BACKGROUND

Trastuzumab-d病变体(T-DXd; DS-8201), seen as a first-in-class pembrolizumab-like drug, is a novel molecule composed of three components: (i) a humanized anti-human epidermal growth factor receptor 2 (HER2) monoclonal antibody (mAb) composed of the same amino acid sequence as trastuzumab, covalently linked to (ii) a bispecific linker polypeptide, and (iii) a payload. In each molecule, the HER2-targeting antibody is attached to a tandemly repeated (five copies) diacidic payload.

T-DXd was approved for patients with previously treated HER2-positive recurrent or metastatic breast cancer by the Ministry of Health, Labour and Welfare in Japan in September 2020 and by the Food and Drug Administration in January 2021 based on the randomized, phase 3 DESTINY-Gastric01 trial (NCT03299363). T-DXd is approved in the US with boxed warnings for interstitial lung disease and employment liability.

OBJECTIVE

This post hoc analysis evaluated the overall effect of treatment differences on the quality of survival after discounting for time spent with toxicities or disease progressions.

METHODS

The analysis population included all randomized subjects who received ≥1 dose of study treatment and had ≥1 postdose assessment for objective response.

RESULTS

Patient Disposition

Among the 187 patients in the analysis population, 125 were randomized to T-DXd (6-4 mg/kg in 3-week cycle) and 62 were randomized to PC for trastuzumab (cycling dosage of 140 mg/m² every 2 weeks or palliative starting dose of 80 mg/m² weekly).

Mean Duration of Health States

Table 2 presents the unweighted mean duration of each health state, by treatment arm, for the primary analysis (10.1-month truncation; data cutoff, November 8, 2020) and the sensitivity analysis (4.3-month truncation; data cutoff, June 30, 2020).

Mean duration of health states

<table>
<thead>
<tr>
<th>Health state</th>
<th>T-DXd</th>
<th>PC</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Progression-free survival</td>
<td>10.48</td>
<td>8.88</td>
<td>&lt;0.0001</td>
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<tr>
<td>Time without symptoms and toxicities</td>
<td>1.80</td>
<td>1.37</td>
<td>0.0019</td>
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<td>Overall survival</td>
<td>7.91</td>
<td>7.42</td>
<td>0.0021</td>
</tr>
</tbody>
</table>

CONCLUSIONS

For patients with advanced gastric cancer, T-DXd resulted in greater utility compared with PC, which was statistically and clinically meaningful.

REFERENCES

10. Feinberg School of Medicine, University of Chicago, Chicago, IL, USA; Daichi Sankyo Inc., Basking Ridge, NJ, USA; Daichi Sankyo Europe GmbH, Munich, Germany; KTI Health Solutions, Research Triangle Park, NC, USA; Daichi Sankyo Co., Ltd., Undeclared, Japan; National Cancer Center Hospital East, Kashiwa, Chiba, Japan

Figure 1. Partitioned Survival Plot, 4.3-Month Truncation

Figure 2. Threshold Utility Plot

Figure 3. Time to Event Without Symptoms or Toxicities (TWiST) for patients with HER2-positive advanced gastric cancer. T-DXd patients had a longer median TWiST compared with PC patients (10.1 vs. 9.1 months, respectively).

Figure 4. Health State Utility Weights

Figure 5. Q-TWiST Differences Between Treatment Groups in Months, TDX = All Grade 3+ AE, Sensitivity Analysis (H3.4-Month Truncation)

Figure 6. Q-TWiST Differences Between Treatment Groups in Months, TDX = All Grade 3+ AE, Sensitivity Analysis (H3.4-Month Truncation)