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Completed

A Study to Assess the Safety and the Efficacy of IV Fosnetupitant/ Palonosetron (260 mg/0.25 mg) Combination Compared to Oral Netupitant/ Palonosetron (300 mg/0.5 mg) Combination for the Prevention of CINV in AC Chemotherapy in Women With Breast Cancer

ClinicalTrials.gov ID NCT03403712

Sponsor Helsinn Healthcare SA

Information provided by Helsinn Healthcare SA (Responsible Party)

Last Update Posted 2020-06-01

Study Details Tab

Study Overview

Brief Summary

Multicenter, randomized, double-blind, double-dummy, parallel group, stratified study assessing the safety and describing the efficacy of a single dose of intravenous (IV) fosnetupitant/palonosetron (260 mg/0.25 mg) infusion [test] versus oral netupitant/palonosetron (300 mg/0.5 mg) combination [control]; each administered with oral dexamethasone prior to initial and repeated cycles of AC chemotherapy in female breast cancer patients.

Official Title

A Multicenter, Randomized, Double-blind, Double-dummy, Active-controlled, Parallel Group Phase 3b Study to Assess the Safety and to Describe the Efficacy of IV Fosnetupitant/Palonosetron (260 mg/0.25 mg) Combination (IV NEPA FDC) Compared to Oral Netupitant/Palonosetron (300 mg/0.5 mg)

HELSINN EXHIBIT 2024
Azurity Pharmaceuticals, Inc. v. Helsinn Healthcare S.A.
IPR2025-00946

Combination (Akynzeo®) for the Prevention of Chemotherapy-induced Nausea and Vomiting in Initial and Repeated Cycles of Anthracycline-cyclophosphamide (AC) Chemotherapy in Women With Breast Cancer

Conditions

Chemotherapy-induced Nausea and Vomiting

Intervention / Treatment

- Drug: fosnetupitant/ palonosetron
- Drug: netupitant/palonosetron
- Drug: dexamethasone

Other Study ID Numbers

Study Start (Actual)

2018-03-16

Primary Completion (Actual)

2018-09-19

Study Completion (Actual)

2018-09-19

Enrollment (Actual)

404

Study Type

Interventional

Phase

Phase 3

Resource links provided by the National Library of Medicine

MedlinePlus Genetics (https://medlineplus.gov/genetics/) related topics: Breast cancer (https://medlineplus.gov/genetics/condition/breast-cancer)

MedlinePlus (https://medlineplus.gov/) related topics: Nausea and Vomiting (https://medlineplus.gov/nauseaandvomiting.html)

Drug Information (https://dailymed.nlm.nih.gov/dailymed/) available for:
Dexamethasone (https://dailymed.nlm.nih.gov/dailymed/search.cfm?labeltype=human&query=Dexamethasone)
Palonosetron (https://dailymed.nlm.nih.gov/dailymed/search.cfm?labeltype=human&query=Palonosetron)

FDA Drug and Device Resources (https://clinicaltrials.gov/fda-links)

Contacts and Locations

This section provides contact details for people who can answer questions about joining this study, and information on where this study is taking place.

To learn more, please see the Contacts and Locations section in How to Read a Study Record (https://clinicaltrials.gov/study-basics/how-to-read-study-record#contacts-and-locations).

This study has 40 locations

United States

Arizona Locations

- **Tucson, Arizona, United States, 85745**
  The Oncology Inst. Of Hope and Innovation

Arkansas Locations

- **Little Rock, Arkansas, United States, 72205**
  Carti Cancer Center

California Locations

- **Anaheim, California, United States, 92801**
  Pacific Cancer Medical Center, Inc.
- **Bakersfield, California, United States, 93309**
  CBCC Global Research, INC at Comprehensive Blood and Cancer Center
- **Corona, California, United States, 92882**
  The Oncology Tnstitute of Hope and Innovation
- **Inglewood, California, United States, 90305**
  Uptimum Medical Group Inc.
- **Long Beach, California, United States, 90805**

The Oncology Institute of Hope and Innnovation

- **Los Angeles, California, United States, 90033**
  Hao Wei Zhang M.D.
- **Redlands, California, United States, 92373**
  Emad Ibrahim, MD, INC.

Florida Locations

- **Lakeland, Florida, United States, 33805**
  Watson Clinic LLP
- **Orange City, Florida, United States, 32763**
  Mid Florida Hematology and Oncology Center

Georgia Locations

- **Athens, Georgia, United States, 30607**
  University Cancer & Blood Center, LLC
- **Dublin, Georgia, United States, 31021**
  Cancer Center of !\!liddle Georgia
- **Rome, Georgia, United States, 30165**
  Harbin Clinic
- **Savannah, Georgia, United States, 31404**
  Summit Cancer Care

Illinois Locations

- **Skokie, Illinois, United States, 60076**
  Edward H. Kaplan MD & Associates
- **Skokie, Illinois, United States, 60077**
  Presence Infusion Care - Skokie

Indiana Locations

- **Fort Wayne, Indiana, United States, 46845**
  Fort Wayne Medical Oncology and Hematology, Inc.
- **Lafayette, Indiana, United States, 47904**
  TU Health Arnett Cancer Center
- **New Albany, Indiana, United States, 47150**
  Baptist Health Cancer Center

Kansas Locations

- **Topeka, Kansas, United States, 66606**
  Cotton O'Neil Clinical Res. Ctr., Hematology & Oncology
- **Wichita, Kansas, United States, 67214**
  Cancer Center of Kansas

Kentucky Locations

Ashland, Kentucky, United States, 41101
Ashland-Bellefonte Cancer Center

Louisiana Locations

Shreveport, Louisiana, United States, 71105
CHRISTUS Cancer Treatment Center

Maryland Locations

Baltimore, Maryland, United States, 21202
Mercy Medical Center, Medical Oncology and Hematology

Mississippi Locations

Hattiesburg, Mississippi, United States, 39401
Hattiesburg Clinic Hematology Oncology

Missouri Locations

Joplin, Missouri, United States, 64804
Cornell-Beshore Cancer Institute

Springfield, Missouri, United States, 65807
Cox Mcdical ·Centers

New Jersey Locations

Elizabeth, New Jersey, United States, 07207
Trinitas Cancer Center

New Mexico Locations

Farmington, New Mexico, United States, 87401
San Juan Oncology Associates

Ohio Locations

Columbus, Ohio, United States, 43219
Mid Ohio Oncology/Hematology Inc. DBA The Mark H. Zangmeister Center

Toledo, Ohio, United States, 43623
Toledo Clinic Cancer Center - Toledo

Pennsylvania Locations

Monongahela, Pennsylvania, United States, 15063
Monongahela Valley Hospital

South Carolina Locations

Rock Hill, South Carolina, United States, 29732
Carolina Blood and Cancer Care Associates, P.A.

Tennessee Locations

Germantown, Tennessee, United States, 38138
The West Clinic, PC dba West Cancer Center

Wyoming Locations

Cheyenne, Wyoming, United States, 82001
Cheyenne Regional Medical Center

Georgia

Kutaisi, Georgia, 4600
JSC Saint Nikolozi Surgery and Oncological Centre

Tbilisi, Georgia, 0159
LTD Institute of Clinical Oncology

Tbilisi, Georgia, 0159
LTD Tbilisi Oncology Dispensary

Tbilisi, Georgia, 0179
LTD S.Khechinashvili University Hospital

Participation Criteria

Researchers look for people who fit a certain description, called eligibility criteria. Some examples of these criteria are a person's general health condition or prior treatments.

For general information about clinical research, read Learn About Studies (https://clinicaltrials.gov/study-basics/learn-about-studies).

Eligibility Criteria

Description

Inclusion Criteria:

Cycle 1:

The following inclusion criteria must be checked prior to inclusion at Cycle 1:

1. Patient read, understood and signed the written informed consent before any study related activity, agreeing to participate in the study and to comply with study requirements.
2. Female patient of at least 8 years of age.
3. Histologically or cytologically confirmed breast cancer, including recurrent or metastatic.
4. Naïve to moderately or highly emetogenic antineoplastic agents.
5. Scheduled to receive at least 4 consecutive cycles of an AC combination regimen.

   Notes:

   1. additional not emetogenic, minimally or low emetogenic antineoplastic agents are permitted at any time after start of AC combination on Day 1.
   2. additional highly or moderately emetogenic antineoplastic agents are only allowed on Day 1 after the start of AC combination, provided their administration is completed within 6 hours from the start of the AC combination administration.
6. ECOG Performance Status of 0 or 1.
7. Patient shall be: a) of non-childbearing potential or b) of childbearing potential using reliable contraceptive measures and having a negative urine pregnancy test within 24 hours prior to dose of investigational product.

   Notes:

   1. Female patients of non-childberaring potential are defined as being in post-menopausal state since at least 1 year; or having documented surgical sterilization or hysterectomy at least 3 months before study participation.
   2. Reliable contraceptive measures include implants, injectables, combined oral contraceptives, intrauterine devices, vasectomized partner or complete (long term) sexual abstinence;
8. Hematologic and metabolic status adequate for receiving a cycle of AC chemotherapy based on investigator's assessment.
9. If the patient has a known hepatic or renal impairment, she may be enrolled in the study at the discretion of the Investigator.
10. Able to read, understand, follow the study procedure and complete the patient diary.

All inclusion criteria will be checked at screening visit (Visit 1 of Cycle 1); inclusion criteria 7 will be re-checked at Day 1 (Visit 2).

Cycles 2 to 4:

The following inclusion criteria must be checked prior to inclusion at each repeated cycle:

1. Participation in the study during the next cycle of chemotherapy is considered appropriate by the Investigator and does not pose unwarranted risk to the patient.
2. Scheduled to receive an AC chemotherapy regimen or AC chemotherapy together with other chemotherapies as defined in Inclusion criterion #5 for Cycle 1.
3. Patient shall be: a) of non-childbearing potential or b) of childbearing potential using reliable contraceptive measures and having a negative urine pregnancy test within 24 hours prior to dosing of investigational product.
4. Adequate hematologic and metabolic status for receiving a cycle of AC chemotherapy according to the Investigator's opinion.

All inclusion criteria will be checked at screening visit (Visit 1); inclusion criterion #3 will be re-checked at Day 1 (Visit 2).

Exclusion Criteria:

Cycle 1:

The following exclusion criteria must be checked prior to inclusion at Cycle 1:

1. Lactating patient.
2. Current use of illicit drugs or current evidence of alcohol abuse.
3. Scheduled to receive moderately or highly emetogenic antineoplastic agent in addition to the AC regimen, from 6 hours after the start of the AC chemotherapy on Day 1 and up to Day 1 of Cycle 2.
4. Received or is scheduled to receive radiation therapy to the abdomen or the pelvis within 1 week prior to the start of AC chemotherapy administration on Day 1 or between Days 1 to 5, inclusive.
5. Any vomiting, retching, or nausea (grade 1 as defined by National Cancer Institute) within 24 hours prior to the start of AC chemotherapy administration on Day 1.
6. Symptomatic primary or metastatic central nervous system (CNS) malignancy.
7. Active peptic ulcer disease, gastrointestinal obstruction, increased intracranial pressure, hypercalcemia, an active infection or any illness or medical conditions (other than malignancy) that, in the opinion of the Investigator, may confound the results of the study, represent another potential etiology for emesis and nausea (other than chemotherapy-induced nausea and vomiting [CINV]) or pose unwarranted risks in administering the study drugs to the patient.
8. Known hypersensitivity or contraindication to 5 hydroxytryptamine type 3 (5-HT3) receptor antagonists (e.g., palonosetron, ondansetron, granisetron, dolasetron, tropisetron, ramosetron), to dexamethasone, or to neurokinin-1 (NK1) receptor antagonists (e.g., aprepitant, rolapitant).
9. Known contraindication to the IV administration of 50 mL 5% glucose solution.

10. Participation in a previous clinical trial involving IV fosnetupitant or oral netupitant administered alone or in combination with palonosetron.
11. Any investigational drugs taken within 4 weeks prior to Day 1, and/or is scheduled to receive any investigational drug (other than those planned by the study protocol) during the present study.
12. Systemic corticosteroid therapy within 72 hours prior to the start of AC chemotherapy administration on Day 1, except the dexamethasone provided as additional study drug. However, topical and inhaled corticosteroids are permitted.
13. Scheduled to receive bone marrow transplantation and/or stem cell rescue therapy during the study participation.
14. Other than as administered as part of the study protocol, any medication with known or potential antiemetic activity within 24 hours prior to the start of AC chemotherapy administration on Day 1, including:
    - 5-HT3 receptor antagonists (e.g., ondansetron, granisetron, dolasetron, tropisetron, ramosetron, palonosetron)
    - NK1 receptor antagonists (e.g., aprepitant, fosaprepitant, rolapitant or any other new drug of this class)
    - benzamides (e.g., metoclopramide, alizapride)
    - phenothiazines (e.g., prochlorperazine, promethazine, fluphenazine, perphenazine, thiethylperazine, chlorpromazine)
    - benzodiazepines (except if the subject is receiving such medication for sleep or anxiety and has been on a stable dose for at least seven days prior to Day 1).
    - butyrophenones (e.g., haloperidol, droperidol)
    - anticholinergics (e.g., scopolamine, with the exception of inhaled anticholinergics for respiratory disorders, e.g., ipratropium bromide)
    - antihistamines (e.g., cyclizine, hydroxyzine, diphenhydramine, chlorpheniramine)
    - domperidone
    - mirtazapine
    - olanzapine
    - prescribed cannabinoids (e.g., tetrahydrocannabinol or nabilone)
    - Over The Counter (OTC) antiemetics, OTC cold or OTC allergy medications.
15. Scheduled to receive any strong or moderate inhibitor of CYP3A4 during the efficacy assessment period (Day 1 to Day 5, inclusive) or its intake within 1 week prior to Day 1.
16. Scheduled to receive any CYP3A4 inducer during the efficacy assessment period (Day 1 to Day 5, inclusive) or its intake within 4 weeks prior to Day 1, with the exception of corticosteroids (for which exclusion criterion #12 applies).
17. History or predisposition to cardiac conduction abnormalities, except for incomplete right bundle branch block.
18. History of risk factors for Torsades de Pointes (heart failure, hypokalemia, family history of Long QT Syndrome).
19. Severe or uncontrolled cardiovascular diseases, including myocardial infarction within 3 months prior to Day 1, unstable angina pectoris, significant valvular or pericardial disease,

history of ventricular tachycardia, symptomatic Congestive Heart Failure (CHF) New York Heart Association (NYHA) class III-IV, and severe uncontrolled arterial hypertension.

All exclusion criteria with the exception of criteria #5, #12, and #14 will be checked at screening visit (Visit 1). Exclusion criteria #5, #12, and #14 will be checked at Day 1 (Visit 2) only.

Exclusion criteria #3, #4, #7, #11, #13, #15, and #16 need to be re-checked at Day 1 (Visit 2).

Cycles 2 to 4:

The following exclusion criteria must be checked prior to inclusion at each repeated cycle:

1. Scheduled to receive moderately or highly emetogenic antineoplastic agent in addition to the AC regimen, from 6 hours after the start of the AC chemotherapy on Day 1 of current cycle and up to Day 1 of the next cycle.
2. Active infection or uncontrolled disease that may pose unwarranted risks in administering the study drugs to the patient.
3. Started any of the prohibited medications.
4. Any vomiting, retching, or nausea (grade ≥ 1 as defined by National Cancer Institute) within 24 hours prior to the start of AC chemotherapy administration on Day 1.
5. Received or is scheduled to receive radiation therapy to the abdomen or the pelvis within 1 week prior to the start of AC chemotherapy administration on Day 1 or between Days 1 to 5.
6. Symptomatic primary or metastatic CNS malignancy.
7. Any illness or medical condition that, in the opinion of the investigator, may confound the results of the study or pose unwarranted risks in administering the investigational product or dexamethasone to the patient.

All exclusion criteria, with exception of criterion #4, will be checked at screening visit (Visit 1). Exclusion criterion #4 will be checked at Day 1 (Visit 2) only. Exclusion criteria #2, #3 and #5 need to be re-checked at Day 1 (Visit 2).

Ages Eligible for Study

18 Years and older (Adult, Older Adult)

Sexes Eligible for Study

Female

Accepts Healthy Volunteers

No

Study Plan

This section provides details of the study plan, including how the study is designed and what the study is measuring.

How is the study designed?

Design Details

Primary Purpose : Prevention
Allocation : Randomized
Interventional Model : Parallel Assignment
Masking : Quadruple (Participant, Care Provider, Investigator, Outcomes Assessor)

Arms and Interventions

Participant Group/Arm	Intervention/Treatment
Experimental: Test group intravenous fosnetupitant/ palonosetron (260 mg/0.25 mg) fixed-dose combination, administered as a 30-minute infusion of a 50 mL solution, on Day 1 of each cycle. Oral dexamethasone will be administered on Day 1 of each cycle (12 mg)	Drug: fosnetupitant/ palonosetron • intravenous fosnetupitant/ palonosetron (260 mg/0.25 mg) fixed-dose combination • Other Names: ◦ IV NEPA FDC Drug: dexamethasone • Oral dexamethasone (12 mg)
Active Comparator: Control group oral netupitant/palonosetron (300 mg/0.50 mg) fixed-dose combination on Day 1 of each cycle. Oral dexamethasone will be administered on Day 1 of each cycle (12 mg)	Drug: netupitant/palonosetron • oral netupitant/palonosetron (300 mg/0.50 mg) fixed-dose combination • Other Names: ◦ Akynzeo capsules Drug: dexamethasone • Oral dexamethasone (12 mg)

What is the study measuring?

Primary Outcome Measures

Outcome Measure	Measure Description	Time Frame
Number of Participants With Treatment-emergent AEs at Cycle 1		At the end of Cycle 1 (each cycle is 21 days)
Number of Participants With Treatment-emergent AEs All Cycles		At the end of Cycle 4 (each cycle is 21 days)
Number of Participants With Severe (i.e., CTCAE Grade ≥3) TEAEs Reported for ≥2% of Patients in Either Treatment Group and Overall Throughout the Study		At the end of Cycle 4 (each cycle is 21 days)

Number of Participants With Study-Drug-Related TEAEs Reported for ≥2% of Patients in Either Treatment Group Throughout the Study		At the end of Cycle 4 (each cycle is 21 days)

Secondary Outcome Measures

Outcome Measure	Measure Description	Time Frame
Complete Response in Cycle 1 During the Acute Phase	defined as no emetic episodes [vomit or retch] and no rescue medication	24 hours after the start of AC chemotherapy administration
Complete Response in Cycle 1 During the Delayed Phase	defined as no emetic episodes [vomit or retch] and no rescue medication	120 hour after the start of AC chemotherapy

		administration
Complete Response in Cycle 1 During the Overall Phase	defined as no emetic episodes [vomit or retch] and no rescue medication	0-120 hours after the start of AC chemotherapy
Overall Percentage of Patients With NIDL Based on FLIE Scores for Cycles 1	Percentage (including two-sided 95% CI using Wilson score method) of patients with NIDL based on FLIE scores (overall, by domain, and by individual item) are summarized by treatment group. NIDL was defined as a score greater than 108 points, 54 points, and 6 points for total FLIE score, domain score, and single item score, respectively. Differences between treatment groups for total FLIE score and domain scores (nausea and vomiting) were presented with two-sided 95% CIs using the CMH method adjusted for region and age class strata and also using Newcombe-Wilson's method without strata adjustment. No Impact on Daily Life (NIDL) Based on Functional Living Index-Emesis (FLIE) Scores. The FLIE is a nausea and vomiting specific self report instrument comprised of two domains (nausea and vomiting) with nine identical items in each domain	cycle 1

Collaborators and Investigators

This is where you will find people and organizations involved with this study.

Sponsor

Helsinn Healthcare SA

Collaborators

- George Clinical Pty Ltd
- The Physicians' Services Incorporated Foundation

Study Record Dates

These dates track the progress of study record and summary results submissions to ClinicalTrials.gov. Study records and reported results are reviewed by the National Library of Medicine (NLM) to make sure they meet specific quality control standards before being posted on the public website.

Study Registration Dates

First Submitted

2018-01-04

First Submitted that Met QC Criteria

2018-01-10

First Posted

2018-01-19

Results Reporting Dates

Results First Submitted

2020-03-17

Results First Posted with QC Comments

2020-03-31

Results First Submitted that Met QC Criteria

2020-04-02

Results First Posted

2020-04-15

Study Record Updates

Last Update Submitted that met QC Criteria

2020-05-15

Last Update Posted

2020-06-01

Last Verified

2020-05

More Information

Terms related to this study

Additional Relevant MeSH Terms

Signs and Symptoms, Digestive
Nausea
Vomiting
Anti-Inflammatory Agents
Antiemetics
Autonomic Agents
Peripheral Nervous System Agents
Physiological Effects of Drugs
Gastrointestinal Agents
Glucocorticoids
Hormones
Hormones, Hormone Substitutes, and Hormone Antagonists
Antineoplastic Agents, Hormonal
Antineoplastic Agents
Serotonin 5-HT3 Receptor Antagonists
Serotonin Antagonists
Serotonin Agents
Neurotransmitter Agents
Molecular Mechanisms of Pharmacological Action
Dexamethasone
Palonosetron

HHS Vulnerability Disclosure

Plan for Individual Participant Data (IPD)

Plan to Share Individual Participant Data (IPD)?

Undecided

Drug and device information, study documents, and helpful links

Studies a U.S. FDA-Regulated Drug Product

Yes

Studies a U.S. FDA-Regulated Device Product

No

Study Documents ⓘ **Provided by Helsinn Healthcare SA**

- Study Protocol (https://cdn.clinicaltrials.gov/large-docs/12/NCT03403712/Prot_000.pdf) [PDF, 2.01MB, 2017-11-30]
- Statistical Analysis Plan (https://cdn.clinicaltrials.gov/large-docs/12/NCT03403712/SAP_001.pdf) [PDF, 1.24MB, 2018-12-12]