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[C2H2404] Summary of cost-effectiveness evaluation of Zolbetuximab (Vyloy)

1. Indications

Claudin-18.2 (CLDN18.2)-positive unresectable advanced or recurrent gastric cancer

2. Price of the drug

Zolbetuximab has been reimbursed since May 2024, and its price as of October 2025 is JPY 65,190. The price is determined using the Similar Efficacy Comparison Method (I), with a usefulness premium (II) of 5%. The product was designated as an item for cost-effectiveness evaluation using the H1 classification.

3. Scope of Cost-effectiveness Evaluation

This product is used to treat patients with human epidermal growth factor receptor 2 (HER2)-negative CLDN18.2-positive unresectable advanced or recurrent gastric cancer. The scope of evaluation, as agreed upon at the first session of the Expert Committee of Cost-Effectiveness Evaluation (ECCEE), is described below:

Target population	(a) Patients with programmed cell death-ligand 1 (PD-L1) combined positive score (CPS) ≥5 (b) Patients with PD-L1 CPS <5
Comparator	(a) Nivolumab with chemotherapy (CAPOX) (b) Chemotherapy (CAPOX)

4. Evaluation of additional benefits

Population (a): Patients with PD-L1 CPS ≥5

The manufacturer conducted an indirect comparison using the results of the

subgroup analysis of patients with CPS≥5 in the GLOW trial and from the CheckMate 649 trial. The 95% credible intervals (CrI) of the hazard ratios (HR) for both OS and PFS crossed 1. However, due to uncertainties such as the small number of subjects in whom CPS was measured in the GLOW trial, the manufacturer concluded that it was difficult to assess the additional benefit of zolbetuximab with CAPOX over nivolumab with CAPOX. The academic group performed sensitivity analyses using the data from the intention-to-treat (ITT) population in the GLOW trial to address the uncertainty of the indirect comparison, as the efficacy of zolbetuximab has not been shown to differ according to PD-L1 CPS status. The HR (95% CrI) for OS and PFS were 1.10 (0.83, 1.47) and 0.97 (0.74, 1.27), and these results aligned with the manufacturer's findings. Although there may be uncertainty about these results, it is difficult to determine whether zolbetuximab with CAPOX is more effective than nivolumab with CAPOX based on current evidence. Therefore, the academic group concluded that additional benefits of zolbetuximab have not been shown in this population group.

Population (b): Patients with PD-L1 CPS <5
The manufacturer concluded that zolbetuximab with CAPOX demonstrated additional benefits over CAPOX, as the OS and PFS in the PD-L1 CPS <5 subgroup of the GLOW trial showed statistically significant differences, consistent with the results of the ITT population. The academic group determined that the manufacturer's analysis was generally appropriate and accepted the results.

5. Results of the cost-effectiveness analysis
The manufacturer conducted a cost-minimization analysis for target population (a) and a cost-effectiveness analysis for the target population (b) using a partitioned survival model consisting of three health states: pre-progression, post-progression, and death. The academic group replaced the prices of zolbetuximab and other drugs with the latest data, and excluded the testing costs of HER2 and CLDN18.2. The results were as follows:

Population	Comparator	ICER (JPY/QALY)
(a) Patients with PD-L1 CPS ≥5	Nivolumab with CAPOX	Cost increase
(b) Patients with PD-L1 CPS <5	CAPOX	17,614,324