# A221602

# Olanzapine With or Without Fosaprepitant for the Prevention of Chemotherapy Induced Nausea and Vomiting (CINV)in Patients Receiving Highly Emetogenic Chemotherapy (HEC): A Phase III Randomized, Double Blind, Placebo-Controlled Trial

**ClinicalTrials.gov Identifier: NCT03578081**

## Study Background

### Trial Description

This randomized phase III trial studies how well olanzapine with or without fosaprepitant work in preventing chemotherapy induced nausea and vomiting in cancer patients receiving chemotherapy that causes vomiting. Olanzapine and fosaprepitant dimeglumine may help control nausea and vomiting in patients during chemotherapy. Olanzapine is usually given in combination with other drugs, including fosaprepitant dimeglumine. It is not yet known if olanzapine when given with other drugs, is still effective without using fosaprepitant dimeglumine for controlling nausea and vomiting.

### Arms:

Arm I (fosaprepitant dimeglumine, olanzapine): (Experimental): Patients receive palonosetron hydrochloride IV over 30 seconds or ondansetron hydrochloride IV over 2-5 minutes or PO on day 1, dexamethasone PO on days 1-4, fosaprepitant dimeglumine IV over 20-30 minutes on day 1, and olanzapine PO on days 1-4. Treatment may repeat every 4 days for up to 3 courses in the absence of disease progression or unacceptable toxicity.

Arm II (placebo, olanzapine): (Active Comparator): Patients receive palonosetron hydrochloride IV over 30 seconds or ondansetron hydrochloride IV over 2-5 minutes or PO on day 1, dexamethasone PO on days 1-4, placebo IV over 20-30 minutes on day 1, and olanzapine PO on days 1-4. Treatment (with no placebo) may repeat every 4 days for up to 3 courses in the absence of disease progression or unacceptable toxicity.

**Objectives:**

- PRIMARY OBJECTIVES:
  I. To compare between the two study arms the proportion of patients with no nausea for the overall (0-120 hours post-chemotherapy), acute (0-24 hours post-chemotherapy), and delayed periods (24-120 hours postchemotherapy) for patients receiving highly emetogenic chemotherapy (HEC).

- SECONDARY OBJECTIVES:
  I. To compare between the two study arms the complete response (CR) rates (no emetic episodes and no use of rescue medication) in the acute, delayed, and overall periods.
  II. To compare between the two study arms, the incidences of potential toxicities that have been ascribed to olanzapine.
  III. To perform an economic evaluation of olanzapine and fosaprepitant dimeglumine (fosaprepitant) versus (vs.) olanzapine in patients receiving HEC (noting that all patients will also receive dexamethasone and a 5HT3 receptor antagonist).
  IV. To explore the efficacy of olanzapine in chemotherapy cycles two to four, for patients who elect to continue on the same antiemetic regimen received in cycle one, in chemotherapy cycles two to four (continuation phase), by documenting nausea and complete response.
  V. To explore the safety of olanzapine in chemotherapy cycles two to four, for patients who elect to continue on the same antiemetic regimen received in cycle one, in chemotherapy cycles two to four (continuation phase), by recording any adverse events or drug related toxicities.

- OUTLINE: Patients are randomized to 1 of 2 arms.

  ARM I: Patients receive palonosetron hydrochloride intravenously (IV) over 30 seconds or ondansetron hydrochloride IV over 2-5 minutes or orally (PO) on day 1, dexamethasone PO on days 1-4, fosaprepitant dimeglumine IV over 20-30 minutes on day 1, and olanzapine PO on days 1-4. Treatment may repeat every 4 days for up to 3 courses in the absence of disease progression or unacceptable toxicity.

  ARM II: Patients receive palonosetron hydrochloride IV over 30 seconds or ondansetron hydrochloride IV over 2-5 minutes or PO on day 1, dexamethasone PO on days 1-4, placebo IV over 20-30 minutes on day 1,

and olanzapine PO on days 1-4. Treatment (with no placebo) may repeat every 4 days for up to 3 courses in the absence of disease progression or unacceptable toxicity. After completion of study, patients are followed up periodically.

## Study Milestones:

Start date: November 20, 2018

Primary Completion Date: November 8, 2021

## Publication Information:

Analysis Type: Primary

PubMed ID: 37284847

Citation: The Oncologist. 2023 June 7;28(8):722-9. doi: 10.1093.

Associated Datasets: NCT03578081-D1-Dataset.csv (primary), NCT03578081-D2-Dataset.csv (continuation), NCT03578081-D3-Dataset.csv (ae)

## Dataset Information:

Dataset Name: NCT03578081-D3-Dataset.csv (ae)

Description: This dataset, NCT03578081-D3-Dataset.csv, is one of 4 datasets associated with PubMed ID 37284847, and contains data related to adverse events. Dataset NCT03578081-D1-Dataset.csv contains data presented in the consort diagram, baseline characteristics table, primary analysis, and supplementary material. Dataset NCT03578081-D2-Dataset.csv contains daily nausea severity scores for patients that continued with the regimen in cycles 2-4. Dataset NCT02116530-D1 associated with this publication contains data from a previous study, A221301, which is presented in Figure 3 and Supplemental Table 2.

Data can be used to approximate published study findings, but exact reproduction of previous manuscripts may not be possible in some cases (e.g., when data must be modified for de-identification purposes or have undergone further data cleaning).

Blank values indicate data not applicable or missing, except where otherwise noted.

## NCT03578081-D3-Dataset.csv (ae) Data Dictionary:

| LABEL | NAME | ELEMENTS | COMMENTS |
|---|---|---|---|
| Data Center ID | dcntr_id | | |
| Arm | arm | Fosaprepitant, Placebo | Was not assigned for adverse events reported in cycle 0 (baseline). |
| Cycle | cycle | 0, 1, 2, 3, 4 | |
| Toxicity | toxicity | | |
| Toxicity Code | toxcode | | |
| General System Organ Class | soc | | |
| Grade | grade | 0, 1, 2, 3, 4, 5 | |
| Relationship to Study Medication | relation | DEFINITE, NOT RELATED, POSSIBLE, PROBABLE, UNLIKELY | Was not assigned for adverse events reported in cycle 0 (baseline). |