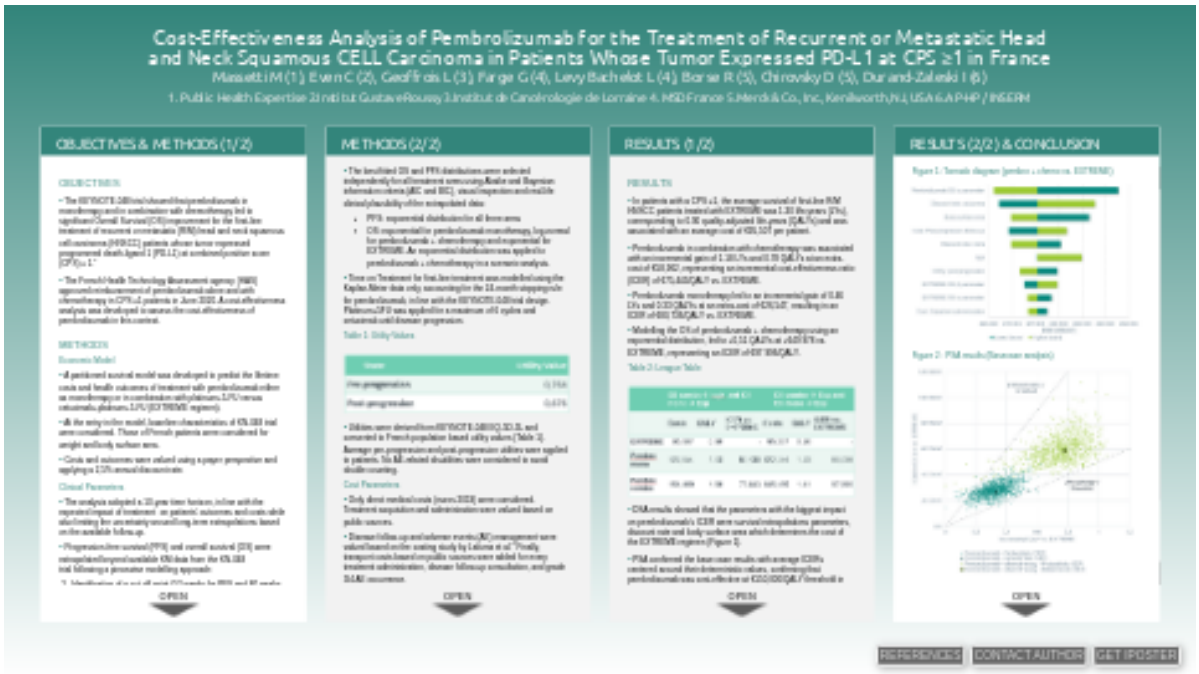
Cost-Effectiveness Analysis of Pembrolizumab for the Treatment of Recurrent or Metastatic Head and Neck Squamous CELL Carcinoma in Patients Whose Tumor Expressed PD-L1 at CPS ≥1 in France



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PRESENTED AT:

OBJECTIVES & METHODS (1/2)

OBJECTIVES

• The KEYNOTE-048 trial showed that pembrolizumab in monotherapy and in combination with chemotherapy led to significant Overall Survival (OS) improvement for the first-line treatment of recurrent or metastatic (R/M) head and neck squamous cell carcinoma (HNSCC) patients whose tumor expressed programmed death-ligand 1 (PD-L1) at combined positive score (CPS) ≥ 1.[1]

• The French Health Technology Assessment agency (HAS) approved reimbursement of pembrolizumab alone and with chemotherapy in CPS ≥1 patients in June 2020. A cost-effectiveness analysis was developed to assess the cost-effectiveness of pembrolizumab in this context.

METHODS

Economic Model

• A partitioned survival model was developed to predict the lifetime costs and health outcomes of treatment with pembrolizumab either as monotherapy or in combination with platinum+5-FU versus cetuximab+platinum+5-FU (EXTREME regimen).

• At the entry in the model, baseline characteristics of KN-048 trial were considered. Those of French patients were considered for weight and body surface area.

• Costs and outcomes were valued using a payer perspective and applying a 2,5% annual discount rate.

Clinical Parameters

• The analysis adopted a 10-year time horizon, in line with the expected impact of treatment on patients' outcomes and costs while also limiting the uncertainty around long-term extrapolations based on the available follow-up.

• Progression-free survival (PFS) and overall survival (OS) were extrapolated beyond available KM data from the KN-048 trial following a piecewise modelling approach:

1. Identification of a cut-off point (52 weeks for PFS and 80 weeks for OS) beyond which the KM curve becomes more stable using statistical tests and visual inspection;
2. Extrapolation of the KM curve beyond this point to the 10-year time horizon, using parametric survival models.

METHODS (2/2)

• The best fitted OS and PFS distributions were selected independently for all treatment arms using Akaike and Bayesian information criteria (AIC and BIC), visual inspection and real-life clinical plausibility of the extrapolated data:

- PFS: exponential distribution for all three arms
- OS: exponential for pembrolizumab monotherapy, log-normal for pembrolizumab + chemotherapy and exponential for EXTREME. An exponential distribution was applied to pembrolizumab + chemotherapy in a scenario analysis.

• Time on Treatment for first-line treatment was modelled using the Kaplan-Meier data only, accounting for the 24-month stopping rule for pembrolizumab, in line with the KEYNOTE-048 trial design. Platinum+5FU was applied for a maximum of 6 cycles and cetuximab until disease progression.

Table 1: Utility Values

State	Utility Value
Pre-progression	0,764
Post-progression	0,676

• Utilities were derived from KEYNOTE-048 EQ-5D-3L and converted to French population based utility values (Table 1). Average pre-progression and post-progression utilities were applied to patients. No AE-related disutilities were considered to avoid double counting.

Cost Parameters

• Only direct medical costs (euros 2019) were considered. Treatment acquisition and administration were valued based on public sources.

• Disease follow-up and adverse events (AE) management were valued based on the costing study by Lafuma et al.[2] Finally, transport costs based on public sources were added for every treatment administration, disease follow-up consultation, and grade 3/4 AE occurrence.

Model Outputs

• Incremental cost-effectiveness ratio (ICER) was calculated as cost per quality-adjusted life year (QALY) gained.

• To assess the robustness of the results, deterministic sensitivity analysis (DSA) was conducted for key variables and probabilistic sensitivity analysis (PSA) was undertaken with 1,000 Monte-Carlo model iterations. Scenario analysis were conducted around main assumptions, including similar OS distributions for both pembrolizumab arms.

RESULTS (1/2)

RESULTS

• In patients with a CPS ≥1, the average survival of first-line R/M HNSCC patients treated with EXTREME was 1.30 life-years (LYs), corresponding to 0.90 quality-adjusted life-years (QALYs) and was associated with an average cost of €95,507 per patient.

• Pembrolizumab in combination with chemotherapy was associated with an incremental gain of 1.18 LYs and 0.78 QALYs at an extra-cost of €58,962, representing an incremental cost-effectiveness ratio (ICER) of €75,443/QALY vs. EXTREME.

• Pembrolizumab monotherapy led to an incremental gain of 0.46 LYs and 0.33 QALYs at an extra-cost of €26,547, resulting in an ICER of €80,736/QALY vs. EXTREME.

• Modelling the OS of pembrolizumab + chemotherapy using an exponential distribution, led to +0,51 QALYs at +€49 978 vs. EXTREME, representing an ICER of €97 996/QALY.

Table 2: League Table

	OS combo→ logN and OS mono → Exp			OS combo → Exp and OS mono → Exp		
	Costs	QALY	ICER vs. EXTREME	Costs	QALY	ICER vs. EXTREME
EXTREME	95,507	0.90	-	95,507	0.90	-
Pembro mono	122,054	1.23	80,736	122,054	1.23	80,736
Pembro combo	154,469	1.68	75,443	145,485	1.41	97,996

• DSA results showed that the parameters with the biggest impact on pembrolizumab's ICER were survival extrapolations parameters, discount rate and body surface area which determines the cost of the EXTREME regimen (Figure 1).

• PSA confirmed the base case results with average ICERs centered around their deterministic values, confirming that pembrolizumab was cost-effective at €150,000/QALY threshold in more than 95% of simulations (Figure 2).

• The willingness-to-pay threshold should reach €110,000/QALY and €94,000/QALY to have >80% probability of being cost-effective, respectively for pembrolizumab mono-therapy and pembrolizumab in combination vs. EXTREME.

RESULTS (2/2) & CONCLUSION

Figure 1: Tornado diagram (pembro + chemo vs. EXTREME)

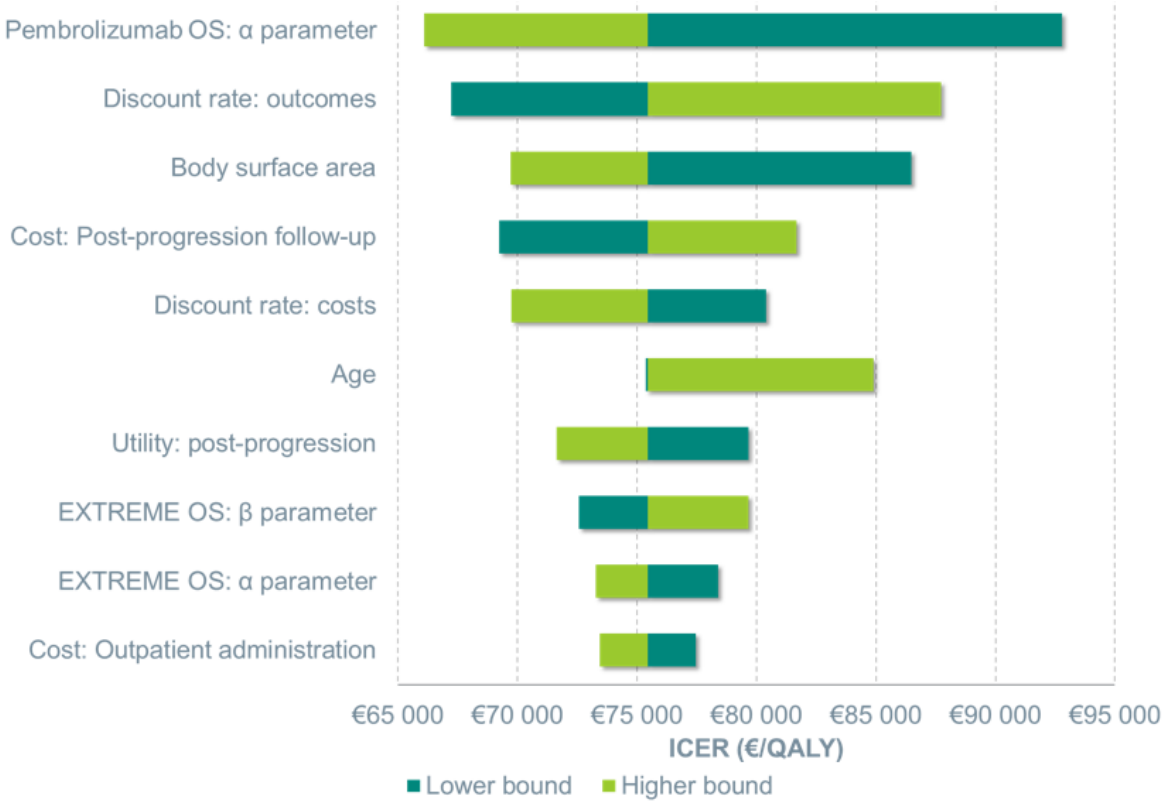
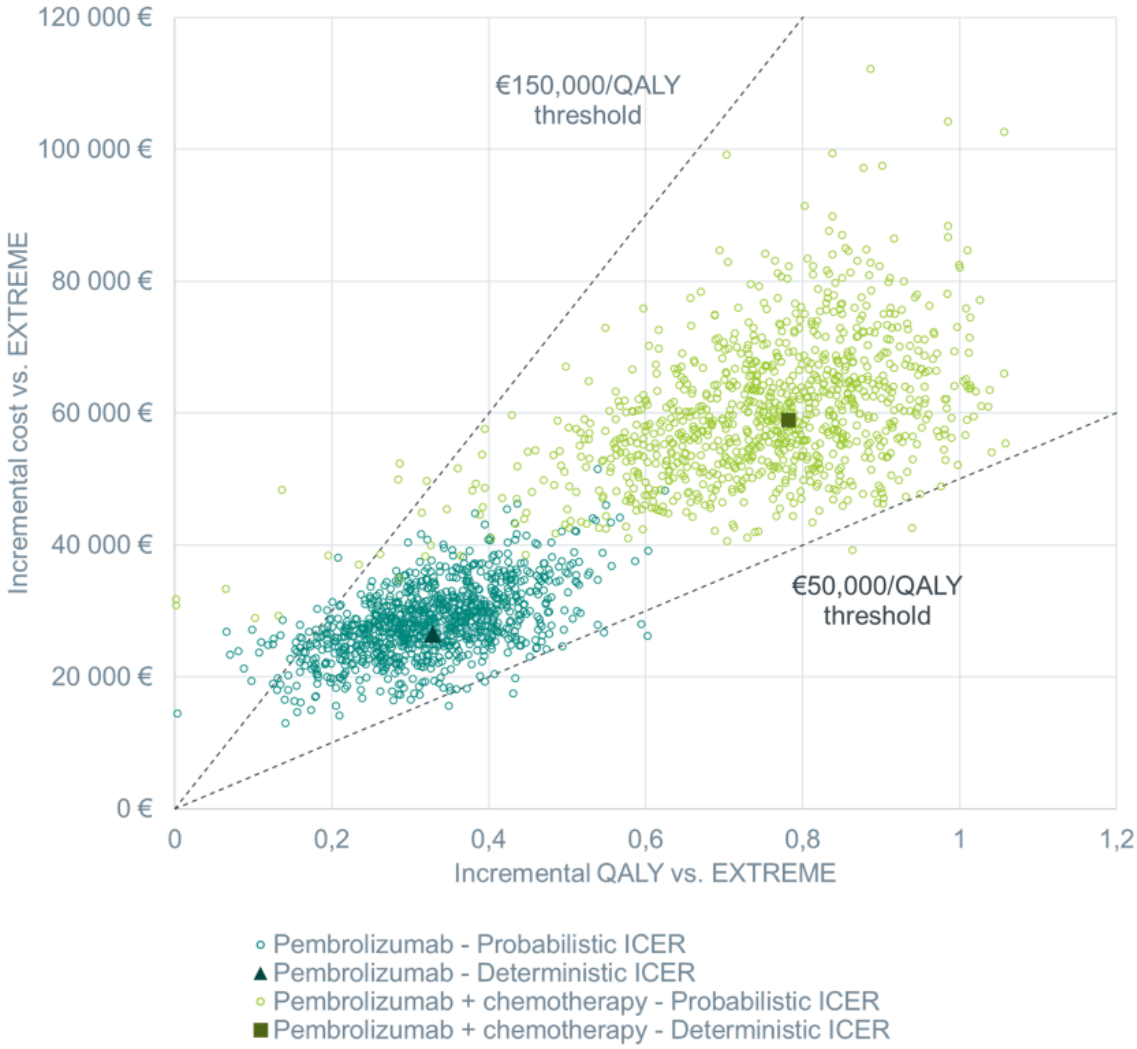


Figure 2 : PSA results (Basecase analysis)



CONCLUSION

In the first-line treatment of R/M HNSCC patients with PD-L1 expression at CPS≥1, pembrolizumab extends patients' survival and improves their quality of life at ICERs consistent with other published results in oncology in France.

AUTHOR INFORMATION

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