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Recruiting

Study With IV NEPA (Fosnetupitant/Palonosetron) for the Prevention of Chemotherapy-induced Nausea and Vomiting in Paediatric Cancer Patients Undergoing Highly Emetogenic Chemotherapy (HEC)

ClinicalTrials.gov ID NCT06904235

Sponsor Helsinn Healthcare SA

Information provided by Helsinn Healthcare SA (Responsible Party)

Last Update Posted 2025-07-28

Study Details Tab

Study Overview

Brief Summary

Chemotherapy often causes nausea and vomiting (CINV), and this is a major problem for the children being treated for cancer. To prevent this, a combination of two substances in fixed proportion (IV NEPA) was developed. The two substances are: palonosetron, an antagonist of 5 HT3 receptors, and fosnetupitant, an antagonist of NK1 receptors that transforms into netupitant in the body. The medication is administered through intravenous injection (IV- drip).

This study is built from 2 parts:

Part 1: phase 2, open label Part 2: phase 3 double blind

The detailed description, study design, study milestones and eligibility criteria will reflect the Part 1 requirements

Feedback

HELSINN EXHIBIT 2029
Azurity Pharmaceuticals, Inc. v. Helsinn Healthcare S.A.
IPR2025-00947

Detailed Description

Part I of the study is a Phase 2, open-label, randomised (for Cohort 1 only), single chemotherapy cycle study which will compare single-dose of IV NEPA to another treatment (fosaprepitant/ondansetron) considered as a standard of care, in patients receiving single-day chemotherapy that has a high possibility to generate a vomiting episode (HEC) (Cohort 1) and assess repeated dose of IV NEPA in patients receiving multi day HEC chemotherapy (Cohort 2).

Because this will be the first study testing the IV NEPA in children, Part I will enroll patients from older to younger age groups with safety checks before moving to the next group.

Official Title

A Multicentre, Multinational, Pharmacokinetic, Safety, and Efficacy Study With IV NEPA (Fosnetupitant/Palonosetron) for the Prevention of Chemotherapy-induced Nausea and Vomiting in Paediatric Cancer Patients Undergoing Highly Emetogenic Chemotherapy (HEC). A 2-part Study With Phase 2, Open-label, Randomised, Single-dose IV NEPA vs Fosaprepitant/Ondansetron in Single-day HEC and Repeated-dose IV NEPA in Multi-day HEC (Part I, Single Cycle) and With Phase 3, Double-blind, Randomised, Repeated-dose IV NEPA vs Fosaprepitant/Ondansetron in Multi-day HEC (Part II, Repeated Cycles)

Conditions

Nausea and Vomiting Chemotherapy-Induced | Nausea Post Chemotherapy

Intervention / Treatment

- Drug: IV NEPA (fosnetupitant/palonosetron)
- Drug: Reference Treatment: IV ondansetron infusion
- Drug: Reference Treatment: IV fosaprepitant infusion

Other Study ID Numbers

- 2024-514321-39 (EudraCT Number)

Study Start (Actual)

2025-07-07

Primary Completion (Estimated)

2027-10

Study Completion (Estimated)

2027-12

Enrollment (Estimated)

95

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:
Ondansetron (https://dailymed.nlm.nih.gov/dailymed/search.cfm?labeltype=human&query=Ondansetron)
Palonosetron (https://dailymed.nlm.nih.gov/dailymed/search.cfm?labeltype=human&query=Palonosetron)
Fosaprepitant (https://dailymed.nlm.nih.gov/dailymed/search.cfm?labeltype=human&query=Fosaprepitant)

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).

Study Contact

Name: Tulla Spinelli Head of Clinical Affairs, PharmD, PhD
Phone Number: +41919852121
Email: tulla.spinelli@helsinn.com

This study has 18 locations

Greece

Athens, Greece
Not yet recruiting
Aghia Sophia Children's Hospital, Pediatric Hematology/ Oncology Unit (POHemU)

Thessaloniki, Greece
Not yet recruiting
"AHEPA" University General Hospital of Thessaloniki, 2nd Department of Pediatrics

Poland

Bialystok, Poland
Recruiting
Department of Pediatrics, Oncology and Hematology University Children's Clinical Hospital them. Ludwik Zamenhof in Bialystok

Olsztyn, Poland
Not yet recruiting
Clinical Department of Paediatric Oncology and Haematology VOIVODSHIP SPECIALIST CHILDREN'S HOSPITAL them. prof. dr. Stanisław Popowski in Olsztyn

Poznan, Poland
Recruiting
Department of Pediatric Oncology, Hematology and Transplantation Clinical Hospital them. Karol Jonscher Medical University them. Karol Marcinkowski in Poznań

Szczecin, Poland
Not yet recruiting
Department of Paediatrics and Paediatric Haemato-Oncology University Clinical Hospital No. 1 them. prof. Tadeusz Sokołowski Pomeranian Medical University

Szczecin, Poland
Recruiting
Department of Paediatrics, Oncology and Paediatric Immunology, University Clinical Hospital No. 1 them. prof. Tadeusz Sokołowski Pomeranian Medical University in Szczecin

Warsaw, Poland
Recruiting
Department of Oncology and Surgical Oncology

for Children and Youth Institute Mother and Child

Warsaw, Poland
Recruiting
Department of Oncology Institute "Monument - Child Health Center"

Łodz, Poland
Not yet recruiting
Clinic of Pediatrics, Oncology and Hematology University Pediatric Center them M. Konopnicka SP ZOZ Central Clinical Hospital Medical University of Lodz

Romania

Bucharest, Romania
Recruiting
Fundeni Clinical Institute, Pediatric Hematology and BMT

Bucharest, Romania
Recruiting
Oncology Institute "Prof. Dr. Al. Trestioreanu", Pediatric Oncology

Timisoara, Romania
Recruiting
Emergency Children's Hospital " Louis Turcanu, Oncology-Haematology and BMP department

Turkey

Ankara, Turkey
Not yet recruiting
Gazi University Gazi Hospital Children Hematology and Oncology

Ankara, Turkey
Not yet recruiting
Hacettepe University Hospitals Oncology Hospital 2nd Floor Children Oncology

Faith Locations

Istanbul, Faith, Turkey
Not yet recruiting
Istanbul University Istanbul Faculty of Medicine Topkapı

Mamak Locations

Ankara, Mamak, Turkey

Not yet recruiting
Ankara University Faculty of Medicine Children's Hospital, Department of Children Oncology and Hematology

Melikgazi Locations

Kayseri, Melikgazi, Turkey
Not yet recruiting
Erciyes University Hospitals Kanka Children's Hematology Oncology and Bone Marrow 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:

The following inclusion criteria must be checked prior to study inclusion:

1. Signed written Informed Consent Form (ICF) by parent(s)/legal guardian of the paediatric patient in compliance with the local laws and regulations. In addition, the signed children's Assent Form according to local requirements.
2. Male or female in- or out-patient from 0 months (newborns) to <18 years on the date of enrolment (Day 1).
3. Cohort 1: Patient < 6 months weighing at least 4 kg or patient ≥ 6 months weighing at least 6 kg.

   Cohort 2: Patient weighing at least 4 kg.
4. Patient with a predicted life expectancy ≥3 months according to Investigator's opinion.
5. Patient naïve or non-naïve to chemotherapy, with histologically and/or cytologically (or imaging in the case of brain tumours and nephroblastomas) confirmed malignant disease.
6. Cohort 1: Patient scheduled and eligible to receive at least 1 cycle of single-day HEC.

   Cohort 2: Patient scheduled and eligible to receive at least 1 cycle of multi-day HEC.

   (For the level of emetogenicity of the chemotherapeutic agents, refer to the POGO January 2021 guideline).
7. For patients aged ≥10 years: Eastern Cooperative Oncology Group Performance Status (ECOG PS) ≤2.
8. For patient with known hepatic impairment: the patient may be enrolled provided the serum ALT and AST are ≤2.5 ULN, the total bilirubin is ≤1.5 ULN, and in the Investigator's opinion the impairment is not expected to jeopardize the patient's safety during the study.
9. For patient with known renal impairment: the patient may be enrolled provided the estimated glomerular filtration rate (eGFR) is ≥70 mL/min/1.73m2 (≥50 mL/min/1.73m2 for children <3 months old) (the eGFR should be calculated using the modified Schwartz equation) and in the Investigator's opinion the impairment is not expected to jeopardize the patient's safety during the study.
10. For patient with known history or predisposition to cardiac abnormalities: as per the Investigator's opinion, the history/predisposition should not jeopardize patient's safety during the study.
11. Patient with non-clinically significant abnormal laboratory values or with clinically relevant abnormal laboratory values may be enrolled if in the Investigator's opinion the patient's safety is not expected to be jeopardized.

12. Female patient shall: a) not have attained menarche yet or b) have attained menarche and have a negative serum pregnancy test at the Screening Visit and a negative urine pregnancy test at Day 1.
13. 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 guardian must be counselled on the importance of avoiding pregnancy before and during the study.

Exclusion Criteria:

1. The patient and/or parent(s)/legal guardian 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; or 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 on Day 1 (Cohort 1 patients) or within 168 h (for Cohort 2 patients receiving the last IV NEPA on Day 3) or 216 h (for Cohort 2 patients receiving the last IV NEPA on Day 5) from start of chemotherapy on Day 1.
3. Known history of allergy to any component of the study treatments or other contraindications to any NK1-RAs or 5-HT3-RAs.
4. Active infection.
5. Any illness or condition that, in the opinion of the Investigator, may pose unwarranted risks in administering the investigational product to the patient.
6. Uncontrolled medical condition (e.g., uncontrolled insulin-dependent diabetes mellitus).
7. Patient experiencing ongoing vomiting from any organic aetiology (including patients with history of gastric outlet obstruction or intestinal obstruction due to adhesions or volvulus), or patient with hydrocephalus.
8. Patient who experienced any vomiting, retching, or nausea within 24 h prior to the administration of the study treatment on Day 1 (Note: functional vomiting for infants, which is normally seen during the first 3 months of life, is not to be considered as vomiting).
9. Patient who received any drug with potential antiemetic effect within 24 h prior to administration of study treatment on Day 1, including but not limited to the following:
    - NK1-RAs (e.g., (fos)aprepitant or any other drug of this class)
    - 5-HT3-RAs (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 treatment administration on Day 1 or expected to be administered within the efficacy assessment period, except for single doses of midazolam, temazepam, or triazolam
    - Butyrophenones (e.g., droperidol, haloperidol)

- Anticholinergics (e.g., scopolamine, except the inhaled anticholinergics for respiratory disorders e.g., ipratropium bromide)
- Antihistamines (e.g., diphenhydramine, cyclizine, hydroxyzine, chlorphenhyramine, dimenhydrinate, meclizine)
- Domperidone
- Mirtazapine
- Olanzapine
- Prescribed cannabinoids (e.g., tetrahydrocannabinol, nabilone)
- Over-the-counter (OTC) antiemetics, OTC cold medications, or OTC allergy medications
- Herbal preparations containing ephedra or ginger

10. Patient who received palonosetron within 1 week prior to administration of study treatment on Day 1.

11. Patient receiving systemic corticosteroid therapy above 0.14mg/kg or >10 mg of prednisone daily or equivalent.

    Exception:

    Dexamethasone for the prevention of CINV is permitted in association with the study treatment (Test Treatment and Reference Treatment) as per standard of care and applicable guidelines, provided its dosage is reduced by 50% in consideration of known interactions with various NK1 RAs, including fosaprepitant and fosnetupitant.

12. Patient aged <6 years who received any investigational drug (defined as a medication with no marketing authorization granted for any age or 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 patient any age who is expected to receive investigational drugs prior to study completion.
13. Intake of alcohol, food, or beverages (e.g., grapefruit, cranberry, pomegranate, and aloe vera juices; German chamomile) known to interfere with CYP3A4 or CYP2D6 metabolic enzymes within 1 week prior to Day 1 and during the overall study period.
14. Use of any drugs or substances known to be strong inhibitors of CYP3A4 or CYP2D6 enzymes 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 CYP3A4 substrates with narrow therapeutic range within 1 week prior to Day 1 or planned to be used during the overall study period.
16. Use of any drugs or substances known to be strong inducers of CYP3A4 or CYP2D6 enzymes within 4 weeks prior to Day 1 or planned to be used during the overall study period.
17. Lactating female patient.
18. Enrolment in a previous study on netupitant (either administered alone or in combination with palonosetron).
19. Marked baseline prolongation of QTc interval (QTcF>460 millisecond [msec]). At the discretion of the investigator, criterion may be based on automatic interpretation of results.

Ages Eligible for Study

0 Months to 18 Years (Child, 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
Interventional Model Description:

- Cohort 1: Single-day HEC and single-dose administration of Test Treatment (IV NEPA) or administration of Reference Treatment (IV fosaprepitant + IV ondansetron) on Day 1. Due to fosaprepitant and ondansetron not being indicated in patients younger than 6 months of age and due to fosaprepitant not being indicated in patients with body weight <6 kg, in Cohort 1, patients aged <6 months will exclusively receive the Test Treatment. Patients aged ≥6 months and weighing at least 6 kg will be randomly allocated to either Test Treatment or Reference Treatment.
- Cohort 2: Multi-day HEC and repeated-dose administration of Test Treatment (IV NEPA), with the first administration on Day 1. All patients will receive the Test Treatment

Masking : None (Open Label)

Arms and Interventions

Participant Group/Arm	Intervention/Treatment
Experimental: IV NEPA The Test Treatment (IV NEPA) is planned to be administered in Cohort 1 and Cohort 2. IV NEPA Dosing Schedule • Cohort 1 (single-day HEC): Single 30-min infusion on Day 1, before start of chemotherapy. • Cohort 2 (multi-day HEC): Single 30-min infusion on Days 1, 3, and 5 (administration on Day 5 depending on the patient's multi day HEC scheme), before start of chemotherapy or in the morning if no chemotherapy is administered on the same day.	Drug: IV NEPA (fosnetupitant/palonosetron) • In NEPA-22-01, different body weight-based dosages of IV NEPA will be applied to patients below and over 3 months of age: Formulation A (for patients ≥3 months of age; 235 mg fosnetupitant/1.5 mg palonosetron per vial) or Formulation B (for patients <3 months of age; 235 mg fosnetupitant/2.5 mg palonosetron per vial).
Active Comparator: Reference Treatment	Drug: Reference Treatment: IV ondansetron infusion

The Reference Treatment is planned to be administered in Cohort 1 only. The Reference Treatment includes fosaprepitant powder for solution for IV infusion and ondansetron liquid solution for IV infusion.	• IV Ondansetron Dosing Regimen
	  ◦ Day 1 (before start of chemotherapy): One 30-min infusion of 0.15 mg/kg (ondansetron maximum dose: 8 mg per administration)
	  ◦ Day 1 at 4 h and 8 h after the end of first administration: Two 30-min infusions of 0.15 mg/kg (ondansetron maximum dose: 8 mg per administration)
	
	Drug: Reference Treatment: IV fosaprepitant infusion
	
	• Fosaprepitant IV Dosing Regimen
	  ◦ Patients aged 12 years to <18 years: a single dose of IV fosaprepitant 150 mg
	  ◦ Patients aged 2 years to <12 years: a single dose of IV fosaprepitant 4 mg/kg (maximum dose: 150 mg)
	  ◦ Patients aged 6 months to <2 years: a single dose of IV fosaprepitant 5 mg/kg (maximum dose: 150 mg)

What is the study measuring?

Primary Outcome Measures

Outcome Measure	Measure Description	Time Frame
COHORT 1 Neptupitant exposure parameter	Maximum concentration (Cmax)	From time zero (start of IV NEPA

		infusion) to maximum 168 hours
COHORT 1 Neptupitant exposure	Area under the plasma concentration-time curve	From time zero (start of IV NEPA infusion) to maximum 168 hours
COHORT 2 monitoring of AEs (safety and tolerability of IV NEPA)	monitoring of AEs following repeated IV NEPA administration	Up to 31 days

Secondary Outcome Measures

Outcome Measure	Measure Description	Time Frame
COHORT 1: To assess the PK profile of netupitant.	Cmax of netupitant	From Time zero (start of IV NEPA infusion) until

		168 hours
COHORT 1: To assess the PK profile of fosnetupitant.	Cmax of fosnetupitant	From Time zero (start of IV NEPA infusion) until 168 hours
COHORT 1: To assess the PK profile palonosetron.	Cmax of palonosetron	From Time zero (start of IV NEPA infusion) until 168 hours
COHORT 1: To assess the PK profile of netupitant	AUC0-48 of netupitant	From Time zero (start of IV NEPA infusion) until 48 hours

COHORT 1: To assess the PK profile of fosnetupitant.	AUC0-48 of fosnetupitant	From Time zero (start of IV NEPA infusion) until 48 hours
COHORT 1: To assess the PK profile palonosetron.	AUC0-48 of palonosetron	From Time zero (start of IV NEPA infusion) until 48 hours
COHORT 1: To assess the PK profile of netupitant	t1/2 of netupitant	From Time zero (start of IV NEPA infusion) until 168 hours

COHORT 1: To assess the PK profile of palonosetron.	t1/2 of palonosetron	From Time zero (start of IV NEPA infusion) until 168 hours
COHORT 1 and 2: To assess the population PK profile of fosnetupitant.	Clearance (CL) of fosnetupitant	From Time zero (start of IV NEPA infusion) until 168 hours
COHORT 1 and 2: To assess the population PK profile of palonosetron.	CL of palonosetron	From Time zero (start of IV NEPA infusion) until 168 hours
COHORT 1 and 2: To assess the population	CL/F of netupitant	From Time zero (start of

PK profile of netupitant.		IV NEPA infusion) until 168 hours
COHORT 1 and 2: To assess the population PK profile of fosnetupitant	Volume of compartments (V) for fosnetupitant	From Time zero (start of IV NEPA infusion) until 168 hours
COHORT 1 and 2: To assess the population PK profile of palonosetron.	V for palonosetron	From Time zero (start of IV NEPA infusion) until 168 hours
COHORT 1 and 2: To assess the population PK profile of netupitant.	V/F for netupitant	From Time zero (start of IV NEPA infusion) until

		168 hours

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

2024-12-16

First Submitted that Met QC Criteria

2025-03-31

First Posted

2025-04-01

Study Record Updates

Last Update Submitted that met QC Criteria

2025-07-23

Last Update Posted

2025-07-28

Last Verified

2025-07

More Information

Terms related to this study

Keywords Provided by Helsinn Healthcare SA

Prevention of chemotherapy-induced nausea and vomiting
highly emetogenic chemotherapy
HEC
IV NEPA
CINV

HHS Vulnerability Disclosure

Additional Relevant MeSH Terms

Signs and Symptoms, Digestive
Nausea
Vomiting
Antiemetics
Autonomic Agents
Peripheral Nervous System Agents
Physiological Effects of Drugs
Gastrointestinal Agents
Antipruritics
Dermatologic Agents
Serotonin 5-HT3 Receptor Antagonists
Serotonin Antagonists
Serotonin Agents
Neurotransmitter Agents
Molecular Mechanisms of Pharmacological Action

Neurokinin-1 Receptor Antagonists
Ondansetron
Palonosetron
Fosaprepitant
Aprepitant

Plan for Individual Participant Data (IPD)

Plan to Share Individual Participant Data (IPD)?

No

IPD Plan Description

Only global trial data will be shared, not a single patient

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