



## Clinical trial results:

**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.**

### Summary

EudraCT number	2017-004031-37
Trial protocol	DK
Global end of trial date	21 February 2024

### Results information

Result version number	v1 (current)
This version publication date	19 June 2025
First version publication date	19 June 2025

### Trial information

#### Trial identification

Sponsor protocol code	17.14
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#### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03668639
WHO universal trial number (UTN)	-

Notes:

### Sponsors

Sponsor organisation name	Department of oncology, Odense University Hospital
Sponsor organisation address	Kløvervænget 10, indgang 112, 5 sal, Odense C, Denmark, 5000
Public contact	Christina H Bruvik Ruhlmann , Department of oncology, Odense University Hospital, 0045 65413349, christina.ruhlmann@rsyd.dk
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Notes:

### Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

## Results analysis stage

Analysis stage	Final
Date of interim/final analysis	02 February 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 February 2024
Global end of trial reached?	Yes
Global end of trial date	21 February 2024
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

1. The first co-primary objective is to explore the safety of an antiemetic regimen consisting of Akynzeo and dexamethasone during five weeks of fractionated (5 days a week) radiotherapy and concomitant weekly cisplatin at a dose of  $\geq 40$  mg/m<sup>2</sup>.
2. The second co-primary objective investigate Akynzeo and dexamethasone in terms of the proportion of subjects with no vomiting, i.e. sustained no emesis rate - during five weeks of fractionated radiotherapy and concomitant weekly cisplatin at a dose of  $\geq 40$  mg/m<sup>2</sup>.

Protection of trial subjects:

A signed, written informed consent was obtained prior to any study procedures or assessments being initiated. The study was approved by the Ethics Committee (Acadre number: 17/35157) and the Danish Medicines Agency (EudraCT number: 2017-004031-37). It was conducted in accordance with the principles of Good Clinical Practice, as well as all applicable patient privacy requirements in Denmark (protection by the "Act on Processing of Personal Data" and the "Health Care Act"), and the guiding principles of the Declaration of Helsinki. Data were entered into a logged, web-based REDCap database hosted by Open Patient data Explorative Network (OPEN), Odense, Denmark.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	08 October 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	Denmark: 73
Worldwide total number of subjects	73
EEA total number of subjects	73

Notes:

### Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0

Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	61
From 65 to 84 years	12
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

Patients were recruited from two departments of oncology in Denmark. From October 8, 2018, to January 2, 2024, 154 patients were screened, and 73 patients were eligible and received at least one dose of the study medication.

### Pre-assignment

Screening details:

Patients with a diagnosis of cervical cancer, naïve to chemo- and radiotherapy and who are scheduled to receive fractionated radiotherapy and concomitant weekly cisplatin at a dose of  $\geq 40$  mg/m<sup>2</sup> for at least five weeks, will be screened for eligibility and asked for study participation when the patients attend a planned visit.

### Period 1

Period 1 title	Recruitment (Overall period) (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

### Arms

Arm title	netupitant/palonosetron plus dexamethasone
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Arm description:

Intention to treat

Arm type	Experimental
Investigational medicinal product name	Dexamethason
Investigational medicinal product code	PR1
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Day 1, weeks 1-5

- At one hour prior to cisplatin  $\geq 40$  mg/m<sup>2</sup>, the subject will be administered Akynzeo (netupitant 300 mg / palonosetron 0.5 mg) orally and 30 minutes before cisplatin 3 tablets of dexamethasone 4 mg, 12 mg in total.

Days 2-3, weeks 1-5

- The subject will be instructed to take 2 tablets dexamethasone from the bottle to a total of 8 mg, in the morning on Days 2-3.

Day 4, weeks 1-5

- The subject will be instructed to take 1 tablet of dexamethasone 4 mg from the bottle in the morning on Day 4.

Investigational medicinal product name	Akynzeo
Investigational medicinal product code	PR2
Other name	Palonosetron Hydrochloride
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Day 1, weeks 1-5

- At one hour prior to cisplatin  $\geq 40$  mg/m<sup>2</sup>, the subject will be administered Akynzeo (netupitant 300 mg / palonosetron 0.5 mg) orally and 30 minutes before cisplatin 3 tablets of dexamethasone 4 mg, 12 mg in total.

Days 2-3, weeks 1-5

- The subject will be instructed to take 2 tablets dexamethasone from the bottle to a total of 8 mg, in the morning on Days 2-3.

Day 4, weeks 1-5

- The subject will be instructed to take 1 tablet of dexamethasone 4 mg from the bottle in the morning

on Day 4.

<b>Number of subjects in period 1</b>	netupitant/palonosetron plus dexamethasone
Started	73
Completed	37
Not completed	36
Adverse Events (not serious)	8
Adverse event (Serious, not fatal)	3
Consent withdrawn by subject	5
Physician decision	20

## Baseline characteristics

### Reporting groups

Reporting group title	Recruitment (Overall period)
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Reporting group description: -

Reporting group values	Recruitment (Overall period)	Total	
Number of subjects	73	73	
Age categorical Units: Subjects			

Age continuous Units: years median full range (min-max)	47 23 to 82	-	
Gender categorical Units: Subjects			
Female	73	73	

## End points

### End points reporting groups

Reporting group title	netupitant/palonosetron plus dexamethasone
Reporting group description:	
Intention to treat	

### Primary: Safety of the antiemetic regimen NEPA and DEX

End point title	Safety of the antiemetic regimen NEPA and DEX <sup>[1]</sup>
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End point description:

TRAEs occurring in  $\geq 2\%$  of patients are shown. No grade 4 or 5 TRAEs were observed. The column All grades represents the number of patients with grade 1, 2, and/or 3 TRAEs, counted once per patient regardless of the number of different grades experienced.

End point type	Primary
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End point timeframe:

The proportion of patients experiencing Treatment Related Adverse Events (TRAEs) measured from the first dose of study medication to the end of cycle 5.

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Safety were assessed using descriptive analyses on the intention-to-treat (ITT) population, consisting of all patients who received at least one dose of study medication and had at least one AE registration after treatment administration.

<b>End point values</b>	netupitant/palonosetron plus dexamethasone			
Subject group type	Reporting group			
Number of subjects analysed	73			
Units: Counts				
Grade 1	68			
Grade 2	44			
Grade 3	7			

### Statistical analyses

No statistical analyses for this end point

### Primary: proportion of subjects with no vomiting (i.e. sustained no emesis rate)

End point title	proportion of subjects with no vomiting (i.e. sustained no emesis rate) <sup>[2]</sup>
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End point description:

End point type	Primary
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End point timeframe:

five weeks after initiating chemo-radiotherapy

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The co-primary outcome regarding efficacy was described using a Kaplan–Meier plot showing the cumulative incidence of patients (ITT population) who sustained no emesis after initiating chemo-radiotherapy.

<b>End point values</b>	netupitant/palo nosetron plus dexamethason e			
Subject group type	Reporting group			
Number of subjects analysed	73			
Units: subjects with no vomiting				
no emesis episodes	63			

## Statistical analyses

No statistical analyses for this end point

## Secondary: Mean time to first emetic episode

End point title	Mean time to first emetic episode
End point description:	
End point type	Secondary
End point timeframe:	
Measured from first dose to study drug until last AE-evaluation (days)	

<b>End point values</b>	netupitant/palo nosetron plus dexamethason e			
Subject group type	Reporting group			
Number of subjects analysed	73			
Units: day				
arithmetic mean (standard deviation)	9 (± 9.3)			

## Statistical analyses

No statistical analyses for this end point

## Secondary: Complete responses

End point title	Complete responses
End point description:	
End point type	Secondary



End point timeframe:

Proportion of patients with Complete respons during Day 1-5 and Day 1-35.

<b>End point values</b>	netupitant/palo nosetron plus dexamethason e			
Subject group type	Reporting group			
Number of subjects analysed	73			
Units: per patient				
Day 1-5	56			
Day 1-35	38			

### Statistical analyses

No statistical analyses for this end point

### Secondary: No vomiting

End point title	No vomiting
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End point description:

End point type	Secondary
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End point timeframe:

No vomiting episodes experienced between first dose and day 35.

<b>End point values</b>	netupitant/palo nosetron plus dexamethason e			
Subject group type	Reporting group			
Number of subjects analysed	73			
Units: per patient				
Day 1-5	68			
Day 1-35	63			

### Statistical analyses

No statistical analyses for this end point

### Secondary: No significant nausea

End point title	No significant nausea
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End point description:

End point type	Secondary
End point timeframe:	
From first dose to day 35	

<b>End point values</b>	netupitant/palonosetron plus dexamethasone			
Subject group type	Reporting group			
Number of subjects analysed	73			
Units: per patient				
Day 1-5	63			
Day 1-35	45			

### Statistical analyses

No statistical analyses for this end point

### Secondary: No nausea

End point title	No nausea
End point description:	
End point type	Secondary
End point timeframe:	
From first dose to day 35.	

<b>End point values</b>	netupitant/palonosetron plus dexamethasone			
Subject group type	Reporting group			
Number of subjects analysed	73			
Units: per patient				
Day 1-5	36			
Day 1-35	13			

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

The follow-up period was defined as the period from the first study drug dose to the last AE evaluation.

Adverse event reporting additional description:

Investigators evaluated a list of 34 items representing potential adverse events (AEs) and their relation to the study drug at baseline (prior to study initiation). AEs were considered treatment-related adverse events (TRAEs) if the relationship to NEPA or NEPA/DEX was deemed as definitely, probably or possibly related, or if it was missing.

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	5.0
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### Reporting groups

Reporting group title	Intention to treat group
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Reporting group description: -

Serious adverse events	Intention to treat group		
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 73 (6.85%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
General disorders and administration site conditions			
Malaise			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders, other (Diverticulitis)			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			

Urticaria			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 2 %

<b>Non-serious adverse events</b>	Intention to treat group		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	69 / 73 (94.52%)		
Investigations			
Liver transaminases increased			
subjects affected / exposed	11 / 73 (15.07%)		
occurrences (all)	12		
Vascular disorders			
Flushing			
subjects affected / exposed	2 / 73 (2.74%)		
occurrences (all)	3		
Cardiac disorders			
Cardiac disorders, other			
subjects affected / exposed	2 / 73 (2.74%)		
occurrences (all)	2		
Nervous system disorders			
Dizziness			
subjects affected / exposed	22 / 73 (30.14%)		
occurrences (all)	24		
headache			
subjects affected / exposed	17 / 73 (23.29%)		
occurrences (all)	18		
Tremor			

subjects affected / exposed occurrences (all)	2 / 73 (2.74%) 2		
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all)	19 / 73 (26.03%) 23		
Eye disorders Eye disorders, other subjects affected / exposed occurrences (all)	3 / 73 (4.11%) 3		
Gastrointestinal disorders diarrhea subjects affected / exposed occurrences (all)  constipation subjects affected / exposed occurrences (all)  abdominal pain subjects affected / exposed occurrences (all)  dyspepsia subjects affected / exposed occurrences (all)  Nausea subjects affected / exposed occurrences (all)  Flatulence subjects affected / exposed occurrences (all)  Gastrointestinal disorders, Other subjects affected / exposed occurrences (all)	3 / 73 (4.11%) 3  49 / 73 (67.12%) 55  13 / 73 (17.81%) 14  28 / 73 (38.36%) 35  2 / 73 (2.74%) 2  10 / 73 (13.70%) 10  4 / 73 (5.48%) 4		
Respiratory, thoracic and mediastinal disorders Hiccups subjects affected / exposed occurrences (all)	10 / 73 (13.70%) 10		

Skin and subcutaneous tissue disorders Palmar-plantar erythrodysesthesia syndrome subjects affected / exposed occurrences (all)  Urticaria subjects affected / exposed occurrences (all)	4 / 73 (5.48%)  4   4 / 73 (5.48%)  4		
Psychiatric disorders insomnia subjects affected / exposed occurrences (all)	36 / 73 (49.32%)  46		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	7 / 73 (9.59%)  9		

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 May 2023	Amended in protocol version 3. Inclusion will end December 31, 2023, and End of Study (follow -up completed for all subjects) will be February 26, 2024. The number of enrolled patients at End of Study will constitute the ITT population. This is a descriptive and non-comparative study (no null hypothesis to test), and therefore the 61 eligible patients will be equal to the ITT population in order to reflect the real world setting where patients do not necessarily receive 5 cycles/weeks of chemotherapy and hence antiemetics/study drug. The ITT population will form the basis for all safety data analyses. Efficacy data analyses will be performed based on both the ITT population and on the primary per-protocol cohort (completing five cycles/weeks of chemotherapy/antiemetics/study drug).

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
31 March 2020	Covid-19	20 April 2020

Notes:

### Limitations and caveats

None reported

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### Online references

<http://www.ncbi.nlm.nih.gov/pubmed/40437122>