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Completed

Oral Akynzeo® Vs Standard of Care in Preventing CINV in High-risk MEC Patients (MyRisk) (CINV)

ClinicalTrials.gov ID NCT04817189

Sponsor Helsinn Healthcare SA

Information provided by Helsinn Healthcare SA (Responsible Party)

Last Update Posted 2024-12-04

Study Details Tab

Study Overview

Brief Summary

MyRisk: Efficacy and safety evaluation of oral Akynzeo® in patients receiving MEC at high risk of developing CINV based on a prediction tool. A multinational and multicenter study.

Antiemetic guidelines recommendations are based on the emetogenic potential of the chemotherapy. Chemotherapy (CT) agents are divided in Highly, Moderately, Low and Minimally Emetogenic potential.

In addition to type of chemotherapy, several patient-related risk factors can increase the risk of CINV (chemotherapy-induced nausea and vomiting). Currently, there is limited consensus surrounding the most relevant patient risk factors that may predict the risk of CINV. Based on a recent study by Dranitsaris et al. (Dranitsaris et al. Ann Oncol. 2017 Jun 1; 28(6):1260-1267.), eight (8) predictive factors have been identified and an algorithm has been developed to incorporate these factors into the optimal selection of prophylactic antiemetics:

Feedback

HELSINN EXHIBIT 2026
Azurity Pharmaceuticals, Inc. v. Helsinn Healthcare S.A.
IPR2025-00945

1. nausea and/or vomiting in the prior cycle of chemotherapy
2. use of non-prescribed antiemetics at home in the prior cycle of chemotherapy
3. platinum or anthracycline-based chemotherapy
4. age < 60 years
5. expectations for (anticipating) nausea and/or vomiting
6. <7 h of sleep the night before chemotherapy
7. history of morning sickness during previous pregnancy
8. cycle of chemotherapy (A negative association between risk and number of cycles was identified where the hazard for CINV was highest in cycles 1 and 2, with a gradual decline and plateau from cycle 3 onward).

The clinical application of this prediction tool has the potential to be an important resource for clinicians and may help to enhance patient care by optimizing the use of the antiemetics in a proactive manner.

Detailed Description

Antiemetic guideline recommendations are based on the emetogenic potential of chemotherapy and involve 4 levels of classification of intravenous chemotherapy agents, i.e., high, moderate, low and minimal; these have been accepted by major organisations. Moderate emetogenic chemotherapy (MEC) results in acute vomiting in 30% to 90% of cancer patients in the absence of antiemetic therapy. In addition to the chemotherapy type, several patient-related risk factors and clinical characteristics can increase CINV risk. These can include use of antiemetics inconsistent with international guidelines, younger age, prechemotherapy nausea, no complete CINV response in an earlier cycle, history of nausea/vomiting, (trait) anxiety, fatigue experience, and expectations of nausea/vomiting. Other studies have largely confirmed some of the key risk factors for CINV (history of vomiting during pregnancy, history of motion sickness, age, gender) and added other factors such as (chronic) alcohol consumption, body surface area, fewer hours slept the night prior to infusion, or advanced stage cancer. Currently, there is a limited consensus surrounding the most relevant patient risk factors that may predict CINV risk. Based on a recent study by Dranitsaris et al. eight predictive factors have been identified, and an algorithm has been developed to combine these patient-related risk factors into the optimal treatment of prophylactic antiemetics. These include:

1. nausea and/or vomiting in the prior cycle of chemotherapy
2. use of non-prescribed antiemetics at home in the prior cycle of chemotherapy
3. platinum or anthracycline-based chemotherapy
4. age < 60 years
5. expectations for (anticipating) nausea and/or vomiting
6. <7 h of sleep the night before chemotherapy
7. history of morning sickness during previous pregnancy
8. cycle of chemotherapy (A negative association between risk and number of cycles was identified where the hazard for CINV was highest in cycles 1 and 2, with a gradual decline and plateau from cycle 3 onward).

Akynzeo®, an oral combination of the neurokinin 1 receptor antagonists (NK1 RA), netupitant and the 5-hydroxytryptamine (HT3) receptor antagonists (5-HT3 RA), palonosetron, is recommended by guidelines for the prevention of CINV. Akynzeo® has been evaluated in a multicentre, randomised, double-blind, double-dummy phase II clinical trial at various dose ranges among 694 cisplatin-treated cancer patients from 44 sites (two countries); each NEPA (netupitant-palonosetron) dose significantly improves CINV prevention in cancer patients. Similar results were obtained in another international, randomised, double-blind and parallel group phase III clinical trial; NEPA prevented CINV in patients receiving MEC.

The current study primarily aimed to evaluate whether Akynzeo® leads to a higher response rate compared with standard care in MEC regimen-treated patients who are identified to be at high risk based on the algorithm.

Official Title

MyRisk: Efficacy and Safety Evaluation of Oral Akynzeo® in Patients Receiving MEC At High Risk of Developing CINV Based on a Prediction Tool: a Multinational and Multicenter Study

Conditions

Chemotherapy-induced Nausea and Vomiting

Intervention / Treatment

- Drug: NEPA (300mg netupitant/0.5mg palonosetron)
- Drug: Granisetron, 2 mg (oral) or 1 mg (IV) OR Palonosetron, 0.5 mg (oral), 0.25mg (IV) OR Ondansetron, 16 mg (oral) or 8 mg (IV) OR Dolasetron 100 mg (oral) OR Tropisetron 5 mg (oral or IV)
- Drug: Dexamethasone, 8 mg (oral) or equivalent IV dose

Other Study ID Numbers

Study Start (Actual)

2021-02-01

Primary Completion (Actual)

2024-07-02

Study Completion (Actual)

2024-07-02

Enrollment (Actual)

414

Study Type

Interventional

Phase

Phase 4

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 19 locations

China

Shanghai, China
Shanghai Chest Hospital

Shanghai, China
Shanghai Ninth People´s Hospital

Shanghai, China
Shanghai Obstetrics and Gynecology Hospital

Czechia

Prague, Czechia
General University Hospital in Prague

Praha, Czechia, 14059
Thomayerova nemocnice

Germany

Essen, Germany
Evang. Kliniken Essen-Mitte

Mannheim, Germany
Universitätsmedizin Mannheim

München, Germany
München Klinik Neuperlach

Paderborn, Germany
Frauenklinik St. Louise

Potsdam, Germany
Klinikum Ernst von Bergmann gemeinnützige GmbH

Greece

Athens, Greece
Sotiria General Hospital, 3rd Deúpartment of Medicine, School of Medicine, National and Kapodistrian University of Athens

Heraklion, Greece
General University Hospital of Heraklion

Spain

A Coruña, Spain, 15006
Complejo Hospitalario Universitario de A Coruña

Barcelona, Spain, 0802
Hospital de la Santa Creu i Sant Pau

Madrid, Spain, 28007
Hospital General Universitario Gregorio Marañón

Salamanca, Spain, 37007
Hospital Universitario de Salamanca

Switzerland

Basel, Switzerland
University Hospital Basel

Genolier, Switzerland
Swiss Medical Network - Clinique de Genolier

United Kingdom

London, United Kingdom
The Royal Marsden 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:

- Adult patients aged ≥18 years
- Patients with a risk score of ≥ 13 as calculated by the algorithm - see 3.6.3.1. Baseline/screening: VISIT 0
- Signed Informed consent
- Both sexes
- Patients with diagnosis of any cancer scheduled and intended to be treated for three consecutive cycles with a single dose of any IV MEC regimen, per cycle, including adjuvant or neo-adjuvant chemotherapy
- Patients with Eastern Cooperative Oncology Group (ECOG) performance status 0, 1 or 2
- Use of Standard of Care defined as a 5-HT3 RA + Dexamethasone (or equivalent corticosteroid) based-regimen on day 1 of chemotherapy for CINV prevention
- Naïve and non- naïve to chemotherapy
- The enrolled women should be a) of non-childbearing potential or b) of childbearing potential using reliable contraceptive measures and having a negative urine pregnancy test done by health care team within 1-24 hours before dosing the antiemetic treatment in both arms and outcome recorded in the medical records
- Able to comply with study requirements

Exclusion Criteria:

- Patients receiving highly emetogenic chemotherapy (including anthracycline+cyclophosphamide-based chemotherapy)
- Patients receiving oral moderately emetogenic chemotherapy drugs
- Patients receiving opioids within 2 weeks prior to trial enrollment (longer use allowed)
- Use of olanzapine as prophylaxis of CINV
- Patients scheduled to receive radiotherapy concurrently with chemotherapy
- Any illness or condition that, in the opinion of the physician, may confound the results of the study or pose unwarranted risks in administering the investigational product to the patient.
- Patients with mechanical risk factors for nausea (i.e. intestinal obstruction)
- Patients with liver disease (as nausea is a common presenting symptom)
- Patients with metabolic risk factors for nausea (i.e. electrolyte imbalances causing nausea/vomiting)
- Chronic treatment with steroids (with the exception of inhaled or topical steroids)
- Pregnancy and/or breast-feeding women
- Women of childbearing potential refusing to use effective contraception during the whole study treatment and up to one month after study treatment with Akynzeo®
- Use of Standard of Care including an NK-1 RA-based regimen to prevent CINV

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 : Supportive Care
Allocation : Randomized
Interventional Model : Parallel Assignment
Interventional Model Description: interventional, open label, randomized, active controlled, parallel arms, multicenter and multinational study
Masking : None (Open Label)

Arms and Interventions

Participant Group/Arm	Intervention/Treatment

Experimental: NEPA (300mg netupitant/0.5mg palonosetron) + Dexamethasone 8 mg
 	
Oral netupitant/palonosetron (300 mg/0.50 mg) fixed-dose combination on Day 1 of each cycle.
 	
Dexamethasone (8 mg) will be administered on Day 1 of each cycle.
	Drug: NEPA (300mg netupitant/0.5mg palonosetron)
	• Oral netupitant/palonosetron (300 mg/0.50 mg) fixed-dose combination on Day 1 of each cycle.
	• Other Names:
	  ◦ Akynzeo® capsules
	Drug: Dexamethasone, 8 mg (oral) or equivalent IV dose
	• Dexamethasone (8 mg) will be administered on Day 1 of each cycle.
	• Other Names:
	  ◦ corticosteroid

Active Comparator: Standard of care + Dexamethasone 8 mg Dexamethasone (or equivalent corticosteroids) 8 mg administered by the oral route (or equivalent IV dose) on Day 1, approximately 1 hour before chemotherapy and one of the 5-HT3-RAs recommended by European Society for Medical Oncology	Drug: Granisetron, 2 mg (oral) or 1 mg (IV) OR Palonosetron, 0.5 mg (oral), 0.25mg (IV) OR Ondansetron, 16 mg (oral) or 8 mg (IV) OR Dolasetron 100 mg (oral) OR Tropisetron 5 mg (oral or IV) • Standard of care will be administered on Day 1 of each cycle. • Other Names: ◦ 5-HT3 RA Drug: Dexamethasone, 8 mg (oral) or equivalent IV dose • Dexamethasone (8 mg) will be administered on Day 1 of each cycle.

(ESMO) and Multinational Association of Supportive Care in Cancer (MASCC) guidelines (standard of care), i.e. either: Granisetron, 2 mg (oral) or 1 mg (IV) OR Palonosetron, 0.5 mg (oral), 0.25mg (IV) OR Ondansetron, 16 mg (oral) or 8 mg (IV) OR Dolasetron 100 mg (oral) OR Tropisetron 5 mg (oral or IV)	• Other Names: ◦ corticosteroid

What is the study measuring?

Primary Outcome Measures

Outcome Measure	Measure Description	Time Frame
The proportion of complete responses over three cycles of chemotherapy after the start of the MEC administration	To evaluate if the use of NEPA (netupitant and palonosetron) in patients treated with IV moderately emetogenic chemotherapy and at high risk of CINV is more effective in preventing CINV than a standard of care antiemetics over three cycles of chemotherapy.	At the end of all three chemotherapy cycles. The length of a cycle depends on the treatme

		nt being given (cycles range from 2 to 6 weeks).

Secondary Outcome Measures

Outcome Measure	Measure Description	Time Frame

Evaluation of acute (0 to 24 hours), delayed (>24 to 120 hours), and overall (0-120 hours) CINV indicators in each cycle of chemotherapy	Proportion of: • No emetic episode during the acute, delayed, and overall phase and daily in each cycle • Number of vomiting episodes during the acute, delayed, and overall phase in each cycle • No rescue medication during the acute, delayed, and overall phase and daily in each cycle • No significant nausea (maximum MAT scale = 2) during the acute, delayed, and overall phase and daily in each cycle; • No nausea (MAT scale = 0) during the acute, delayed, and overall phase and daily in each cycle; • Complete protection (no emetic episode, no rescue medication, and no significant nausea) during the acute, delayed, and overall phase and daily in each cycle Time 0 is defined as the start time of the chemotherapy administration on Day 1 of each of the three cycles.	At the end of each cycle and after all 3 chemotherapy cycles. The length of a cycle depends on the treatment being given (cycles range from 2 to 6 weeks).
Evaluation of the predictive role of potential risk factors in the development of CINV over three cycles of chemotherapy	Analysis of the development of CINV as a dependent variable will be performed to identify additional potential risk factors of CINV thought to be increasing the risk of CINV in patients receiving MEC. The outcome measure is the development of CINV, defined as any occurrence of nausea or a vomiting episode.	At the end of each cycle and after all 3 chemotherapy cycles. The

	The data on the development of CINV will be taken from data collection tools, patients' diaries and MASCC Antiemesis Tool (MAT).	length of a cycle depends on the treatment being given (cycles range from 2 to 6 weeks).
Evaluation of the safety profile of the antiemetic drug over three cycles of chemotherapy - the frequency of adverse events (AE)	An overall summary of adverse events (AE) will be presented, including the frequency of patients with: • Any treatment-emergent adverse event • Any treatment-emergent adverse event related to a study drug • Any treatment-emergent adverse event leading to chemotherapy dose reductions or interruptions • Any treatment-emergent serious adverse event All AEs will be summarized by their: • Severity • Seriousness • Relationship to a drug	At the end of all 3 chemotherapy cycles. The length of a cycle depends on the treatment being given (cycles range from 2 to 6 weeks).

Evaluation of the safety profile of the antiemetic drug over three cycles of chemotherapy - the percentage of adverse events (AE)	An overall summary of adverse events (AE) will be presented, including the percentage of patients with: • Any treatment-emergent adverse event • Any treatment-emergent adverse event related to a study drug • Any treatment-emergent adverse event leading to chemotherapy dose reductions or interruptions • Any treatment-emergent serious adverse event All AEs will be summarized by their: • Severity • Seriousness • Relationship to a drug	At the end of all 3 chemotherapy cycles. The length of a cycle depends on the treatment being given (cycles range from 2 to 6 weeks).
Evaluation of the frequency of discontinuations due to adverse events	The frequency of discontinuations due to adverse events (AE) will be presented. All AEs leading to discontinuation will be summarized by their: • Severity • Seriousness • Relationship to a drug	At the end of all 3 chemotherapy cycles. The length of a cycle depends on the treatment being given (cycles

		range from 2 to 6 weeks).
Evaluation of the percentage of discontinuations due to adverse events	The percentage of patients with discontinuations due to adverse events (AE) will be presented. All AEs leading to discontinuation will be summarized by their: • Severity • Seriousness • Relationship to a drug	At the end of all 3 chemotherapy cycles. The length of a cycle depends on the treatment being given (cycles range from 2 to 6 weeks).
Evaluation of frequency of on treatment deaths due to adverse events	The frequency of on treatment deaths due to adverse events (AE) will be presented. All AEs leading to on treatment deaths will be summarized by their: • Severity • Seriousness • Relationship to a drug	At the end of all 3 chemotherapy cycles. The length of a cycle depend

		s on the treatment being given (cycles range from 2 to 6 weeks).
Evaluation of the percentage of patients with on treatment death due to adverse events	The percentage of patients with on treatment death due to adverse events (AE) will be presented. All AEs leading to on treatment death will be summarized by their: • Severity • Seriousness • Relationship to a drug	At the end of all 3 chemotherapy cycles. The length of a cycle depends on the treatment being given (cycles range from 2 to 6 weeks).
Listings concerning the safety profile of the antiemetic drug over three	The following listings will be presented: • All AEs (including pre-treatment AEs) • Serious adverse events	At the end of all 3 chemotherapy cycles.

cycles of chemotherapy	• Adverse events resulting in withdrawn of study drug	The length of a cycle depends on the treatment being given (cycles range from 2 to 6 weeks).
Exploration of the effect of CINV on daily activities and quality of life in patients receiving moderately-emetogenic chemotherapy over three cycles of chemotherapy	Evaluation of the effect of CINV on daily activities and quality of life that will be measured by using the Functional Living Index-Emesis (FLIE) questionnaire, a validated, nausea and vomiting specific, patient-reported outcome instrument. The Functional Living Index-Emesis (FLIE) has 18 questions. These questions are divided into two domains: Nausea (questions 1-9) and Vomiting (questions 10-18). The minimum score for any question is 0 and the maximum score is 100. Higher scores indicate less impairment on daily life as a result of nausea or vomiting.	At the end of all 3 chemotherapy cycles. The length of a cycle depends on the treatment being given (cycles range from 2 to 6 weeks).

Evaluation of resource utilization and health economic outcome - number of days with rescue medication administered for the treatment of CINV	Health economic endpoint, the number of days with rescue medication administered for the treatment of CINV, will be evaluated during the study cycles	At the end of each cycle and after all 3 chemotherapy cycles. The length of a cycle depends on the treatment being given (cycles range from 2 to 6 weeks).
Evaluation of resource utilization and health economic outcome - daily doses of rescue medication administered for the	Health economic endpoint, the daily doses of rescue medication administered for the treatment of CINV, will be evaluated during the study cycles	At the end of each cycle and after all 3 chemotherapy cycles. The length

treatment of CINV		of a cycle depends on the treatment being given (cycles range from 2 to 6 weeks).
Evaluation of resource utilization and health economic outcome - the number of re-hydration bags	Health economic endpoint, the number of re-hydration bags given for at least grade 2 vomiting (more details below), will be evaluated during the study cycles	At the end of each cycle and after all 3 chemotherapy cycles. The length of a cycle depends on the treatment being given (cycles range from 2 to 6 weeks).

Evaluation of resource utilization and health economic outcome - the number of days of unplanned hospitalisations	Health economic endpoint, the number of days of unplanned hospitalizations related to CINV, will be evaluated during the study cycles All hospitalizations will be summarized according to the department of hospitalization (type of ward)	At the end of each cycle and after all 3 chemotherapy cycles. The length of a cycle depends on the treatment being given (cycles range from 2 to 6 weeks).
Evaluation of resource utilization and health economic outcome - the number of outpatient physician visits	Health economic endpoint, the number of outpatient physician visits and health care consultations due to CINV (e.g., general practitioner), will be evaluated during the study cycles	At the end of each cycle and after all 3 chemotherapy cycles. The length

		of a cycle depends on the treatment being given (cycles range from 2 to 6 weeks).
Evaluation of resource utilization and health economic outcome - the number of unplanned laboratory test	Health economic endpoint, the number of unplanned laboratory test including those at unplanned hospitalizations due to CINV, will be evaluated during the study cycles	At the end of each cycle and after all 3 chemotherapy cycles. The length of a cycle depends on the treatment being given (cycles range from 2 to 6 weeks).

Evaluation of resource utilization and health economic outcome - discontinuation of chemotherapy treatment due to CINV	Health economic endpoint, the number of discontinuations of chemotherapy treatment due to CINV, will be evaluated during the study cycles	At the end of each cycle and after all 3 chemotherapy cycles. The length of a cycle depends on the treatment being given (cycles range from 2 to 6 weeks).
Evaluation of resource utilization and health economic outcome - the number of delays of chemotherapy administration due to CINV	Health economic endpoint, the number of delays of chemotherapy administration due to CINV, will be evaluated during the study cycles	At the end of each cycle and after all 3 chemotherapy cycles. The length

		of a cycle depends on the treatment being given (cycles range from 2 to 6 weeks).
Evaluation of resource utilization and health economic outcome - the average length of delay of chemotherapy administration due to CINV	Health economic endpoint, the average length of delay (in days) of chemotherapy administration due to CINV, will be evaluated during the study cycles	At the end of each cycle and after all 3 chemotherapy cycles. The length of a cycle depends on the treatment being given (cycles range from 2 to 6 weeks).

Evaluation of resource utilization and health economic outcome - days of absence from work	Health economic endpoint, the number of days of absence from work, will be evaluated during the study cycles	At the end of each cycle and after all 3 chemotherapy cycles. The length of a cycle depends on the treatment being given (cycles range from 2 to 6 weeks).

Collaborators and Investigators

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

Sponsor

Helsinn Healthcare SA

Investigators

- Study Chair: Alex Molasiotis, prof., University of Derby

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.

HHS Vulnerability Disclosure

Study Registration Dates

First Submitted
2021-03-01

First Submitted that Met QC Criteria
2021-03-24

First Posted
2021-03-26

Study Record Updates

Last Update Submitted that met QC Criteria
2024-12-02

Last Update Posted
2024-12-04

Last Verified
2024-12

More Information

Terms related to this study

Additional Relevant MeSH Terms

Signs and Symptoms, Digestive
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
Antipruritics
Dermatologic Agents
Serotonin 5-HT3 Receptor Antagonists
Serotonin Antagonists
Serotonin Agents
Neurotransmitter Agents
Molecular Mechanisms of Pharmacological Action
Dexamethasone
Ondansetron
Palonosetron
Granisetron
Tropisetron
Dolasetron

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

No

Studies a U.S. FDA-Regulated Device Product

No

Product Manufactured in and Exported from the U.S.

No