Cost effectiveness analysis of nivolumab plus chemotherapy VS chemotherapy in patients with advanced gastric cancer in Japan.

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Background

In Japan, the incidence and mortality rates of gastric cancer are decreasing year by year, but are still high compared to all cancer types. In addition, the incidence of gastric cancer is five times higher than in the United States and Europe.
Nivolumab was recommended as third-line therapy for advanced gastric cancer (AGC) in Japanese practice guidelines, but the CheckMate649 trial provided evidence that nivolumab plus chemotherapy (Niv+Chemo) can be used as first-line therapy. The checkmate649 trial has demonstrated clinical efficacy is high, but has not reported cost-effectiveness. The aim of this study is to assess whether this combination therapy is cost-effective as first-line treatment for patients with AGC, comparing with chemotherapy (FOLFOX, XELOX) in Japanese settings in order to contribute to health policy decision making in Japan.

Method

Model-based cost-effectiveness analysis

A model-based, cost-effectiveness analysis (CEA) was conducted to evaluate the cost-effectiveness of NIV+Chemo compared to chemotherapy such as FOLFOX and XELOX from the perspective of Japanese healthcare payer. We modeled the Japanese patients with AGC assuming the CheckMate649.
A partitioned survival analysis (PartSA) model was developed to predict long-term costs and quality adjusted life years (QALYs) associated with each therapy. In the PartSA, the prognosis of patients with AGC was modeled into three states of "progression-free survival (PFS)", "progressed disease (PD)", and "death".
Outcomes (costs, life years, and QALYs) are evaluated for each health state.

For the base case, we evaluated the ICER of NIV+Chemo in AGC patients. The subgroup analysis on the PD-L1 with a combined positive score (CPS) of five or more and one or more was conducted.
A willingness to pay (WTP) threshold of USD 75,000 per QALY gained was used as the acceptable level of ICER. The time horizon was set to 38 years. Based on the guideline for the cost-effectiveness evaluation in Japan, a discount rate of 2% per annum was applied to long-term costs and QALYs. The cycle length of the model was defined as 1 month. The model was developed and analyzed using TreeAge Pro 2021(R1.2).

Cost

We considered only direct medical costs from the perspective of the Japanese healthcare system. Table 1 summarizes the input values for the cost parameters. All costs were calculated in Japanese yen and converted to US dollars with a currency exchange rate of $1=JPY 100. In this model, the following cost parameters were set: (1) monthly drug costs in PFS, (2) monthly other medical costs in PFS, (3) monthly medical costs in PD, and (4) terminal medical costs (per case). Drug costs for PFS were estimated based on the drug price standard and clinical practice in Japan. Other cost parameters were estimated using the JMDC claims database provided by Japan Medical Data Center Co.,Ld. (JMDC).

Table 1. Costs inputs in simulation model

Cost (USD/month)		Base estimation	Range	
Drug costs in PFS	nivolumab	8,259.80	-10%	10%
	FOFFOX	2,162.39	-10%	10%
	XELOX	1,779.67	-10%	10%
Other medical costs in PFS	FOLFOX	4,889.60	4,807.16	4,972.05
	XELOX	2,732.84	2,681.18	2,784.51
Medical cost in PD	FOLFOX	3,144.17	3,086.83	3,201.53
	XELOX	1,991.85	1,950.23	2,033.48
Terminal care cost (/case)		18,566.47	18,067.27	19,065.67

*PFS: progression-free survival; PD: progressed disease

Utility weight

In this analysis, the utility of "progression-free survival" and "progressed disease" in each treatment group were set as shown in Table 2. The baseline utility weights of "progression-free survival" and "progressed disease" were derived from Shiroiwa T, et al(2011).

Table 2. Utility weights inputs in simulation model

Utility weight		Base estimation	Range	
Progression-free survival	N+C	0.815	-10%	10%
	C	0.797	-10%	10%
Progressed disease	N+C	0.577	-10%	10%
	C	0.577	-10%	10%

*N+C group: Nivolumab plus chemotherapy; C group: Control group

Sensitivity analysis

One-way deterministic sensitivity analyses of each variable were conducted to evaluate the robustness of the base case results. The subgroup analysis on the PD-L1 with a combined positive score (CPS) of five or more and one or more was conducted. In addition, the scenario analysis was conducted to reduce the price of nivolumab by 25% and 50%.

Results

Base case analysis

The ICER of NIV+Chemo compared to chemotherapy was above USD 75,000 per QALY gained which is normally considered a cost-effective threshold of Japanese resources. (Table 3)

Table 3. Base case analysis

	QALY	Incremental QALY	Cost	Incremental Cost (USD)	ICER (USD/QALY)
chemotherapy	1.07	-	102,107	-	-
NIV+Chemo	1.37	0.30	241,317	139,210	458,114

Sensitivity analysis

The tornado diagrams showed that the base case analyses were considered robust enough for decision making, where parameters' end ranges were far away from the willingness to pay. (Figure 1)

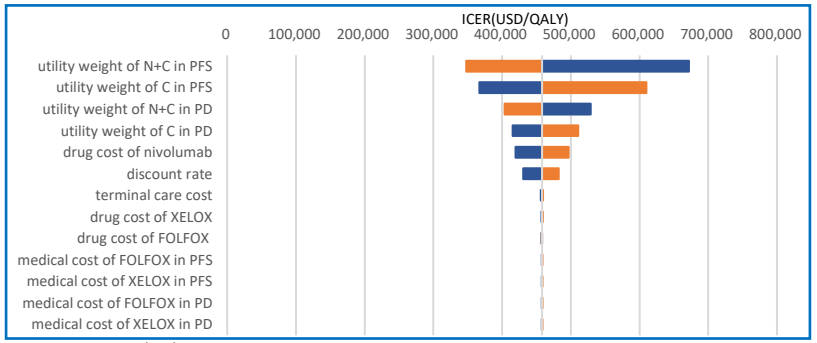

Figure 1. Tornado diagrams
*N+C group: Nivolumab plus chemotherapy; C group: Control group; PFS: progression-free survival; PD: progressed disease

Table 4. Subgroup analysis

	Incremental QALY	Incremental Cost (USD)	ICER (USD/QALY)
PD-L1 CPS of five or more	0.46	166,321	359,134
PD-L1 CPS of one or more	0.34	144,049	424,698

Table 5. Scenario analysis

	Incremental QALY	Incremental Cost (USD)	ICER (USD/QALY)
25% reduction in the price of nivolumab	0.30	109,824	361,410
50% reduction in the price of nivolumab	0.30	80,438	264,707

Conclusion

Applying the willingness to pay threshold of USD 75,000 per QALY, nivolumab plus chemotherapy (NIV+Chemo) therapy might not be cost-effective for the first-line therapy of AGC compared with chemotherapy.

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