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Completed

PK/PD Study of Netupitant and Palonosetron in Pediatric Patients for Prevention of Chemotherapy-induced Nausea and Vomiting (CINV)

ClinicalTrials.gov ID NCT03204279

Sponsor Helsinn Healthcare SA

Information provided by Helsinn Healthcare SA (Responsible Party)

Last Update Posted 2024-06-25

Study Details Tab

Study Overview

Brief Summary

This study is Phase 2 pharmacokinetic (PK) and pharmacodynamic (PD) dose-finding study of oral netupitant administered concomitantly with oral palonosetron in pediatric cancer patients for the prevention of nausea and vomiting associated with emetogenic chemotherapy. Two different netupitant dosages will be tested in patients aged from 3 months to < 18 years: 1.33 mg/kg up to a maximum of 100 mg, and 4 mg/kg up to a maximum of 300 mg. All netupitant doses in all age classes will be concomitantly administered with palonosetron 20 µg/kg (up to a maximum dose of 1.5 mg) which is the IV palonosetron dose approved by USA FDA for the pediatric population. The primary objective is to investigate the PK/PD relationship between netupitant exposure (AUC, Cmax) and antiemetic efficacy (CR in delayed phase) after a single oral netupitant administration, concomitantly with oral palonosetron in pediatric cancer patients receiving Moderately Emetogenic Chemotherapy (MEC) or Highly Emetogenic Chemotherapy (HEC) cycles. Efficacy parameter to be used in the correlation is the

Feedback

HELSINN EXHIBIT 2023
Azurity Pharmaceuticals, Inc. v. Helsinn Healthcare S.A.
IPR2025-00949

proportion of patients with Complete Response (CR i.e., no emetic episodes and no rescue medication) during (> 24-120 h after the start of chemotherapy on Day 1).

The secondary objectives are to assess the safety and tolerability after single oral administration of netupitant given concomitantly with a single oral administration of palonosetron; to evaluate the pharmacokinetic (AUC, Cmax, tmax and t1/2) of oral palonosetron at the fixed dose of 20 µg/kg in pediatric patients with the concomitant administration of netupitant. A total of 92 pediatric cancer patients receiving either HEC or MEC will be enrolled in the study.

Official Title

A Multicenter Multinational Randomized Double Blind PK/PD Dose-finding Study of Oral Netupitant Given With Oral Palonosetron in Pediatric Cancer Patients for Prevention of Nausea and Vomiting Associated With Emetogenic Chemotherapy

Conditions

Chemotherapy-induced Nausea and Vomiting (CINV)

Intervention / Treatment

- Drug: Netupitant
- Drug: Palonosetron
- Drug: Netupitant
- Drug: Palonosetron

Other Study ID Numbers

Study Start (Actual)

2017-08-31

Primary Completion (Actual)

2019-09-30

Study Completion (Actual)

2019-09-30

Enrollment (Actual)

67

Study Type

Interventional

Phase

Phase 2

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: 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 17 locations

United States

Delaware Locations

Wilmington, Delaware, United States, 19803
Nemours/A.I. duPont Hospital for Children

Florida Locations

Jacksonville, Florida, United States, 32207
Nemours Children's Clinic

Orlando, Florida, United States, 32827
Nemours Children's Hospital - Orlando

Maine Locations

Scarborough, Maine, United States, 04074
Maine Medical Center - Cancer Medicine and Blood Disorders - Scarborough

South Carolina Locations

Charleston, South Carolina, United States, 29425
Medical University of South Carolina

Russian Federation

Chelyabinsk, Russian Federation
Chelyabinsk Regional Children's Clinical Hospital

Krasnodar, Russian Federation
Children's Territorial Clinical Hospital

Moscow, Russian Federation
Dmitry Rogachev National Scientific and Practical Center for Pediatric Hematology, Oncology and Immunology

St. Petersburg, Russian Federation
City Clinical Hospital #31

St. Petersburg, Russian Federation
First I.P. Pavlov State Medical University of St. Petersburg

Voronezh, Russian Federation, 394024
Voronezh Regional Children's Cinical Hospital #1

Yekaterinburg, Russian Federation
Regional Children's Clinical Hospital #1

Serbia

Belgrade, Serbia
University Children's Hospital, Center for Pediatrics, Department of Hematology and Oncology

Nis, Serbia
Clinical Center Nis, Clinic of Pediatric Internal Diseases

Ukraine

Dnipro, Ukraine, 49100
Dnipropetrovsk Regional Children's Clinical Hospital

Kyiv, Ukraine

National Institute of Cancer, Research
Department of Pediatric Oncology

Lviv, Ukraine
West Ukrainian Specialized Children's Medical
Center, Department of Pediatric Surgery

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:

1. Signed written informed consent by parent(s)/legal guardians of the pediatric patient in compliance with the local laws and regulations. In addition signed children's assent form according to local requirements.
2. Male or female in- or out-patient from birth to < 18 years at the time of randomization.
3. Patient weight at least 3.3 kg.
4. Naïve or non-naïve patient with histologically, and/or cytologically (or imaging in the case of brain tumors) confirmed malignant disease.
5. Scheduled and eligible to receive at least one moderately or highly emetogenic chemotherapeutic agent on Day 1 only or for multiple days.
6. For patient aged ≥ 10 years: Eastern Cooperative Oncology Group Performance Status (ECOG PS) ≤ 2.
7. For patient aged 2 years with known mild to moderate hepatic impairment: in the Investigator's opinion the impairment does not jeopardize patient's safety during the study.
8. For patient aged 2 years with known mild to moderate renal impairment: in the Investigator's opinion the impairment should not jeopardize patient's safety during the study.
9. For patient with known history or predisposition to cardiac abnormalities: in the Investigator's opinion the history/predisposition should not jeopardize patient's safety during the study.
10. If the patient is female, she shall: a) not have attained menarche yet or b) have attained menarche and have a negative pregnancy test at the screening visit and at Day 1.
11. Male or female fertile patient using reliable contraceptive measures (such measures, for patient and sexual partner, include: implants, injectables, combined oral contraceptives, intrauterine devices, vasectomized/sterilized partner, use of a double-barrier method or sexual abstinence). The patient and his/her parent(s)/legal guardians must be counseled on the importance of avoiding pregnancy before or during the study.

Exclusion Criteria:

1. The patient and/or parents/caregivers are expected by the Investigator to be non-compliant with the study procedures.
2. Patient has received or is scheduled to receive total body irradiation, total nodal irradiation, upper abdomen radiotherapy, half or upper body irradiation, radiotherapy of the cranium, craniospinal regions, head and neck, lower thorax region or the pelvis within 1 week prior to study entry (Day 1) or within 120 h after start of chemotherapy administration on Day 1.
3. Known history of allergy to any component or other contraindications to any Neurokinin-1 (NK1) or 5-hydroxytryptamine 3 (5-HT3) receptor antagonists.
4. Active infection.

5. Uncontrolled medical condition (e.g., uncontrolled insulin dependent diabetes mellitus).
6. Patient suffering from ongoing vomiting from any organic etiology (including patients with history of gastric outlet obstruction or intestinal obstruction due to adhesions or volvulus, patients with a symptomatic central nervous system(CNS) tumor causing nausea and/or vomiting) or patient with hydrocephalus.
7. Patient who experienced any vomiting, retching, or nausea within 24 h prior to the administration of the study drug

8. Patient who received any drug with potential anti-emetic effect within 24 h prior to the start of reference chemotherapy, including but not limited to:

   NK1- receptor antagonists (e.g., aprepitant or any other new drug of this class); 5-HT3 receptor antagonists (e.g., ondansetron, granisetron, dolasetron, tropisetron, ramosetron); Benzamides (e.g., metoclopramide, alizapride); Phenothiazines (e.g., prochlorperazine, promethazine, perphenazine, fluphenazine, chlorpromazine, thiethylperazine); Benzodiazepines initiated 48 h prior to study drug administration or expected to be received within 120 h following initiation of chemotherapy, except for single doses of midazolam, temazepam or triazolam; Butyrophenones (e.g., droperidol, haloperidol); Anticholinergics (e.g., scopolamine, with the exception of inhaled anticholinergics for respiratory disorders e.g., ipratropium bromide); Antihistamines (e.g., diphenhydramine, cyclizine, hydroxyzine, chlorpheniramine, dimenhydrinate, meclizine); Domperidone; Mirtazapine; Olanzapine; Prescribed cannabinoids (e.g., tetrahydrocannabinol, nabilone); Over the Counter (OTC) antiemetics, OTC cold or OTC allergy medications; Herbal preparations containing ephedra or ginger.

9. Patient who received palonosetron within 1 week prior to administration of study drug.
10. Patient who has been started on systemic corticosteroid therapy within 72 h prior to study drug administration or is planned to receive a corticosteroid as part of the chemotherapy regimen
11. Patient aged < 6 years who received any investigational drug (defined as a medication with no marketing authorization granted for any age class and any indication) within 90 days prior to Day 1, or patient aged 6 years who received any investigational drug within 30 days prior to Day 1 or is expected to receive investigational drugs prior to study completion.
12. Intake of alcohol, food or beverages (e.g., grapefruit, cranberry, pomegranate and aloe vera juices, German chamomile) known to interfere with either CYP3A4 or CYP2D6 metabolic enzymes within 1 week prior to Day 1 and during the overall study period.
13. Use of any drugs or substances known to be strong or moderate inhibitors of CYP3A4 and CYP2D6 enzymes within 1 week prior to Day 1 or planned to be used during the overall study period.
14. Use of any drugs or substances known to be CYP3A4 substrates with narrow therapeutic range within 1 week prior to Day 1, or planned to be used during the overall study period.
15. Use of any drugs or substances known to be inducers of CYP3A4 enzymes within 4 weeks prior to Day 1 or planned to be used during the overall study period.
16. Lactating female patient.

17. Patient with clinically relevant abnormal laboratory values that in the Investigator's opinion jeopardize the patient's safety during the study.
18. Patient aged < 2 years with known hepatic impairment (any grade), or patient aged 2 years with known severe hepatic impairment.
19. Patient aged < 2 years with known renal impairment (any grade), or patient aged 2 years with known severe renal impairment.
20. Enrolment in a previous study with netupitant (either alone or in combination with palonosetron).

Ages Eligible for Study

up to 17 Years (Child)

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 : Triple (Participant, Care Provider, Investigator)

Arms and Interventions

Participant Group/Arm	Intervention/Treatment
Experimental: Netupitant 1.33 mg/kg plus Palonosetron Single oral dose of Netupitant 1.33 mg/kg up to a maximum of 100 mg (for patients < 3 months of age the netupitant dose will be 0.8 mg/kg) administered with single oral dose of 20 µg/kg palonosetron up to a maximum of 1.5 mg.	Drug: Netupitant • Netupitant 1.33 mg/kg oral suspension up to a maximum of 100 mg Drug: Palonosetron • Palonosetron 20 µg/kg solution for oral use up to a maximum of 1.5 mg

Experimental: Netupitant 4 mg/kg plus Palonosetron Single oral dose of Netupitant 4 mg/kg up to a maximum of 300 mg (for patients < 3 months of age the netupitant dose will be 2.4 mg/kg) administered with single oral dose 20 µg/kg palonosetron up to a maximum of 1.5 mg.	Drug: Netupitant • Netupitant 4 mg/kg oral suspension up to a maximum of 300 mg Drug: Palonosetron • Palonosetron 20 µg/kg solution for oral use up to a maximum of 1.5 mg

What is the study measuring?

Primary Outcome Measures

Outcome Measure	Measure Description	Time Frame
Area Under the Plasma Concentration Versus Time Curve From Time Zero to Infinity (AUC0-inf) of Netupitant	Mean values of area under the plasma Concentration versus time curve from time zero to infinity (AUC0-inf) of netupitant after a single oral netupitant administration, concomitantly with oral palonosetron, in pediatric cancer patients receiving HEC or MEC cycles. AUC estimates are obtained by non-compartmental analysis of population model-predicted individual plasma concentration-time profiles.	within 168 hours after netupitant administration. A sampling windows

		approach will be used by collecting a single blood sample from each patient in one of these time windows: from 2 to 8 h, from 24 to 48 h, from 72 to 96 h and from 120 to 168 h.
Maximum Plasma Concentration (Cmax) of Netupitant	Mean values of maximum plasma concentration (Cmax) of netupitant after a single oral netupitant administration, concomitantly with oral palonosetron, in pediatric cancer patients receiving HEC or MEC cycles. Cmax estimates are obtained by non-compartmental analysis of population model-predicted individual plasma concentration-time profiles	within 168 hours after netupitant administration. A sampling window

		s approach will be used by collecting a single blood sample from each patient in one of these time windows: from 2 to 8 h, from 24 to 48 h, from 72 to 96 h and from 120 to 168 h
Exposure - Response Analysis for Netupitant	Exposure - Response analysis for netupitant performed by assessing the relationships between exposure parameters AUC0-inf and Cmax with the primary efficacy endpoint, i.e., the CR in the delayed phase. Graphical exposure-response analysis for netupitant performed by assessing the relationship between individual exposure parameters (AUC0-inf) and Cmax) with the	> 24-120 hours after the start of chemotherapy on Day 1

	primary efficacy endpoint, i.e the CR in the delayed phase.	

Secondary Outcome Measures

Outcome Measure	Measure Description	Time Frame
Percentage of Pediatric Patients With Complete Response During the Delayed Phase	Percentage of Pediatric Patients with complete response (CR, i.e., no emetic episodes and no rescue medication) during the delayed phase (> 24 to 120 h after the start of chemotherapy on Day 1) after a single oral netupitant administration, concomitantly with oral palonosetron, in pediatric cancer patients receiving HEC or MEC cycles.	> 24-120 hours after the start of chemotherapy on Day 1

Collaborators and Investigators

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

Sponsor

Helsinn Healthcare SA

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

2017-06-14

First Submitted that Met QC Criteria

2017-06-28

First Posted

2017-07-02

Results Reporting Dates

Results First Submitted

2020-09-16

Results First Posted with QC Comments

2020-10-12

Results First Submitted that Met QC Criteria

2020-12-03

Results First Posted

2020-12-07

Study Record Updates

HHS Vulnerability Disclosure

Last Update Submitted that met QC Criteria

2024-06-24

Last Update Posted

2024-06-25

Last Verified

2020-12

More Information

Terms related to this study

Additional Relevant MeSH Terms

Signs and Symptoms, Digestive

Nausea

Vomiting
Antiemetics
Autonomic Agents
Peripheral Nervous System Agents
Physiological Effects of Drugs
Gastrointestinal Agents
Serotonin 5-HT3 Receptor Antagonists
Serotonin Antagonists
Serotonin Agents
Neurotransmitter Agents
Molecular Mechanisms of Pharmacological Action
Palonosetron

Plan for Individual Participant Data (IPD)

Plan to Share Individual Participant Data (IPD)?

No

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 and Statistical Analysis Plan (https://cdn.clinicaltrials.gov/large-docs/79/NCT03204279/Prot_SAP_001.pdf) [PDF, 3.02MB, 2019-02-11]