

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-D1-Dataset.csv (primary)

Description: This dataset, NCT03578081-D1-Dataset.csv, is one of 4 datasets associated with PubMed ID 37284847 and 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 NCT03578081-D3-Dataset.csv contains data related to adverse events. 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-D1-Dataset.csv (primary) Data Dictionary:

LABEL	NAME	ELEMENTS	COMMENTS
Data Center ID	dcntr_id		
Arm	arm	Fosaprepitant, Placebo	
Evaluable for Primary Endpoint	eval	No, Yes	
Withdrew prior to starting protocol treatment	cancel	No, Yes	
Ineligible	inelig	No, Yes	
Had a major violation	mv	No, Yes	
Age (years)	age		

LABEL	NAME	ELEMENTS	COMMENTS
Race	race	American Indian or Alaskan Native, Asian, Black or African American, More Than One Race, Native Hawaiian or Pacific Islander, Unknown or Not reported: Patient refused or not available, White and Hispanic, White and not Hispanic, White and unknown, not reported ethnicity	An error in the published manuscript states that there are 12 total White and Hispanic origin unknown individuals in the study. There should be 24 total White and Hispanic origin unknown individuals.
ECOG Performance Score	ecogps	0, 1, 2	
Chemotherapy Regimen	chemoreg	Cisplatin-containing regimen, Doxorubicin and cyclophosphamide	In Supplemental Table 3, nomenclature changes to anthracycline and cyclophosphamide instead of doxorubicin and cyclophosphamide as doxorubicin is an anthracycline class medication.
Sex	gender	Female, Male	
5-HT receptor antagonist	antrecpt	Ondasetron, Palonosetron	

LABEL	NAME	ELEMENTS	COMMENTS
Worst nausea over the past 24 hours (baseline)	nausea_r	0, 1, 2, 3, 4, 5, 6, 7, 9, 10	
Undesired sedation trouble over the past 24 hours (baseline)	sedationtrb_r	0, 1, 2, 3, 4, 5, 6, 7, 10	
Undesired appetite increase over the past 24 hours (baseline)	appetite_r	0, 1, 2, 3, 4, 5, 6, 7, 8, 10	
Has Nausea in Acute Period	nausea_acute	No, Yes	
Has Nausea in Delayed Period	nausea_delayed	No, Yes	
Has Nausea in Overall Period	nausea_overall	No, Yes	
Nausea Score Day 1	nausea2	0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10	
Nausea Score Day 2	nausea3	0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10	
Nausea Score Day 3	nausea4	0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10	
Nausea Score Day 4	nausea5	0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10	

LABEL	NAME	ELEMENTS	COMMENTS
Nausea Score Day 5	nausea6	0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10	
Sedation Trouble Score Day 1	sedationtrb2	0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10	
Sedation Trouble Score Day 2	sedationtrb3	0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10	
Sedation Trouble Score Day 3	sedationtrb4	0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10	
Sedation Trouble Score Day 4	sedationtrb5	0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10	
Sedation Trouble Score Day 5	sedationtrb6	0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10	
Undesired Appetite Increase Score Day 1	appetite2	0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10	
Undesired Appetite Increase Score Day 2	appetite3	0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10	
Undesired Appetite Increase Score Day 3	appetite4	0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10	

LABEL	NAME	ELEMENTS	COMMENTS
Undesired Appetite Increase Score Day 4	appetite5	0, 1, 2, 3, 4, 5, 6, 7, 8, 10	
Undesired Appetite Increase Score Day 5	appetite6	0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10	
Complete Response in the Acute Period	cr_acute	No, Yes	
Complete Response in the Delayed Period	cr_delayed	No, Yes	
Complete Response in the Overall Period	cr_overall	No, Yes	
Number of Rescue Meds Day 1	num-pills2	0, 1, 2, 3	
Number of Rescue Meds Day 2	num-pills3	0, 1, 2, 3	
Number of Rescue Meds Day 3	num-pills4	0, 1, 2, 3	
Number of Rescue Meds Day 4	num-pills5	0, 1, 2, 3	

LABEL	NAME	ELEMENTS	COMMENTS
Number of Rescue Meds Day 5	numpills6	0, 1, 2, 3	
Had Vomiting in Overall Period	vomiting_overall	No, Yes	
Had Vomiting in Acute Period	vomiting_acute	No, Yes	
Had Vomiting in Delayed Period	vomiting_delayed	No, Yes	
Continued with Regimen in Cycles 2-4	continued	No, Yes	It was reported that 71% of patients in each arm agreed to continue with the regimen. 71% of evaluable patients in the Fosaprepitant arm continued while 73% of evaluable patients in the Placebo arm continued.