Background

Neratinib, an irreversible kinase inhibitor of HER1, HER2, and HER4, is used for the treatment of early-stage HER2-positive breast cancer after trastuzumab-based treatment.

- The international, randomized, placebo-controlled phase III ExteNET trial showed that 240 mg/day neratinib for 1 year (13 cycles) increased the risk of grade 3–4 adverse events compared with placebo, which was not observed in the corresponding phase II control trial.

Methods

All patients with stage I–III breast cancer who had completed ≥6 cycles of trastuzumab were eligible. The study was a randomized, double-blind, placebo-controlled, phase III, international, multicenter trial. The patients were randomized 1:1:1 to loperamide monotherapy, loperamide plus budesonide, or loperamide plus colestipol. All patients were required to use a diary to record intake of prophylaxis.

CONTROL, an international, open-label, sequential-cohort study, is investigating the effect of adding budesonide or colestipol to loperamide prophylaxis on neratinib-associated diarrhea in patients with HER2+ breast cancer. The study is ongoing.

Results

The study is still ongoing and results will be presented at a future conference.

Table 2. Characteristics of treatment-emergent diarrhea (Safety population)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Loperamide</th>
<th>Loperamide with budesonide</th>
<th>Loperamide with colestipol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade ≥2</td>
<td>8%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Grade ≥3</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Discontinuation</td>
<td>2%</td>
<td>2%</td>
<td>2%</td>
</tr>
<tr>
<td>Hospitalization</td>
<td>3%</td>
<td>3%</td>
<td>3%</td>
</tr>
</tbody>
</table>

Conclusions

The addition of colestipol to loperamide prophylaxis resulted in the greatest reduction in treatment-emergent diarrhea events compared with placebo and loperamide plus budesonide in the ExteNET trial, and may further diminish the duration of diarrhea.

References


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