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Efficacy of Casopitant, a Novel Neurokinin-1 Receptor Antagonist, for Antiemesis Over Repeated Cycles of Moderately Emetogenic Therapy

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INTRODUCTION
Chemotherapy-induced nausea and vomiting (CINV) associated with anthracycline-cyclophosphamide (AC), frequently used to treat breast cancer, is considered to be among the most difficult CINV to prevent.

Casopitant is a potent and selective neurokinin 1 receptor antagonist that is currently in development for prevention of CINV and postoperative nausea and vomiting. Phase II and phase III trials have evaluated the safety and efficacy of casopitant added to a 2-drug (ondansetron and dexamethasone) antiemetic regimen in patients receiving moderately or highly emetogenic chemotherapy (MEC or HEC).

A phase III study performed in patients receiving MEC (primarily AC) demonstrated a significant benefit with single oral, 3-day oral, and 3-day intravenous (IV) oral casopitant added to ondansetron plus dexamethasone during the first cycle of chemotherapy.

This post report the results of a post hoc analysis of data from the multiple-cycle extension of the study.

METHODS

Study Design
- Phase III, multinational, multicentre, randomised, double-blind, active-controlled, 4-arm, parallel-group study

Figure 1. Study Schematic

RESULTS

Patient Disposition
- Generally balanced across the 4 treatment groups for the ITT population
- 98% were female and 95%–97% had a diagnosis of breast cancer
- Overall, 96% of participants completed cycle 1 of treatment and 76% completed all planned cycles

Patient Demographics and Baseline Characteristics (ITT Population)

Table 1. Demographics and Baseline Characteristics (ITT Population)

| Treatment Group | Gender | Age (years) | Bodyweight (kg) | Performance Status
|-----------------|--------|-------------|-----------------|-------------------|
| Ondansetron & dexamethasone + casopitant 3-day IV/oral | Female | >18 | 60 | 0–2
| Ondansetron & dexamethasone + casopitant 3-day oral | Female | >18 | 60 | 0–2
| Ondansetron & dexamethasone | Female | >18 | 60 | 0–2
| Ondansetron & dexamethasone + casopitant 3-day IV | Female | >18 | 60 | 0–2

Note: All patients received ondansetron 8 mg orally twice daily on Days 1-3 and a single dose of dexamethasone 8 mg IV on Day 1. Follow-up for safety was at least through end of cycle.

Efficacy in Cycle 1
- Casopitant added to standard antiemetic therapy significantly increased the percentage of patients who achieved a CR in cycle 1 for all 3 dosing regimens

Table 3. Probability of CR During Any MEC Cycle With Casopitant Added to Standard Antiemetic Therapy

<table>
<thead>
<tr>
<th>Treatment Group</th>
<th>Casopitant Added</th>
<th>Casopitant Not Added</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ondansetron &amp; dexamethasone</td>
<td>90%</td>
<td>80%</td>
<td>.001</td>
</tr>
<tr>
<td>Ondansetron &amp; dexamethasone + casopitant 3-day IV/oral</td>
<td>90%</td>
<td>80%</td>
<td>.001</td>
</tr>
<tr>
<td>Ondansetron &amp; dexamethasone + casopitant 3-day oral</td>
<td>90%</td>
<td>80%</td>
<td>.001</td>
</tr>
</tbody>
</table>

RESULTS (cont’d)

Statistical Analyses
- Primary endpoint
  - Percentage of patients with complete response (CR) (no vomiting/retching, and no rescue therapy) during the first 120 hours following the initiation of their first cycle of MEC regimen
- Secondary endpoints
  - CR during first 120 hours for cycles 2, 3, and 4
  - No formal testing was provided for these analyses

A subject diary was used to record efficacy data (including emesis, nausea, and rescue medications) during the 120-hour assessment phase of each cycle of chemotherapy.

Need for antiemetic rescue medication (any drug taken specifically for nausea and/or emesis) during the 120-hour assessment period was considered a treatment failure.

CONCLUSIONS
- Casopitant added to ondansetron plus dexamethasone consistently increased overall CR (0–120) rates over repeated chemotherapy cycles
- No difference in protection from nausea was seen during multiple cycles
- Casopitant was well tolerated across all cycles

REFERENCES