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Unknown status

Verified **2021-12** by Christina Ruhlmann, Odense University Hospital

Last known status was: Recruiting

Safety and Antiemetic Efficacy of Akynzeo Plus Dexamethasone During Radiotherapy and Concomitant Weekly Cisplatin

ClinicalTrials.gov ID NCT03668639

Sponsor Christina Ruhlmann

Information provided by Christina Ruhlmann, Odense University Hospital (Responsible Party)

Last Update Posted 2021-12-14

Study Details Tab

Study Overview

Brief Summary

This is a multicentre, single-arm, phase II study to investigate the safety and antiemetic efficacy of Akynzeo (a fixed dose combination of palonosetron and netupitant) plus dexamethasone in patients receiving concomitant chemo-radiotherapy with weekly cisplatin for at least five weeks.

Detailed Description

Akynzeo contains a combination of the neurokinin-1 receptor antagonist netupitant and the serotonin receptor antagonist palonosetron. Akynzeo is approved as antiemetic prophylaxis in patients receiving high emetogenic chemotherapy e.g. high dose cisplatin administered every three weeks.

Feedback

HELSINN EXHIBIT 2025
Azurity Pharmaceuticals, Inc. v. Helsinn Healthcare S.A.
IPR2025-00945

From a previous clinical trial (GAND-emesis trial) we know that patients receiving radiotherapy and concomitant weekly cisplatin 40 mg/m2 are better protected against nausea and vomiting when a triplet antiemetic prophylaxis (neurokinin-1 receptor antagonist, serotonin receptor antagonist, and corticosteroid) is applied.

In the Akynzeo phase III clinical trials, Akynzeo was administered every three weeks. The neurokinin-1 receptor antagonist, netupitant, has a long plasma half-life (approx. 90 hours), and theoretically the drug could accumulate when administered on a weekly basis.

The DANGER-emesis trial is designed to collect safety and efficacy data in patients receiving Akynzeo weekly as antiemetic prophylaxis in combination with dexamethasone in patients treated for cervical cancer with radiotherapy and concomitant weekly cisplatin 40 mg/m2.

Official Title

A Study to Investigate the Safety and Antiemetic Efficacy of Akynzeo Plus Dexamethasone in Patients Receiving Concomitant Chemo-radiotherapy With Weekly Cisplatin for at Least Five Weeks

Conditions

Chemotherapy-induced Nausea and Vomiting | Adverse Event | Cervical Cancer

Intervention / Treatment

- Drug: Akynzeo
- Drug: Dexamethasone

Other Study ID Numbers

Study Start (Actual)

2018-09-05

Primary Completion (Estimated)

2023-03-01

Study Completion (Estimated)

2023-04-15

Enrollment (Estimated)

80

Study Type

Interventional

Phase

Phase 2
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) Dexamethasone sodium phosphate (https://dailymed.nlm.nih.gov/dailymed/search.cfm?labeltype=human&query=Dexamethasone+sodium+phosphate) Dexamethasone acetate (https://dailymed.nlm.nih.gov/dailymed/search.cfm?labeltype=human&query=Dexamethasone+acetate)

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: Christina H. Ruhlmann, MD, PhD
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Study Contact Backup

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This study has 1 location

Denmark

Odense, Denmark, 5000

Recruiting

Department of Oncology, Odense University Hospital

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Principal Investigator : Christina H. Ruhlmann, MD, PhD

Sub-Investigator : Anja Ør Knudsen, MD

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. The patient has a diagnosis of cervical cancer.
2. The patient understands the nature and purpose of this study and the study procedures and has signed informed consent.
3. The patient is aged ≥ 18 years.
4. The patient must be both chemo- and radiotherapy (RT) naïve. NB: previously low voltage RT or electron RT for non-melanoma skin cancers is allowed.
5. The patient is scheduled to receive fractionated radiotherapy and concomitant weekly cisplatin at a dose of ≥ 40 mg/m2 for at least five weeks.
6. Brachy therapy is scheduled to be initiated after the third cycle of weekly cisplatin, and preferentially after the fifth week of treatment.
7. Chemotherapy with an emetic risk potential of minimal or mild (up to 30%) is allowed on days 1-4 (see ref. 14).
8. The patient has a WHO Performance Status of ≤ 2.
9. Hematologic and metabolic status must be adequate for receiving weekly cisplatin in a dose of ≥ 40 mg/m2, and meet the following criteria:
    - Total neutrophils ≥ 1500/mm3 (Standard units : ≥1.5 x 109/L)
    - Platelets ≥ 100,000/mm3 (Standard units: ≥100.0 x 109/L)
    - Bilirubin ≤ 1.5 x ULN (Upper Limits of Normal)
    - Aspartate aminotransferase (AST) and/or alanine aminotransferase (ALT) ≤ 2.5 x ULN
    - GFR ≥ 50 ml/min
10. The patient is able to read, understand, and complete questionnaires and daily components of the Patient Diary for each study cycle.
11. For patients of childbearing potential, urine human chorionic gonadotropin (hCG) (urine dipstick pregnancy test) or blood hCG results must be negative at screening, and these patients must agree to one of the following methods of contraception:
    - Hormonal contraceptives (contraceptive pills, implants, transdermal patches, hormonal vaginal devices or injections with prolonged release).
    - Male partner who is sterile prior to the patient's entry into the study and is the sole sexual partner for that patient.
    - Complete abstinence from intercourse for two weeks before study entry and throughout the study period plus a period after the trial to account for elimination of the drug (minimum of eight days). Abstinence is only an acceptable contraception form, when it reflects the usual and preferred lifestyle of the patient.

Exclusion Criteria:

1. The patient has a current malignant diagnosis other than cervical cancer, with exception of non-melanoma skin cancers.
2. The patient is pregnant or lactating.
3. The patient has experienced emesis (i.e., vomiting and/or retching) or clinically significant nausea (defined as nausea graded as moderate or severe) in the 24 hours preceding the first dose of study medication.
4. The patient has a history active peptic ulcer disease, gastrointestinal obstruction, gastrointestinal carcinoma, increased intracranial pressure, hypercalcemia, or any uncontrolled medical condition (other than malignancy) which in the opinion of the Investigator may confound the results of the study, represent another potential etiology for emesis and nausea (other than CINV/RINV) or pose an unwarranted risk to the patient.
5. The patient has a known hypersensitivity or contraindication to palonosetron, another 5-HT3 receptor antagonist, dexamethasone, or netupitant.
6. The patient has previously received an NK1 receptor antagonist.
7. The patient has received an investigational drug in the previous 30 days or is scheduled to receive any investigational drug during the study period.
8. The patient has taken/received any medication of moderate or high emetogenic potential within the 48 hours prior to the first dose of study medications. Opiate drugs for cancer pain will be permitted if the patient has been on a stable dose and has not experienced emesis or clinically significant nausea from the narcotics in the 24 hours preceding the first dose of study medication.

9. The patient has taken/received any medication with known or potential antiemetic activity within the 24-hour period prior to receiving study drugs. This includes, but is not limited to:

    - 5-HT3 receptor antagonists (e.g., ondansetron, granisetron, dolasetron, tropisetron, ramosetron). Palonosetron is not permitted within 7 days prior to receiving study drugs.
    - Benzamide / benzamide derivatives (e.g., metoclopramide, alizapride).
    - Benzodiazepines (except if the patient is receiving such medication for sleep or anxiety and has been on a stable dose for at least seven days prior to the first dose of study medications).
    - Phenothiazines (e.g., prochlorperazine, promethazine, metopimazine, fluphenazine, perphenazine, thiethylperazine, chlorpromazine).
    - Butyrophenone (e.g., haloperidol, droperidol).
    - Corticosteroids (e.g., dexamethasone, methylprednisolone, prednisolone; with the exception of topical steroids for skin disorders, inhaled steroids for respiratory disorders).
    - Anticholinergics (e.g., scopolamine).
    - Antihistamines (e.g., cyclizine, hydroxyzine, diphenhydramine).
    - Domperidone.
    - Cannabinoids.

- Mirtazapine.
- Olanzapine.

10. The patient has taken/received strong or moderate inhibitors of CYP3A4 within seven (7) days prior to administration of study drugs (see Section 10.3.1., "Inhibitors of CYP3A4").
11. The patient has taken/received inducers of CYP3A4 within thirty (30) days prior to the administration of study drugs (see Section 10.3.2., "Inducers of CYP3A4").

Gender-based Eligibility

Yes

Gender Eligibility for Study

Patients with cervical cancer.

Ages Eligible for Study

18 Years and older (Adult, Older Adult)

Sexes Eligible for Study

Female

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 : N/A
Interventional Model : Single Group Assignment
Masking : None (Open Label)

Arms and Interventions

Participant Group/Arm	Intervention/Treatment
Other: Akynzeo plus dexamethasone Akynzeo (capsule 300mg/0.5mg) Day 1 plus dexamethasone 12 mg Day 1, 8 mg Day 2-3, and 4 mg Day 4 to be administered weekly for five weeks.	Drug: Akynzeo • Weekly administration of akynzeo for five weeks. Drug: Dexamethasone • Weekly administration of dexamethasone 12 mg Day 1, 8 mg Day 2-3, and 4 mg Day 4 for five weeks.

What is the study measuring?

Primary Outcome Measures

Outcome Measure	Measure Description	Time Frame
Safety of weekly administration of Akynzeo measured by incidence of treatment-emergent adverse events	Measurement of incidence of treatment-emergent adverse events.	Five weeks.
Efficacy of weekly administration of Akynzeo	Measurement of incidence of nausea and vomiting and use of rescue antiemetics.	Five weeks.

measured by incidence of nausea and vomiting and use of rescue antiemetics		

Secondary Outcome Measures

Outcome Measure	Measure Description	Time Frame
Complete response in terms of the proportion of subjects with complete response	To investigate Akynzeo and dexamethasone in terms of the proportion of subjects with complete response (defined as no vomits, no dry retches and no need for rescue medication) in the 5 days and the 35 days following initiation of fractionated radiotherapy and concomitant weekly cisplatin at a dose of ≥ 40 mg/m2.	Five days and five weeks.
No significant nausea in terms of the proportion of subjects with no significant nausea	To investigate Akynzeo and dexamethasone in terms of the proportion of subjects with no significant nausea (none or mild nausea) in the 5 days and the 35 days following initiation of fractionated radiotherapy and concomitant weekly cisplatin at a dose of ≥ 40 mg/m2.	Five days and five weeks.
No nausea in terms of the proportion of subjects with no nausea	To investigate Akynzeo and dexamethasone in terms of the proportion of subjects with no nausea in the 5 days and the 35 days following initiation of fractionated radiotherapy and concomitant weekly cisplatin at a dose of ≥ 40 mg/m2.	Five days and five weeks.

Time to first emetic episode	To investigate Akynzeo and dexamethasone in terms of time to first emetic episode.	Five weeks.

Collaborators and Investigators

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

Sponsor

Christina Ruhlmann

Collaborators

- Helsinn Healthcare SA

Investigators

- Principal Investigator: Christina H. Ruhlmann, MD, PhD, Odense University Hospital

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

2018-01-28

First Submitted that Met QC Criteria

2018-09-10

First Posted

2018-09-12

Study Record Updates

Last Update Submitted that met QC Criteria

2021-12-12

Last Update Posted

2021-12-14

Last Verified

2021-12

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
Dexamethasone

HHS Vulnerability Disclosure

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