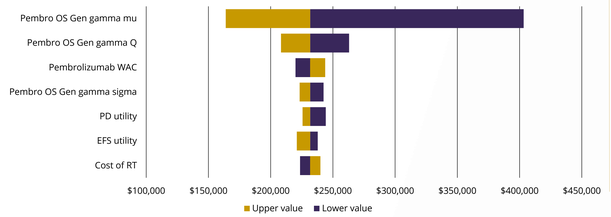
Results

Table 2. Results

	Cost	QALYs	ICER
Base Case			
Pembrolizumab	$523,700	7.44	
Standard of Care	$162,100	5.81	
Incremental	$361,600	1.63	**$220,800**
"Best Case" Scenario Analysis			
Pembrolizumab	$519,900	7.49	
Standard of Care	$162,100	5.81	
Incremental	$357,800	1.68	**$212,800**
"Worst Case" Scenario Analysis			
Pembrolizumab	$545,800	6.64	
Standard of Care	$162,100	5.81	
Incremental	$383,700	0.83	**$462,000**

- Compared to standard of care, the addition of neoadjuvant and adjuvant pembrolizumab was associated with incremental QALYs of 1.63, 1.68, and 0.83 in the base case and scenario analyses respectively, resulting in an **ICER of $220,800 in the base case scenario and ICERs of $108,700 and $462,000 in the "best case" and "worst case" scenario analyses respectively**

Figure 2. Base Case One-Way Sensitivity Analysis (OWSA)



Results (cont.)

- In the OWSA, survival curve parameters and acquisition cost of pembrolizumab had the greatest effect on the base case value, with no value resulting in an ICER that was cost-effective under a $150,000 willingness-to-pay (WTP) threshold
- In the probabilistic sensitivity analysis, pembrolizumab had a 50% chance of being considered cost-effective at a ~$200,000 WTP threshold for the base case

Limitations

- Limited follow-up time from KEYNOTE-689 (median time of 38 months) resulting in uncertainty modeling survival curves
- Utility values were sourced from another analysis evaluating metastatic or recurrent HNSCC, as trial-specific quality of life data were not available at the time of this analysis
- Treatment mixture for trial patients in the PD state was not available and therefore sourced from the literature

Key Takeaways

- This preliminary analysis suggests **pembrolizumab in addition to standard of care may not be cost-effective for LA-HNSCC** at a WTP threshold of $150,000/QALY from a US payer perspective, though there is a **high level of uncertainty based on survival curve projection**
- Results were **most sensitive to survival curve parameters for pembrolizumab**
- The primary limitation to this analysis was the **limited follow-up time from KEYNOTE-689**
- Future analyses should incorporate more **mature survival data** to accurately model a cure fraction scenario as well as utility values derived from quality-of-life surveys in the trial population

Disclosures

- JL is supported by a Genentech-sponsored fellowship
- DV is supported in part by a Genentech-sponsored training program and has served as a consultant to Genentech
- No funding was provided for this study

References