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Abstract P3-09-01: NEPA, a fixed-dose combination of netupitant and palonosetron, prevents chemotherapy-induced nausea and vomiting (CINV) more effectively and reduces the impact on daily living for breast cancer patients compared with palonosetron

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Abstract

Background:

Breast cancer (BC) patients receiving anthracycline-cyclophosphamide (AC) chemotherapy (CT) are at risk for developing CINV due not only to the emetogenicity of the CT but also to young age and gender. As recommended by international antiemetic guidelines, targeting multiple molecular pathways involved in emesis related to AC is important for maximizing control of CINV and improving the functional status of BC patients during CT. NEPA is a fixed-dose combination of netupitant (NETU), a highly-selective NK_1 receptor antagonist (RA), and palonosetron (PALO), a pharmacologically distinct 5-HT_3 RA, that targets dual antiemetic pathways with a convenient single day dose.

Methods:

This was a multinational, randomized, double-blind, phase 3 study evaluating the efficacy and safety of a single oral dose of NEPA (NETU 300 mg + PALO 0.50 mg) versus a single oral 0.50 mg dose of PALO in chemotherapy-naive patients receiving AC. All patients received oral dexamethasone (DEX) on day 1 (12 mg NEPA arm; 20 mg PALO arm). The primary efficacy endpoint was complete response (CR: no emesis, no rescue medication) in the delayed phase, 25-120h after CT. The Functional Living Index-Emesis (FLIE) questionnaire with a 5-day recall period was used to assess the impact of CINV on patients' daily lives as a secondary endpoint. The FLIE consists of 9 nausea-specific (nausea domain) and 9 vomiting-specific (vomiting domain) items that address the effect of nausea and vomiting on daily life. Each item is scored on a 7-point 100 mm visual analog scale with anchors of "none/not at all" and "a great deal". The proportion of patients with an average item score >6 reflecting "no impact on daily life" (NIDL) (ie, total FLIE score >108, nausea/vomiting domain score >54) was compared for NEPA vs PALO using a Cochran-Maentel-Haenszel test stratified by age class and region.

Results:

1455 patients with a mean age of 54 were randomized to receive NEPA or PALO. Treatment groups were similar; 98% were females with BC (97%).

As previously reported (ASCO 2013), NEPA showed superior CR rates compared to PALO for the acute 0-24h (88% vs 85%; p = 0.047), delayed (77% vs 70%; p = 0.001) and overall 0-120h (74% vs 67%; p = 0.001) phases.

A greater proportion of NEPA-treated patients reported NIDL for nausea, vomiting and combined domains compared to PALO.

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The adverse event (AE) profile was comparable between groups. Most frequently reported treatment-related AEs for NEPA and PALO, respectively, were headache (3.3%, 3.0%) and constipation (2.1%, 2.1%).

Conclusions:

In this large Phase 3 study of predominantly females with BC receiving AC, NEPA was superior to PALO in preventing CINV and reducing the negative impact of CINV on patients' daily lives. As a fixed-dose antiemetic drug combination including an NK_1 RA and $5\text{-}HT_3$ RA, NEPA offers improved efficacy over PALO alone, with a convenient single-day dose, and oral DEX only on day 1.

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