Margetuximab is an investigational Fc-engineered anti-human epidermal growth factor receptor 2 (HER2) monoclonal antibody designed to improve the antibody-dependent cellular cytotoxicity (ADCC) and Fcγ receptor (FcyR) interactions for the treatment of patients with HER2+ metastatic breast cancer after prior anti-HER2 therapies. The current study was an adaptive design study that included three phases to assess the safety and tolerability of margetuximab at different infusion times (30, 60, 90 min) and to determine the fastest safe infusion time after a 120-min margetuximab infusion at Cycle 1 (C1). The study included patients who had received prior trastuzumab, pertuzumab, and ado-trastuzumab emtansine (T-DM1) and were enrolled in a 3-arm adaptive phase 1b study. The primary objective was to determine the incidence of grade ≥3 infusion-related reactions (IRRs) by the end of Cycle 2 (C2) when margetuximab was administered as monotherapy or in combination with chemotherapy (CTX) as well as the overall rate of IRRs. Enrolled patients received a 120-min margetuximab infusion, with or without CTX, at Cycle 1 (C1), then 60- or 30-min infusions at C2 and beyond. The choice of backbone CTX was made by the treating physician based on best judgment and patients' comorbidities. The study demonstrated acceptable safety and tolerability of margetuximab across all infusion times, with the overall rate of IRRs being 21% (18/88) (95% CI: 14%–29%). There were no margetuximab-related deaths. The study results support the ongoing phase 3 SOPHIA study of margetuximab plus CTX vs trastuzumab and CTX in patients with HER2+ metastatic breast cancer after prior anti-HER2 therapies.

### Methods

#### Objectives

- To evaluate the safety and tolerability of margetuximab across different infusion times
- To determine the fastest safe infusion time after a 120-min margetuximab infusion at Cycle 1 (C1)

#### Study Design

- **Phase 1 (C1):** 120-min margetuximab infusion at C1, followed by the fastest safe infusion time at C2 and beyond, either 30 min or 60 min
- **Stage A1:** 18 patients, 120-min infusion at C1
- **Stage A2:** 60-min infusion at C2
- **Stage B:** 30 min at C2 and beyond

#### Table 6:陈莉丽

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Margetuximab Alone</th>
<th>Margetuximab + CTX</th>
<th>Trastuzumab + CTX</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade ≥3 TEAE</td>
<td>36 (47)</td>
<td>31 (48)</td>
<td>32 (48)</td>
</tr>
<tr>
<td>Margetuximab-related AE</td>
<td>33 (43)</td>
<td>33 (52)</td>
<td>30 (45)</td>
</tr>
<tr>
<td>Margetuximab-related serious AE</td>
<td>7 (9)</td>
<td>6 (9)</td>
<td>5 (7)</td>
</tr>
<tr>
<td>Margetuximab-related Death</td>
<td>0</td>
<td>1 (2)</td>
<td>0</td>
</tr>
<tr>
<td>Total MargetuximabSEA</td>
<td>11 (15)</td>
<td>16 (24)</td>
<td>18 (28)</td>
</tr>
</tbody>
</table>

#### Conclusions

- The study demonstrated acceptable safety and tolerability of margetuximab across all infusion times, with the overall rate of IRRs being 21% (18/88) (95% CI: 14%–29%). There were no margetuximab-related deaths.
- The results support the ongoing phase 3 SOPHIA study of margetuximab plus CTX vs trastuzumab and CTX in patients with HER2+ metastatic breast cancer after prior anti-HER2 therapies.

### References


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