Clinical trial results:
GAND-emesis: A multinational, randomized, double-blind, placebo-controlled, parallel-group study to investigate the efficacy and tolerability of palonosetron and dexamethasone plus the neurokinin1-receptor antagonist, fosaprepitant dimeglumine or placebo in patients receiving radiotherapy and concomitant weekly cisplatin.

Summary

EudraCT number	2009-014691-21
Trial protocol	DK DE
Global end of trial date	24 April 2015

Results information

Result version number	v1 (current)
This version publication date	09 September 2021
First version publication date	09 September 2021

Trial information

Trial identification

Sponsor protocol code	GAND-emesis

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01074697
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Odense University Hospital
Sponsor organisation address	J. B. Winsløws vej 2, entrance 140, basement, Odense C, Denmark, 5000
Public contact	Ida Coordt Elle, Odense University Hospital, 45 29335922, ida.coordt.elle@rsyd.dk
Scientific contact	Christina Ruhlmann, Odense University Hospital, 45 22314446, christina.ruhlmann@rsyd.dk

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	27 November 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	24 April 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to compare an antiemetic regimen consisting of fosaprepitant dimeglumine (Ivemend®), palonosetron (Aloxi®), and dexamethasone (active arm) and a regimen consisting of palonosetron, dexamethasone, and placebo (control arm) with respect to efficacy; the proportion of subjects with no vomiting, i.e. sustained no emesis rate - during five weeks of fractionated (5 days a week) radiotherapy and concomitant weekly cisplatin at a dose of ≥ 40 mg/m2.

Protection of trial subjects:

Only PS 0-2 included.
Patients were
excluded if they had other current malignant diagnoses
apart from non-melanoma skin cancers, total neutrophils
less than 1·5 × 10 cells per L, platelets less than
100 × 10 cells per L, bilirubin greater than 1·5 times
the upper limit of normal (ULN), and aspartate
aminotransferase or alanine aminotransferase greater
than 2·5 times the ULN.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 April 2010
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Norway: 8
Country: Number of subjects enrolled	Denmark: 205
Country: Number of subjects enrolled	Germany: 16
Country: Number of subjects enrolled	Australia: 5
Worldwide total number of subjects	234
EEA total number of subjects	229

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)	196
From 65 to 84 years	38
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Between June 15, 2010, and March 8, 2015, 246 patients from four countries consented to the study and were
randomly assigned. Of these, 234 patients were eligible, having received study medication (118 received fosaprepitant,
116 received placebo).

Pre-assignment

Screening details:

Eligible patients
were 18 years or older, had histologically confirmed
cervical cancer, were scheduled to receive fractionated
radiotherapy (1.8–2.0 Gy per fraction, five fractions per
week to the pelvis) and concomitant weekly cisplatin
40 mg/m² for at least 5 weeks.

Period 1

Period 1 title	Trial period (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Fosaprepitant

Arm description:

Patients were randomly assigned to receive single
doses of fosaprepitant 150 mg intravenously in combination with palonosetron 0·25 mg intravenously and dexamethasone 16 mg orally before cisplatin administration.

Arm type	Experimental
Investigational medicinal product name	Fosaprepitant
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

150mg i.v.

Investigational medicinal product name	Palonosetron
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

0.25mg i.v.

Investigational medicinal product name	Dexamethasone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

16 mg

Arm title	Placebo

Arm description:

Patients were randomly assigned to receive single doses placebo (saline) in combination with palonosetron 0·25 mg intravenously and dexamethasone 16 mg orally before cisplatin administration.

Arm type	Placebo
Investigational medicinal product name	Placebo/saline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

NA

Investigational medicinal product name	Palonosetron
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

0.25mg i.v.

Investigational medicinal product name	Dexamethasone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

16 mg

Number of subjects in period 1	Fosaprepitant	Placebo
Started	118	116
Completed	118	116

Baseline characteristics

Reporting groups	
Reporting group title	Fosaprepitant
Reporting group description:	
Patients were randomly assigned to receive single doses of fosaprepitant 150 mg intravenously in combination with palonosetron 0·25 mg intravenously and dexamethasone 16 mg orally before cisplatin administration.	
Reporting group title	Placebo
Reporting group description:	
Patients were randomly assigned to receive single doses placebo (saline) in combination with palonosetron 0·25 mg intravenously and dexamethasone 16 mg orally before cisplatin administration.	

Reporting group values	Fosaprepitant	Placebo	Total
Number of subjects	118	116	234
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	99	97	196
From 65-84 years	19	19	38
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	118	116	234
Male	0	0	0

Subject analysis sets	
Subject analysis set title	Fosaprepitant patients
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Patients allocated to Fosaprepitant	
Subject analysis set title	Placebo patients
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Patients allocated to placebo	

Reporting group values	Fosaprepitant patients	Placebo patients	
Number of subjects	118	116	
Age categorical Units: Subjects			
In utero	0	0	

Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	99	97	
From 65-84 years	19	19	
85 years and over	0	0	
Gender categorical			
Units: Subjects			
Female	118	116	
Male	0	0	

End points

End points reporting groups

Reporting group title	Fosaprepitant
Reporting group description:	
Patients were randomly assigned to receive single doses of fosaprepitant 150 mg intravenously in combination with palonosetron 0·25 mg intravenously and dexamethasone 16 mg orally before cisplatin administration.	
Reporting group title	Placebo
Reporting group description:	
Patients were randomly assigned to receive single doses placebo (saline) in combination with palonosetron 0·25 mg intravenously and dexamethasone 16 mg orally before cisplatin administration.	
Subject analysis set title	Fosaprepitant patients
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Patients allocated to Fosaprepitant	
Subject analysis set title	Placebo patients
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Patients allocated to placebo	

Primary: Proportion of patients with sustained no emesis

End point title	Proportion of patients with sustained no emesis
End point description:	
The proportion of patients with sustained no emesis at 5 weeks (competing risk analysis).	
End point type	Primary
End point timeframe:	
5 weeks	

End point values	Fosaprepitant	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	118	116		
Units: patients				
number (confidence interval 95%)	65.7 (42.2 to 89.2)	48.7 (25.2 to 72.2)		

Statistical analyses

Statistical analysis title	Fine and Gray’s proportional subhazards model
Statistical analysis description:	
The cumulative incidence of emesis was analysed using Fine and Gray’s proportional subhazards model (competing risk regression).Competing risk (other than patients with emesis, patients completing all five cycles without emesis, or censored events not due to emesis and not competing) was categorised as discontinuation for reasons of study treatment or for any reason.	
Comparison groups	Placebo v Fosaprepitant

Number of subjects included in analysis	234
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	two-sided Pearson χ^2 test with continuit
Parameter estimate	cumulative incidence
Point estimate	60
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	50
upper limit	70
Variability estimate	Standard deviation

Adverse events

Adverse events information

Timeframe for reporting adverse events:

5 weeks

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	Fosaprepitant

Reporting group description:

Patients were randomly assigned to receive single doses of fosaprepitant 150 mg intravenously in combination with palonosetron 0·25 mg intravenously and dexamethasone 16 mg orally before cisplatin administration.

Reporting group title	Placebo

Reporting group description:

Patients were randomly assigned to receive single doses placebo (saline) in combination with palonosetron 0·25 mg intravenously and dexamethasone 16 mg orally before cisplatin administration.

Serious adverse events	Fosaprepitant	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 118 (0.85%)	0 / 116 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Investigations			
Neutrophil count decreased			
subjects affected / exposed	1 / 118 (0.85%)	0 / 116 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Fosaprepitant	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	118 / 118 (100.00%)	116 / 116 (100.00%)	
Investigations			
Alanine aminotransferase increased			

subjects affected / exposed	3 / 118 (2.54%)	0 / 116 (0.00%)	
occurrences (all)	3	0	
Fever			
subjects affected / exposed	5 / 118 (4.24%)	4 / 116 (3.45%)	
occurrences (all)	5	4	
Neutrophil count decreased			
subjects affected / exposed	6 / 118 (5.08%)	4 / 116 (3.45%)	
occurrences (all)	6	4	
Vascular disorders			
Thromboembolic events			
subjects affected / exposed	0 / 118 (0.00%)	2 / 116 (1.72%)	
occurrences (all)	0	2	
Nervous system disorders			
Dizziness			
subjects affected / exposed	57 / 118 (48.31%)	51 / 116 (43.97%)	
occurrences (all)	57	51	
Nervous system symptoms			
subjects affected / exposed	15 / 118 (12.71%)	19 / 116 (16.38%)	
occurrences (all)	15	19	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	102 / 118 (86.44%)	104 / 116 (89.66%)	
occurrences (all)	102	104	
Headache			
subjects affected / exposed	55 / 118 (46.61%)	49 / 116 (42.24%)	
occurrences (all)	55	49	
Pain			
subjects affected / exposed	6 / 118 (5.08%)	4 / 116 (3.45%)	
occurrences (all)	6	4	
Ear and labyrinth disorders			
Hearing impaired			
subjects affected / exposed	12 / 118 (10.17%)	14 / 116 (12.07%)	
occurrences (all)	12	14	
Tinnitus			
subjects affected / exposed	24 / 118 (20.34%)	16 / 116 (13.79%)	
occurrences (all)	24	16	

Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	14 / 118 (11.86%)	18 / 116 (15.52%)	
occurrences (all)	14	18	
Appetite disorder			
subjects affected / exposed	56 / 118 (47.46%)	59 / 116 (50.86%)	
occurrences (all)	56	59	
Constipation			
subjects affected / exposed	51 / 118 (43.22%)	66 / 116 (56.90%)	
occurrences (all)	51	66	
Diarrhoea			
subjects affected / exposed	77 / 118 (65.25%)	72 / 116 (62.07%)	
occurrences (all)	77	72	
Gastrointestinal tract symptoms			
subjects affected / exposed	7 / 118 (5.93%)	12 / 116 (10.34%)	
occurrences (all)	7	12	
Metabolic alterations			
subjects affected / exposed	11 / 118 (9.32%)	5 / 116 (4.31%)	
occurrences (all)	11	5	
Infections and infestations			
Infections			
subjects affected / exposed	13 / 118 (11.02%)	9 / 116 (7.76%)	
occurrences (all)	13	9	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/26952945