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April 26th, 2022

[C2H2003] Summary of cost–effectiveness evaluation of trastuzumab deruxtecan (Enhertu)

1. Indications

· Unresectable or metastatic HER2-positive breast cancer patients who have received chemotherapy

· Unresectable or metastatic HER2-positive gastric cancer patients who have progressed after chemotherapy

2. Price of the drug

Trastuzumab deruxtecan has been reimbursed since May 2020 at JPY 168,434 (as of April 2022). The price is calculated using a similar efficacy comparison method, with a usefulness premium of 5%. This product is designated as an H1 cost–effectiveness evaluation item.

3. Scope of cost–effectiveness evaluation

Hereafter, the scope of evaluation agreed upon at the first session of the Expert Committee of Cost–Effectiveness Evaluation (ECCEE) is described. This product is used for HER2-positive metastatic or gastric cancer. As the effectiveness of trastuzumab deruxtecan for gastric cancer is not likely homogeneous depending on the gene expression, the population was divided into two parts.

Population	Breast cancer Unresectable or metastatic HER2-positive patients who have received prior anti-HER2-based regimens; (a) second-line therapy (b) third- or more line therapy

	Gastric cancer Third-line therapy for unresectable or metastatic HER2-positive patients; (a) patients with HER2-positive (IHC 3+) (b) patients with HER2-positive (IHC 2+ and ISH+)
Comparator	Breast cancer Population (a)/(b): Trastuzumab and chemotherapy with the lowest price Gastric cancer Population (a)/(b): Nivolumab

4. Evaluation of additional benefits

Breast cancer: A systematic review found no clinical studies for population (a), while a single-arm U201 trial was found for population (b). Both the manufacturer and academic group deduced that it is impossible to assess additional benefits in population (a) because of the lack of clinical data. To analyze population (b), the manufacturer compared the U201 trial with the existing cohort studies and randomized controlled trials (RCT) using MAIC (matched-adjusted indirect comparison). Based on the results, the manufacturer insisted trastuzumab deruxtecan has additional benefits to the comparator. Contrarily, the academic group insisted that it is impossible to analyze because the results by MAIC could be largely biased as the randomized DESTINY-Breast 02 trial is ongoing. The third session of the ECCEE indicated that the existing data should be used for the evaluation. Moreover, they concluded that trastuzumab deruxtecan has additional benefits to the comparator based on the results by the manufacturer.

Gastric cancer: The systematic review yielded a randomized J202 trial, which compared trastuzumab deruxtecan with paclitaxel or irinotecan. The manufacturer used MAIC to compare trastuzumab deruxtecan (J202 trial) with the existing cohort study. In contrast, the academic analysis applied indirect comparison using the J202 trial and the results of the network meta-analysis. The third session of the ECCEE concluded that the results of the academic group are more appropriate. Based on the discussion, trastuzumab deruxtecan has additional benefits for population (a) and not population (b).

5. Results of the cost–effectiveness analysis

The manufacturer estimated cost–effectiveness by the partition survival model.

The academic group suggested that the quality of life (QOL) score of patients with breast cancer after third- or more line therapy is too low. In the analysis for gastric cancer, treatment effects estimated by the academic group were used. The ECCEE accepted the following:

Population	ICER (JPY/QALY)
Breast cancer (a) second-line	Impossible to analyze
Breast cancer (b) third- or more line	7,922,603
Gastric cancer (a) IHC 3+	12,235,903
Gastric cancer (b) IHC 2+and ISH+	Cost increase