Journal Watch

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(Pharm D)

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Olanzapine versus aprepitant for the prevention of chemotherapy-induced nausea and vomiting: a randomized Phase III trial.

Narvari RM, Gray SE, Kerr AC. J Supp Oncol 9:5 p188-195 Sept/Oct2011

Abstract

Background: The purpose of the study was to compare the effectiveness of olanzapine (OLN) with aprepitant (APR) for the prevention of chemotherapy-induced nausea and vomiting (CINV) in patients receiving highly emetogenic chemotherapy.

Methods: A phase III trial was performed in chemotherapy-naive patients receiving cisplatin ≥70mg/m^2 or cyclophosphamide ≥ 500mg/m^2 + doxorubicin ≥ 50mg/m^2, comparing OLN to APR in combination with palonosetron (PAL) and dexamethasone (DEX). The OLN, PAL, DEX (OPD) regimen was OLN 10mg po, PAL 0.25mg IV + DEX 20mg IV, pre-chemo day1 & OLN 10 mg po post-chemo days 2-4. The APR, PAL, DEX arm (APD) regimen consisted of APR 125mg po, PAL 0.25mg IV, + DEX 12mg IV day 1 and APR 80mg po days 2 & 3 + DEX 4 mg PO bid days 2-4. 251 patients consented to the protocol and were randomized. 241 patients were evaluable.

Results: Complete response (CR) was defined as no emesis and no rescue was 97% for the acute period (24 hrs post chemotherapy) & 77% for the delayed period (2-5 days post-chemo) & 77% for the overall period (0-120hrs) for 121 patients receiving the OPD regimen. CR was 87% of the acute period, 73% for the delayed period & 73% overall for the 121 patients receiving the APD regimen. Patients without nausea (0 on 1-10 scale M D Anderson Symptom Inventory) were for OPD: 87% acute, 69% delayed & 69% overall. APD was 87% acute, 38% delayed and 38% overall with the APD regimen. There were no grade 3 or 4 toxicities. CR and control of nausea in subsequent chemo cycles were equal to or greater than cycle 1 for both regimens. OPD was comparable to APD in control of CINV. Nausea was better controlled with OPD.

Discussion: In this study OLN was a single dose of DEX and PAL was very effective at acute and delayed CINV in patients receiving highly emetogenic chemotherapy.CR rates were not significantly different from a similar group of patients receiving highly emetogenic chemotherapy and an antiemetic regimen APD.

Strengths:

Not sponsored by industry.

Randomized controlled trial study design was used.

MDASI is a validated tool.

All randomized patients were accounted for, although ITT analysis was not used, drop-out rate was small, and equal in both arms and therefore probably did not affect the results significantly.

Demographic data and patient characteristics appeared equal in each arm.

Weaknesses:

The study was not blinded probably because a double dummy technique would have to be used to maintain blinding, as the regimens are different. The authors did not consider this to be a problem as all the subjects were chemo-naïve.

Palonosetron is not yet available in Canada so 1st generation $5HT_3$ antagonists would have to be substituted in these protocols if we were to try to reproduce the results here.

Relevance to palliative care: As cancer patients are receiving palliative care earlier in the trajectory of their disease, increasing numbers of palliative patients are receiving chemotherapy. It is therefore, important that we recognize which protocols are considered highly or moderately emetogenic (HEC/MEC) to ensure adequate antiemetic treatments are ordered to avoid CINV. Aprepitant is the standard of care for HEC and can be considered in MEC per current guidelines. Aprepitant is expensive, and not always available at the Grey Nuns, thus olanzapine can be considered as an effective alternative. Cost is also a consideration for the large outpatient population at the Cross Cancer Institute who finance their supportive therapies.

Aprepitant is only available in oral form and as fosaprepitant for IV use. Available in oral, oral dissolving and injectable (including subcutaneous routes), olanzapine has the versatility of dosing options required of anti-emetics.

Furthermore, the anti-anxiety properties of olanzapine may be of use in the control of anticipatory CINV and there is demonstrated value in olanzapine's anti-emetic properties for nausea and vomiting for reasons other than CINV. The side effects of olanzapine, such as weight gain are not usually a concern in the palliative population, many of whom are experiencing anorexia and/or cachexia. Sedation may or may not be an issue with this population.