supportive care

MULTICYCLE EFFICACY AND SAFETY OF NEPA, A FIXED-DOSE ANTIEMETIC COMBINATION OF NETUPITANT AND PALONOSETRON, IN PATIENTS RECEIVING CHEMOTHERAPY OF VARYING EMETOGENICITY

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Aim: As emesis is more difficult to suppress once it occurs, preventing chemotherapy-induced nausea and vomiting from the initial cycle through repeated cycles is essential for an optimal patient-centered approach to cancer management. NEPA is a novel, fixed-dose combination of a new NK1 receptor antagonist (RA), netupitant (NETU 300 mg), and palonosetron (PALO 0.50 mg), a pharmacologically distinct 5-HT3 RA. NEPA is designed to overcome barriers hindering guideline adherence by targeting two molecular pathways with a single, oral fixed-dose product. NEPA was previously shown to be superior to PALO after a single chemotherapy (CT) cycle; maintenance of efficacy over multiple cycles has been evaluated in a combined dataset from 2 pivotal trials.

Methods: These large multinational, randomized studies assessed the efficacy/safety of a single oral dose of NEPA (vs PALO or aprepitant+PALO) in chemotherapy-naive patients receiving multiple cycles of either anthracycline-based (AC) moderately emetogenic CT (MEC) [study 1] or non-AC based MEC or highly emetogenic CT (HEC) [study 2]. All patients also received oral dexamethasone (DEX). Efficacy endpoints were complete response (CR: no emesis, no rescue) and no significant nausea (max <25 mm on 100 mm VAS) during the overall (0-120h) phase.

Results: 1033 NEPA-treated patients participated in 4428 total cycles in these two trials; 76% completed at least 4 cycles. Overall CR and no significant nausea rates were high and were maintained across 4 cycles of CT with rates being modestly lower in patients receiving AC MEC compared to non-AC MEC and HEC.

<table>
<thead>
<tr>
<th>Cycle</th>
<th>CR</th>
<th>No Significant Nausea</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>(N=AC/non-AC/HEC)</td>
<td>AC</td>
</tr>
<tr>
<td>Cycle 1 (N=724/235/74)</td>
<td>74%</td>
<td>80%</td>
</tr>
<tr>
<td>Cycle 2 (N=635/212/68)</td>
<td>80%</td>
<td>88%</td>
</tr>
<tr>
<td>Cycle 3 (N=596/196/63)</td>
<td>84%</td>
<td>91%</td>
</tr>
<tr>
<td>Cycle 4 (N=551/181/52)</td>
<td>84%</td>
<td>92%</td>
</tr>
</tbody>
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The type/incidence of AEs was typical for a diverse cancer population receiving chemotherapy and raised no safety concerns.

Conclusions: This is the largest multiple cycle dataset for an antiemetic and provides confidence in the preservation of benefit with NEPA over multiple cycles of AC- and non-AC MEC and HEC. NEPA, a highly convenient, guideline-based antiemetic combination may result in greater adherence and consequently improved emetic control.