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Completed

A Safety Study of Intravenous Pro-Netupitant and Palonosetron Combination for the Prevention of Nausea and Vomiting

ClinicalTrials.gov ID NCT02517021

Sponsor Helsinn Healthcare SA

Information provided by Helsinn Healthcare SA (Responsible Party)

Last Update Posted 2018-06-20

Study Details Tab

Study Overview

Brief Summary

NEPA-15-18 is a clinical study assessing safety of pro-netupitant and palonosetron, two antiemetic drugs, given with oral dexamethasone. The objective of the study is to evaluate if pro-netupitant and palonosetron are safe when administered to prevent nausea and vomiting after administration of repeated cycles of chemotherapy.

Official Title

A Phase 3, Multicenter, Randomized, Double-blind, Active Control Study to Evaluate the Safety and Efficacy of IV Pro-netupitant/Palonosetron (260 mg/0.25 mg) Combination for the Prevention of Chemotherapy-induced Nausea and Vomiting in Repeated Chemotherapy Cycles in Patients Receiving Highly Emetogenic Chemotherapy

Conditions

Feedback

HELSINN EXHIBIT 2031
Azurity Pharmaceuticals, Inc. v. Helsinn Healthcare S.A.
IPR2025-00945

Chemotherapy-Induced Nausea and Vomiting

Intervention / Treatment

- Drug: Pro-netupitant/Palonosetron
- Drug: Netupitant/Palonosetron
- Drug: Dexamethasone

Other Study ID Numbers

Study Start

2015-11

Primary Completion (Actual)

2016-08

Study Completion (Actual)

2016-08

Enrollment (Actual)

405

Study Type

Interventional

Phase

Phase 3

Resource links provided by the National Library of Medicine

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 74 locations

United States

California Locations

Santa Monica, California, United States, 90403-480
Sarcoma Oncology Center

Whittier, California, United States, 90603
The Oncology Institute of Hope and Innovation

Colorado Locations

Grand Junction, Colorado, United States, 81501
St. Mary's Medical Center

Florida Locations

Miami, Florida, United States, 33143
Well Pharma Medical Research Corporation

Illinois Locations

Peoria, Illinois, United States, 61615-7822
Illinois CancerCare

Indiana Locations

Bloomington, Indiana, United States, 47403
Indiana University Health Bloomington

Louisiana Locations

Alexandria, Louisiana, United States, 71301
Christus St. Frances Cabrini Hospital

New York Locations

East Setauket, New York, United States, 11733
North Shore Hematology Oncology Associates PC

Ohio Locations

Canton, Ohio, United States, 44718
Gabrail Cancer Center Research

Tennessee Locations

Germantown, Tennessee, United States, 38138
West Cancer Center

Knoxville, Tennessee, United States, 37909
Provision Center for Biomedical Research

Austria

Graz, Austria, 8036
University Hospital Graz, Department of Internal Medicine

Krems, Austria
Krems Country Hospital

Linz, Austria, 4020
Hospital Elisabethinen Linz GmbH, Internal Department #1 - Hemato-Oncology

Linz, Austria, 4021
General Hospital Linz GmbH, Internal Medicine Department #3 - Center for Hematology and Medical Oncology

St. Poelten, Austria
University Hospital St. Poelten,1st Medical Department

Croatia

Osijek, Croatia
Clinical Hospital Centre Osijek

Varazdin, Croatia
General Hospital Varazdin

Zagreb, Croatia
Clinical Hospital Center "Sestre milosrdnice"

Zagreb, Croatia
University Hospital Centre Zagreb "Jordanovac"

Czechia

Brno, Czechia
University Hospital Brno. Clinic of Pulmonary Diseases and Tuberculosis

Brno, Czechia
University Hospital

Novy Jicin, Czechia
Hospital Novy Jicin, Department of Oncology

Prague, Czechia, 140 59
Thomayer's Hospital, Clinic of Pneumology

Prague, Czechia
Hospital Na Bulovce

Usti nad Labem, Czechia
Masaryk's Hospital Usti nad Labem, Oncology Dept

Germany

Bielefeld, Germany
Onkoligische Schwerpunktpraxis Bielefeld

Hamburg, Germany
OncoResearch Lerchenfeld GmbH

Hannover, Germany
Hannover Medical School

Leipzig, Germany
Universitaetsklinikum Leipzig; Universitaeres Krebszentrum (UCCL)

München, Germany
Staedtisches Klinikum Muenchen GmbH; Klinikum N euperlach

Israel

Ashkelon, Israel
Barziali Medical Center, Oncology Unit

Beer Sheva, Israel
Soroka University Medical Center,Oncology division

Haifa, Israel
Rambam Health Care Campus

Italy

- **Avellino, Italy**
  S. G. Moscati Hospital, Medical Oncology Division
- **Meldola, Italy**
  cientific Institute of Romagna for the Study and Treatment of Cancer (IRST), IRCCS
- **Milan, Italy**
  National Cancer Institute, IRCCS, Medical Oncology Department
- **Monza, Italy**
  Azienda Socio Sanitaria Territoriale-Monza (ASST-Monza) - Oncology Department
- **Potenza, Italy**
  Regional Hospital "San Carlo"
- **Vimercate, Italy**
  Local Healthcare Company of Vimercate (ASST Vimercate)

Poland

- **Gdynia, Poland**
  Provincial Hospitals in Gdynia Sp. z o.o. (LLC)
- **Poznan, Poland, 60-569**
  Lord's Transfiguration Teaching Hospital, Department of Chemotherapy
- **Prabuty, Poland, 82-550**
  Specialist Hospital in Prabuty Sp. z o .o. (LLC), Department of Pulmonology
- **Tarnobrzeg, Poland**
  Zofia Zamoyska nee Tarnowska Provincial Hospital in Tarnobrzeg
- **Torun, Poland**
  Ludwik Rydygier Provincial Hospital
- **Warsaw, Poland, 02-781**
  Maria Sklodowska-Curie Institute of Oncology, Department of Lung and Thoracic Cancers
- **Warsaw, Poland, 03-291**
  MAGODENT Sp. z o .o. (LLC), Branch No. 4, Department of Clinical Oncology/Chemotherapy

Serbia

- **Belgrade, Serbia**

Clinical Center of Serbia, Clinic of Pulmonology

Belgrade, Serbia
Clinical Hospital Center Bezanijska Kosa, Clinic of Oncology

Belgrade, Serbia
Institute of Oncology and Radiology of Serbia, Clinic of Medical Oncology

Belgrade, Serbia
Military Medical Academy

Sremska Kamenica, Serbia
Institute of Pulmonary Diseases of Vojvodina, Pulmonary Oncology Clinic

Sremska Kamenica, Serbia
Oncology Institute of Vojvodina

South Africa

George, South Africa
GVI Outeniqua Oncology Unit

Johannesburg, South Africa
Medical Oncology Centre of Rosebank

Spain

Avila, Spain, 05004
Our Lady of Sonsoles Hospital

Madrid, Spain, 28035
Hospital Puerta de Hierro

Madrid, Spain
Hospital La Paz, Oncology Department

Madrid, Spain
University Hospital Quiron Madrid, Department of Oncology

Andalucia Locations

Sevilla, Andalucia, Spain
Hospital Nuestra Senora de Valme

Ukraine

Chernivtsi, Ukraine, 58013
Chernivtsi Regional Clinical Oncology Center, Day Care Unit

Dnipropetrovsk, Ukraine, 49055
Clinical Oncology Center, Department of Chemotherapy

Dnipropetrovsk, Ukraine, 49102
Dnipropetrovsk City Multispecialty Clinical Hospital #4, Department of Chemotherapy

Ivano-Frankivsk, Ukraine, 76000
Regional Clinical Oncology Center, Chemotherapy Department

Kharkiv, Ukraine, 61024
S.P. Hryhoriev Institute of Medical Radiology, Department of Chemotherapy

Kharkiv, Ukraine, 61070
Kharkiv Regional Clinical Oncology Center, Chemotherapy Department #1

Khmelnytskyi, Ukraine, 29009
Khmelnytskyi Regional Oncology Center, Surgery Department #1

Kryvyi Rih, Ukraine, 50048
Kryvyi Rih Oncology Center, Department of Chemotherapy

Lviv, Ukraine, 79031
Lviv State Regional Treatment and Diagnostics Oncology Center, Department of Chemotherapy

Ternopil, Ukraine, 46023
Ternopil Regional Public Clinical Oncology Center

Uzhhorod, Ukraine, 88000
LTD UNIMED Adjara

Uzhhorod, Ukraine, 88014
Zakarpattia Regional Clinical Oncology Center, Department of Chemotherapy

Vinnytsia, Ukraine, 21029
Vinnytsia Regional Clinical Oncology Center, Department of Chemotherapy

Zaporizhia, Ukraine, 69040
Zaporizhia Regional Clinical Oncology Center, Thoracic Department

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

- Signed written informed consent
- Histologically or cytologically confirmed solid tumor malignancy.
- Naïve to cytotoxic chemotherapy. Previous biological or hormonal therapy will be permitted.
- Scheduled to receive at least 4 repeated consecutive cycles of the following highly emetogenic reference chemotherapies (HEC), alone or in combination with other chemotherapeutic agents on Day 1: cisplatin administered as a single IV dose of ≥ 70 mg/m2; cyclophosphamide ≥1500 mg/m2; carmustine (BCNU) >250mg/m2; dacarbazine (DTIC); mechloretamine (nitrogen mustard)
- Eastern Cooperative Oncology Group (ECOG) Performance Status of 0, 1, or 2 .
- If a patient is female, she shall be of non-childbearing potential or of childbearing potential using reliable contraceptive measures and having a negative urine pregnancy test.
- Hematologic and metabolic status adequate for receiving an highly emetogenic regimen based on laboratory criteria (Total Neutrophils,Platelets, Bilirubin, Liver enzymes, Serum Creatinine or Creatinine Clearance)
- Able to read, understand, follow the study procedure and complete patient diary.

Cycles 2 to 4:

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

- 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.
- Scheduled to receive the same chemotherapy regimen as Cycle 1 or one of the reference chemotherapies as defined in Inclusion criterion 5 for Cycle 1.
- If a patient is female, she shall be of non--childbearing potential or of childbearing potential using reliable contraceptive measures and having a negative urine pregnancy test.
- Adequate hematologic and metabolic status according to the Investigator's opinion.

Exclusion Criteria:

Cycle 1

- Lactating woman.
- Active infection or uncontrolled disease except for malignancy that may pose unwarranted risks in administering the study drugs to the patient.
- Current use of illicit drugs or current evidence of alcohol abuse.
- Scheduled to receive moderately or highly emetogenic chemotherapies from Day 2 to Day 5.

- Received or is scheduled to receive radiation therapy to the abdomen or the pelvis within 1 week prior to the start of the reference chemotherapy administration on Day 1 or between Days 1 to 5.
- Any vomiting, retching, or nausea (grade ≥ 1 as defined by National Cancer Institute) within 24 hours prior to the start of the reference chemotherapy administration on Day 1.
- Symptomatic primary or metastatic CNS malignancy.
- Known hypersensitivity or contraindication to 5-HT3 receptor antagonists, to dexamethasone or to NK-1 receptor antagonists.
- Known contraindication to the IV administration of 50 mL 5% glucose solution.
- Previously received an NK-1 receptor antagonist.
- Participation in a previous clinical trial involving IV pro-netupitant or oral netupitant administered alone or in combination with palonosetron.
- Any investigational drugs (other than those given in this study) taken within 4 weeks prior to Day 1, and/or is scheduled to receive any investigational drug during the present study.
- Systemic corticosteroid therapy at any dose within 72 hours prior to the start of reference chemotherapy administration on Day 1. Topical and inhaled corticosteroids are permitted.
- Scheduled to receive bone marrow transplantation and/or stem cell rescue therapy.
- Scheduled to receive any strong or moderate inhibitor of CYP3A4 or its intake within 1 week prior to Day 1.
- Scheduled to receive any of the following CYP3A4 substrates within 1 week prior to Day 1: terfenadine, cisapride, astemizole, pimozide.
- Received within 4 weeks prior to Day 1 or scheduled to receive any CYP3A4 inducer.
- Any medication with known or potential antiemetic activity within 24 hours prior to the start of reference chemotherapy administration on Day 1 of Cycle 1, including but not limited to 5-HT3 receptor antagonists and NK-1 receptor antagonists
- History or predisposition to cardiac conduction abnormalities, except for incomplete right bundle branch block
- History of Torsade de Point or known history of risk factors for Torsade de Point (heart failure, hypokalemia, family history of Long QT Syndrome).
- Severe cardiovascular diseases diagnosed within 3 months prior to Day 1 of first cycle, including myocardial infarction, 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.
- Any illness or condition that, in the opinion of the Investigator, may confound the results of the study or pose unwarranted risks in administering the investigational product to the patient.
- Concurrent medical condition that would preclude administration of dexamethasone such as systemic fungal infection or uncontrolled diabetes.

Cycles 2 to 4:

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

- Lactating woman.
- Active infection or uncontrolled disease except for malignancy that may pose unwarranted risks in administering the study drugs to the patient.
- Started any of the restricted medications.
- Any vomiting, retching, or nausea (grade ≥ 1 as defined by National Cancer Institute) within 24 hours prior to the start of reference chemotherapy administration on Day 1.
- Received or is scheduled to receive radiation therapy to the abdomen or the pelvis within 1 week prior to the start of the reference chemotherapy administration on Day 1 or between Days 1 to 5.
- Symptomatic primary or metastatic CNS malignancy.

Ages Eligible for Study

18 Years and older (Adult, Older Adult)

Sexes Eligible for Study

All

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: Pro-netupitant/Palonosetron plus Dexamethasone Intravenous Pro-netupitant/Palonosetron (260 mg/0.25 mg) powder for solution for infusion (on Day 1) with oral dexamethasone prior to each scheduled chemotherapy cycle	Drug: Pro-netupitant/Palonosetron • Other Names: ◦ IV NEPA FDC Drug: Dexamethasone
Active Comparator: Netupitant/Palonosetron plus Dexamethasone Oral netupitant/palonosetron (300 mg/0.50 mg) hard capsule (on Day 1) with oral dexamethasone prior to each scheduled chemotherapy cycle	Drug: Netupitant/Palonosetron • Other Names: ◦ Oral NEPA FDC Drug: Dexamethasone

What is the study measuring?

Primary Outcome Measures

Outcome Measure	Measure Description	Time Frame

Percentage of Patients With Adverse Events	This is a safety study where Adverse Events is the primary outcome (defined by the current ICH Guideline for Good Clinical Practice). Patients are randomized according to a 1:1 ratio (IV NEPA FDC : oral NEPA FDC). No formal comparison is planned, the presence of a control in the same patient population helps interpret any unexpected safety finding in the experimental arm. It is expected that the number of patients randomized to the test group, i.e., 200, will allow approximately 100 patients to be treated with the test drug for 4 cycles. Based on 100 patients treated at Cycle 4 with the IV NEPA FDC , if a given Adverse Event (AE) is not observed, an AE incidence of 3% or greater can be excluded with 95% confidence.	Participants will be followed for the duration of the chemotherapy, an expected average duration of up to 14 weeks assuming a maximum of 4 chemotherapy cycles given every 3 weeks.

Secondary Outcome Measures

Outcome Measure	Measure Description	Time Frame
Percentage of Patients With Complete Response (CR)		0-24 hours

Defined as no Emesis, no Rescue Medication, in the Acute Phase		
Percentage of Patients With Complete Response (CR) Defined as no Emesis, no Rescue Medication, in the Delayed Phase		>24-120 hours
Percentage of Patients With Complete Response (CR) Defined as no Emesis, no Rescue Medication, in the Overall Phase		0-120 hours
Percentage of Patients With no Emetic Episodes in the Acute Phase		0-24 hours
Percentage of Patients With		>24-120 hours

no Emetic Episodes in the Delayed Phase		
Percentage of Patients With no Emetic Episodes in the Overall Phase		0-120 hours
Percentage of Patients With no Significant Nausea (VAS <25 mm) During the Acute Phase		0-24 hours
Percentage of Patients With no Significant Nausea (VAS <25 mm) During the Delayed Phase		>24-120 hours
Percentage of Patients With no Significant Nausea (VAS <25 mm) During the Overall Phase		0-120 hours

Collaborators and Investigators

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

Sponsor

Helsinn Healthcare SA

Collaborators

- PSI CRO

Publications

From PubMed

These publications come from PubMed, a public database of scientific and medical articles. This list is automatically created by ClinicalTrials.gov Identifier (NCT Number), and these articles may or may not be about the study.

- Schwartzberg L, Roeland E, Andric Z, Kowalski D, Radic J, Voisin D, Rizzi G, Navari R, Gralla RJ, Karthaus M. Phase III safety study of intravenous NEPA: a novel fixed antiemetic combination of fosnetupitant and palonosetron in patients receiving highly emetogenic chemotherapy. Ann Oncol. 2018 Jul 1;29(7):1535-1540. doi: 10.1093/annonc/mdy169. (https://pubmed.ncbi.nlm.nih.gov/29722791)

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

2015-08-03

First Submitted that Met QC Criteria

2015-08-05

First Posted (Estimated)

2015-08-06

Results Reporting Dates

Results First Submitted

2018-05-09

Results First Submitted that Met QC Criteria

2018-06-18

Results First Posted

2018-06-20

HHS Vulnerability Disclosure

Certification/Extension Dates

Certification/Extension First Submitted

2016-09-07

Certification/Extension First Submitted that Met QC Criteria

2016-09-07

Certification/Extension First Posted (Estimated)

2016-09-08

Study Record Updates

Last Update Submitted that met QC Criteria

2018-06-18

Last Update Posted

2018-06-20

Last Verified

2018-06

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