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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 

## 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/) (<https://medlineplus.gov/>) related topics: [Nausea and Vomiting](https://medlineplus.gov/nauseaandvomiting.html) (<https://medlineplus.gov/nauseaandvomiting.html>)

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

[FDA Drug and Device Resources](https://clinicaltrials.gov/fda-links) (<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) (<https://clinicaltrials.gov/study-basics/how-to-read-study-record#contacts-and-locations>).

This study has 74 locations


### United States

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#### 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

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 **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

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 **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

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-  **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

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-  **Bielefeld, Germany**  
Onkologische 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

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-  **Ashkelon, Israel**  
Barzali Medical Center, Oncology Unit
-  **Beer Sheva, Israel**  
Soroka University Medical Center, Oncology division
-  **Haifa, Israel**  
Rambam Health Care Campus

## Italy

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-  **Avellino, Italy**  
S. G. Moscati Hospital, Medical Oncology  
Division
-  **Meldola, Italy**  
scientific 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

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-  **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 Skłodowska-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

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-  **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

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-  **George, South Africa**  
GVI Outeniqua Oncology Unit
-  **Johannesburg, South Africa**  
Medical Oncology Centre of Rosebank

## Spain

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-  **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

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-  **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
-  **Khmelnyskyi, Ukraine, 29009**  
Khmelnyskyi Regional Oncology Center, Surgery  
Department #1
-  **Kyryvi Rih, Ukraine, 50048**  
Kyryvi 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 \(https://clinicaltrials.gov/study-basics/learn-about-studies\)](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  $\geq 70$  mg/m<sup>2</sup>; cyclophosphamide  $\geq 1500$  mg/m<sup>2</sup>; carmustine (BCNU)  $>250$ mg/m<sup>2</sup>; dacarbazine (DTIC); mechlorethamine (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  $\geq 1$  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  $\geq 1$  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 ⓘ
<p>Experimental: Pro-netupitant/Palonosetron plus Dexamethasone</p> <p>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</p>	<p>Drug: Pro-netupitant/Palonosetron</p> <ul style="list-style-type: none"> <li>• Other Names:                             <ul style="list-style-type: none"> <li>◦ IV NEPA FDC</li> </ul> </li> </ul> <p>Drug: Dexamethasone</p>
<p>Active Comparator: Netupitant/Palonosetron plus Dexamethasone</p> <p>Oral netupitant/palonosetron (300 mg/0.50 mg) hard capsule (on Day 1) with oral dexamethasone prior to each scheduled chemotherapy cycle</p>	<p>Drug: Netupitant/Palonosetron</p> <ul style="list-style-type: none"> <li>• Other Names:                             <ul style="list-style-type: none"> <li>◦ Oral NEPA FDC</li> </ul> </li> </ul> <p>Drug: Dexamethasone</p>

What is the study measuring?

Primary Outcome Measures ⓘ

Outcome Measure	Measure Description	Time Frame

<p>Percentage of Patients With Adverse Events</p>	<p>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.</p>	<p>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.</p>
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Secondary Outcome Measures 

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

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. \(https://pubmed.ncbi.nlm.nih.gov/29722791\).](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-HT<sub>3</sub> Receptor Antagonists  
Serotonin Antagonists  
Serotonin Agents  
Neurotransmitter Agents  
Molecular Mechanisms of Pharmacological Action  
Dexamethasone  
Palonosetron