Clinical trial results:
A Phase III, Randomized, Double-Blind, Active Comparator-Controlled Parallel-Group Study, Conducted Under In-House Blinding Conditions, to Examine the Efficacy and Safety of a Single 150 mg Dose of Intravenous Fosaprepitant Dimeglumine for the Prevention of Chemotherapy-Induced Nausea and Vomiting (CINV) Associated with Moderately Emetogenic Chemotherapy

Due to the EudraCT – Results system being out of service between 31 July 2015 and 12 January 2016, these results have been published in compliance with revised timelines.

Summary

EudraCT number	2012-001718-41
Trial protocol	FI NL ES CZ SE HU IT PT LV PL BG GR NO HR
Global end of trial date	03 November 2014

Results information

Result version number	v1 (current)
This version publication date	06 February 2016
First version publication date	06 February 2016

Trial information

Trial identification

Sponsor protocol code	MK-0517-031

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01594749
WHO universal trial number (UTN)	-
Other trial identifiers	Merck Protocol Number: MK-0517-031

Notes:

Sponsors

Sponsor organisation name	Merck Sharp & Dohme Corp.
Sponsor organisation address	2000 Galloping Hill Road, Kenilworth, NJ, United States, 07033
Public contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com

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	03 November 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 November 2014
Global end of trial reached?	Yes
Global end of trial date	03 November 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This study aims to demonstrate that, when given concomitantly with a 5-hydroxytryptamine 3 (5-HT3) antagonist and a corticosteroid, a single 150 mg intravenous (IV) dose of fosaprepitant given on Day 1 is superior to the control regimen of 5-HT3 antagonist and corticosteroid only, in preventing chemotherapy-induced nausea and vomiting (CINV) associated with moderately emetogenic chemotherapy (MEC).

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

The following additional measure defined for this individual study was in place for the protection of trial subjects: Rescue medication was allowed for established cases of nausea or vomiting.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 September 2012
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	Argentina: 48
Country: Number of subjects enrolled	Bulgaria: 9
Country: Number of subjects enrolled	Canada: 9
Country: Number of subjects enrolled	Chile: 2
Country: Number of subjects enrolled	Colombia: 21
Country: Number of subjects enrolled	Croatia: 13
Country: Number of subjects enrolled	Czech Republic: 42
Country: Number of subjects enrolled	Finland: 10
Country: Number of subjects enrolled	Germany: 46
Country: Number of subjects enrolled	Greece: 60
Country: Number of subjects enrolled	Hungary: 70
Country: Number of subjects enrolled	Italy: 36
Country: Number of subjects enrolled	Latvia: 25

Country: Number of subjects enrolled	Mexico: 9
Country: Number of subjects enrolled	Netherlands: 6
Country: Number of subjects enrolled	Norway: 12
Country: Number of subjects enrolled	Peru: 55
Country: Number of subjects enrolled	Philippines: 26
Country: Number of subjects enrolled	Poland: 36
Country: Number of subjects enrolled	Portugal: 16
Country: Number of subjects enrolled	Puerto Rico: 16
Country: Number of subjects enrolled	Romania: 51
Country: Number of subjects enrolled	Russian Federation: 52
Country: Number of subjects enrolled	South Africa: 19
Country: Number of subjects enrolled	Spain: 64
Country: Number of subjects enrolled	Sweden: 31
Country: Number of subjects enrolled	Thailand: 3
Country: Number of subjects enrolled	Turkey: 32
Country: Number of subjects enrolled	Ukraine: 14
Country: Number of subjects enrolled	United States: 182
Worldwide total number of subjects	1015
EEA total number of subjects	527

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)	634
From 65 to 84 years	376
85 years and over	5

Subject disposition

Recruitment

Recruitment details:

Males and females who were ≥18 years old and were scheduled to receive MEC were enrolled into this study. Additional inclusion and exclusion criteria applied.

Pre-assignment

Screening details:

A total of 14 participants were randomized but did not receive study drug. The source documents for one additional participant were lost.

One participant was randomized to receive Control Regimen, but actually received Fosaprepitant Regimen.

Disposition is by actual treatment group and not by randomized treatment group.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Data analyst, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Fosaprepitant Regimen

Arm description:

On Day 1, participants received fosaprepitant, 150 mg intravenous (IV) infusion, ~30 minutes prior to chemotherapy PLUS dexamethasone 12 mg, orally (PO) ~30 minutes prior to chemotherapy PLUS ondansetron 16 mg total dose: 8 mg PO ~30-60 minutes prior to chemotherapy, followed by 8 mg PO, 8 hours after first dose PLUS dexamethasone placebo, PO ~30 minutes prior to chemotherapy. On Days 2 and 3, participants received ondansetron placebo, PO every 12 hours. Rescue Therapy: For established cases of nausea or vomiting, medications may have been prescribed from these permitted choices: 5-hydroxytryptamine 3 (5-HT3) antagonists (granisetron, dolasetron, tropisetron or ondansetron); phenothiazines (e.g. prochlorperazine, fluphenazine, perphenazine, thiethylperazine, or chlorpromazine); butyrophenones (e.g. haloperidol or droperidol); benzamides (e.g. metoclopramide or alizapride); benzodiazepines; corticosteroids; domperidone.

Arm type	Experimental
Investigational medicinal product name	fosaprepitant
Investigational medicinal product code	MK-0517
Other name	EMEND®
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

fosaprepitant 150 mg IV infusion

Investigational medicinal product name	ondansetron
Investigational medicinal product code	
Other name	ZOFRAN®
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Day 1: ondansetron 8 mg PO + 8 mg PO 8 hours later; Days 2-3: placebo to ondansetron PO every 12 hours

Investigational medicinal product name	dexamethasone
Investigational medicinal product code	
Other name	DECADRON®

Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Day 1: dexamethasone 12 mg PO (3 capsules of dexamethasone 4 mg + 2 capsules of placebo)

Arm title	Control Regimen

Arm description:

On Day 1, participants received fosaprepitant placebo, 150 mL IV infusion, ~30 minutes prior to chemotherapy PLUS dexamethasone 20 mg, PO ~30 minutes prior to chemotherapy PLUS ondansetron 16 mg total dose: 8 mg PO ~30-60 minutes prior to chemotherapy; followed by 8 mg PO, 8 hours after the first dose. On Days 2-3, participants received ondansetron 8 mg, PO every 12 hours. Rescue Therapy: For established cases of nausea or vomiting, medications may have been prescribed from these permitted choices: 5-HT3 antagonists (granisetron, dolasetron, tropisetron or ondansetron); phenothiazines (e.g. prochlorperazine, fluphenazine, perphenazine, thiethylperazine, or chlorpromazine); butyrophenones (e.g. haloperidol or droperidol); benzamides (e.g. metoclopramide or alizapride); benzodiazepines; corticosteroids; domperidone.

Arm type	Active comparator
Investigational medicinal product name	placebo for fosaprepitant
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

150 mL IV infusion

Investigational medicinal product name	ondansetron
Investigational medicinal product code	
Other name	ZOFRAN®
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Day 1: ondansetron 8 mg PO and 8 mg PO 8 hrs later; Days 2-3: ondansetron 8 mg PO every 12 hours

Investigational medicinal product name	dexamethasone
Investigational medicinal product code	
Other name	DECADRON®
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Day 1: dexamethasone 20 mg PO (5 capsules of dexamethasone 4 mg)

Number of subjects in period 1	Fosaprepitant Regimen	Control Regimen
Started	508	507
Treated	504	497
Completed	487	489
Not completed	21	18
Adverse event, serious fatal	9	3
Consent withdrawn by subject	2	2
Physician decision	1	1
Adverse event, non-fatal	2	1

Lost to follow-up	1	-
Non-compliance with Protocol	-	1
Protocol deviation	2	-
Not treated	4	10

Baseline characteristics

Reporting groups	
Reporting group title	Fosaprepitant Regimen

Reporting group description:

On Day 1, participants received fosaprepitant, 150 mg intravenous (IV) infusion, ~30 minutes prior to chemotherapy PLUS dexamethasone 12 mg, orally (PO) ~30 minutes prior to chemotherapy PLUS ondansetron 16 mg total dose: 8 mg PO ~30-60 minutes prior to chemotherapy, followed by 8 mg PO, 8 hours after first dose PLUS dexamethasone placebo, PO ~30 minutes prior to chemotherapy. On Days 2 and 3, participants received ondansetron placebo, PO every 12 hours. Rescue Therapy: For established cases of nausea or vomiting, medications may have been prescribed from these permitted choices: 5-hydroxytryptamine 3 (5-HT3) antagonists (granisetron, dolasetron, tropisetron or ondansetron); phenothiazines (e.g. prochlorperazine, fluphenazine, perphenazine, thiethylperazine, or chlorpromazine); butyrophenones (e.g. haloperidol or droperidol); benzamides (e.g. metoclopramide or alizapride); benzodiazepines; corticosteroids; domperidone.

Reporting group title	Control Regimen

Reporting group description:

On Day 1, participants received fosaprepitant placebo, 150 mL IV infusion, ~30 minutes prior to chemotherapy PLUS dexamethasone 20 mg, PO ~30 minutes prior to chemotherapy PLUS ondansetron 16 mg total dose: 8 mg PO ~30-60 minutes prior to chemotherapy; followed by 8 mg PO, 8 hours after the first dose. On Days 2-3, participants received ondansetron 8 mg, PO every 12 hours. Rescue Therapy: For established cases of nausea or vomiting, medications may have been prescribed from these permitted choices: 5-HT3 antagonists (granisetron, dolasetron, tropisetron or ondansetron); phenothiazines (e.g. prochlorperazine, fluphenazine, perphenazine, thiethylperazine, or chlorpromazine); butyrophenones (e.g. haloperidol or droperidol); benzamides (e.g. metoclopramide or alizapride); benzodiazepines; corticosteroids; domperidone.

Reporting group values	Fosaprepitant Regimen	Control Regimen	Total
Number of subjects	508	507	1015
Age categorical Units: Subjects			
Adults (18-64 years)	311	323	634
From 65-84 years	193	183	376
85 years and over	4	1	5
Age Continuous | Units: Years			
arithmetic mean	60.1	59.2	
standard deviation	± 11.8	± 12.3	-
Gender, Male/Female Units: Participants			
Female	299	301	600
Male	209	206	415

End points

End points reporting groups

Reporting group title	Fosaprepitant Regimen

Reporting group description:

On Day 1, participants received fosaprepitant, 150 mg intravenous (IV) infusion, ~30 minutes prior to chemotherapy PLUS dexamethasone 12 mg, orally (PO) ~30 minutes prior to chemotherapy PLUS ondansetron 16 mg total dose: 8 mg PO ~30-60 minutes prior to chemotherapy, followed by 8 mg PO, 8 hours after first dose PLUS dexamethasone placebo, PO ~30 minutes prior to chemotherapy. On Days 2 and 3, participants received ondansetron placebo, PO every 12 hours. Rescue Therapy: For established cases of nausea or vomiting, medications may have been prescribed from these permitted choices: 5-hydroxytryptamine 3 (5-HT3) antagonists (granisetron, dolasetron, tropisetron or ondansetron); phenothiazines (e.g. prochlorperazine, fluphenazine, perphenazine, thiethylperazine, or chlorpromazine); butyrophenones (e.g. haloperidol or droperidol); benzamides (e.g. metoclopramide or alizapride); benzodiazepines; corticosteroids; domperidone.

Reporting group title	Control Regimen

Reporting group description:

On Day 1, participants received fosaprepitant placebo, 150 mL IV infusion, ~30 minutes prior to chemotherapy PLUS dexamethasone 20 mg, PO ~30 minutes prior to chemotherapy PLUS ondansetron 16 mg total dose: 8 mg PO ~30-60 minutes prior to chemotherapy; followed by 8 mg PO, 8 hours after the first dose. On Days 2-3, participants received ondansetron 8 mg, PO every 12 hours. Rescue Therapy: For established cases of nausea or vomiting, medications may have been prescribed from these permitted choices: 5-HT3 antagonists (granisetron, dolasetron, tropisetron or ondansetron); phenothiazines (e.g. prochlorperazine, fluphenazine, perphenazine, thiethylperazine, or chlorpromazine); butyrophenones (e.g. haloperidol or droperidol); benzamides (e.g. metoclopramide or alizapride); benzodiazepines; corticosteroids; domperidone.

Subject analysis set title	Fosaprepitant Regimen - ITT Set
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The Intent-to-Treat (ITT) efficacy population consisted of all participants in the group to which they were randomized and who received at least one dose of study drug. One participant with missing source documents was excluded from the efficacy analyses.

Subject analysis set title	Fosaprepitant Regimen - Safety Set
Subject analysis set type	Safety analysis

Subject analysis set description:

The safety population consisted of All Participants as Treated (APaT) which includes all randomized participants who received at least one dose of study medication.

Subject analysis set title	Control Regimen - ITT Set
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The ITT efficacy population consisted of all participants in the group to which they were randomized and who received at least one dose of study drug.

Subject analysis set title	Control Regimen - Safety Set
Subject analysis set type	Safety analysis

Subject analysis set description:

The safety population consisted of APaT which includes all randomized participants who received at least one dose of study medication.

Primary: Percentage of participants with Complete Response from 25 to 120 hours after initiation of moderately emetogenic chemotherapy (MEC)

End point title	Percentage of participants with Complete Response from 25 to 120 hours after initiation of moderately emetogenic chemotherapy (MEC)

End point description:

A Complete Response was defined as no vomiting and no use of rescue medication.

End point type	Primary

End point timeframe:

25 to 120 hours after initiation of MEC

End point values	Fosaprepitant Regimen - ITT Set	Control Regimen - ITT Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	502	498		
Units: Percentage of Participants				
number (not applicable)	78.9	68.5		

Statistical analyses

Statistical analysis title	Percentage difference: Fosaprepitant vs. Control
Comparison groups	Fosaprepitant Regimen - ITT Set v Control Regimen - ITT Set
Number of subjects included in analysis	1000
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [1]
Method	Cochran-Mantel-Haenszel

Notes:

[1] - P-value based on Cochran-Mantel-Haenszel (CMH) method with stratification of gender

Primary: Percentage of participants with infusion-site thrombophlebitis

End point title	Percentage of participants with infusion-site thrombophlebitis

End point description:

The percentages of participants with infusion-site thrombophlebitis are presented. Thrombophlebitis was defined as a condition affecting a superficial vein used for an IV infusion, associated with red color, hardness upon palpation, and the presence of a tender cord and possible fever.

End point type	Primary

End point timeframe:

Day 1 through Day 17, inclusive

End point values	Fosaprepitant Regimen - Safety Set	Control Regimen - Safety Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	504	497		
Units: Percentage of Participants				
number (not applicable)	0.6	0		

Statistical analyses

Statistical analysis title	Percentage Difference: Fosaprepitant vs. Control
Comparison groups	Fosaprepitant Regimen - Safety Set v Control Regimen - Safety Set
Number of subjects included in analysis	1001
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.085 [2]
Method	Miettinen & Nurminen method
Parameter estimate	Difference in percentage vs. Control
Point estimate	0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	1.7

Notes:

[2] - P-value based on Miettinen & Nurminen method

Primary: Percentage of participants with severe infusion-site reactions

End point title	Percentage of participants with severe infusion-site reactions[3]

End point description:

The percentages of participants with severe infusion-site reactions, including severe site pain, or severe site redness (erythema) or severe site hardness (induration) are presented.

End point type	Primary

End point timeframe:

Day 1 through Day 17, inclusive

Notes:

[3] - 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: No participants experienced a severe infusion-site reaction, so no statistical analyses were performed.

End point values	Fosaprepitant Regimen - Safety Set	Control Regimen - Safety Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	504	497		
Units: Percentage of Participants				
number (not applicable)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with Complete Response from 0 to 120 hours after initiation of MEC

End point title	Percentage of participants with Complete Response from 0 to 120 hours after initiation of MEC

End point description:

A Complete Response was defined as no vomiting and no use of rescue medication.

End point type	Secondary

End point timeframe:

0 to 120 hours after initiation of MEC

End point values	Fosaprepitant Regimen - ITT Set	Control Regimen - ITT Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	502	498		
Units: Percentage of Participants				
number (not applicable)	77.1	66.9		

Statistical analyses

Statistical analysis title	Percentage Difference: Fosaprepitant vs. Control
Comparison groups	Fosaprepitant Regimen - ITT Set v Control Regimen - ITT Set
Number of subjects included in analysis	1000
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [4]
Method	Cochran-Mantel-Haenszel

Notes:

[4] - P-value based on CMH method with stratification of gender

Secondary: Percentage of participants with Complete Response from 0 to 24 hours after initiation of MEC

End point title	Percentage of participants with Complete Response from 0 to 24 hours after initiation of MEC

End point description:

A Complete Response was defined as no vomiting and no use of rescue medication.

End point type	Secondary

End point timeframe:

0 to 24 hours after initiation of MEC

End point values	Fosaprepitant Regimen - ITT Set	Control Regimen - ITT Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	502	498		
Units: Percentage of Participants				
number (not applicable)	93.2	91		

Statistical analyses

Statistical analysis title	Percentage difference: Fosaprepitant vs. Control
Comparison groups	Fosaprepitant Regimen - ITT Set v Control Regimen - ITT Set
Number of subjects included in analysis	1000
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.184 [5]
Method	Cochran-Mantel-Haenszel

Notes:

[5] - P-value based on CMH method with stratification of gender

Secondary: Percentage of participants with No Vomiting from 0 to 120 hours after initiation of MEC

End point title	Percentage of participants with No Vomiting from 0 to 120 hours after initiation of MEC

End point description:

No Vomiting was defined as no emetic (vomiting) episodes, including no vomiting and no retching or dry heaves (attempts to vomit that are not productive of stomach contents), regardless of use of rescue medication.

End point type	Secondary

End point timeframe:

0 to 120 hours after initiation of MEC

End point values	Fosaprepitant Regimen - ITT Set	Control Regimen - ITT Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	502	498		
Units: Percentage of participants				
number (not applicable)	82.7	72.9		

Statistical analyses

Statistical analysis title	Percentage difference: Fosaprepitant vs. Control
Comparison groups	Fosaprepitant Regimen - ITT Set v Control Regimen - ITT Set
Number of subjects included in analysis	1000
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [6]
Method	Cochran-Mantel-Haenszel

Notes:

[6] - P-value based on CMH method with stratification of gender

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day 1 up to Day 17, inclusive (Up to 2 weeks after last dose of study drug)

Adverse event reporting additional description:

The Safety population consisted of all participants who received study drug. Participants are included in the treatment group based on the study drug they actually received.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	Control Regimen

Reporting group description:

On Day 1, participants received fosaprepitant placebo, 150 mL IV infusion, ~30 minutes prior to chemotherapy PLUS dexamethasone 20 mg, PO ~30 minutes prior to chemotherapy PLUS ondansetron 16 mg total dose: 8 mg PO ~30-60 minutes prior to chemotherapy; followed by 8 mg PO, 8 hours after the first dose. On Days 2-3, participants received ondansetron 8 mg, PO every 12 hours. Rescue Therapy: For established cases of nausea or vomiting, medications may have been prescribed from these permitted choices: 5-HT3 antagonists (granisetron, dolasetron, tropisetron or ondansetron); phenothiazines (e.g. prochlorperazine, fluphenazine, perphenazine, thiethylperazine, or chlorpromazine); butyrophenones (e.g. haloperidol or droperidol); benzamides (e.g. metoclopramide or alizapride); benzodiazepines; corticosteroids; domperidone.

Reporting group title	Fosaprepitant Regimen

Reporting group description:

On Day 1, participants received fosaprepitant, 150 mg IV infusion, ~30 minutes prior to chemotherapy PLUS dexamethasone 12 mg, PO ~30 minutes prior to chemotherapy PLUS ondansetron 16 mg total dose: 8 mg PO ~30-60 minutes prior to chemotherapy, followed by 8 mg PO, 8 hours after first dose PLUS dexamethasone placebo, PO ~30 minutes prior to chemotherapy. On Days 2 and 3, participants received ondansetron placebo, PO every 12 hours. Rescue Therapy: For established cases of nausea or vomiting, medications may have been prescribed from these permitted choices: 5-HT3 antagonists (granisetron, dolasetron, tropisetron or ondansetron); phenothiazines (e.g. prochlorperazine, fluphenazine, perphenazine, thiethylperazine, or chlorpromazine); butyrophenones (e.g. haloperidol or droperidol); benzamides (e.g. metoclopramide or alizapride); benzodiazepines; corticosteroids; domperidone.

Serious adverse events	Control Regimen	Fosaprepitant Regimen	
Total subjects affected by serious adverse events			
subjects affected / exposed	35 / 497 (7.04%)	39 / 504 (7.74%)	
number of deaths (all causes)	2	8	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lung neoplasm malignant			
subjects affected / exposed	0 / 497 (0.00%)	1 / 504 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Metastases to bone			

subjects affected / exposed	1 / 497 (0.20%)	0 / 504 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-small cell lung cancer			
subjects affected / exposed	0 / 497 (0.00%)	1 / 504 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Vascular disorders			
Thrombosis			
subjects affected / exposed	0 / 497 (0.00%)	1 / 504 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	2 / 497 (0.40%)	1 / 504 (0.20%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death			
subjects affected / exposed	0 / 497 (0.00%)	2 / 504 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Disease progression			
subjects affected / exposed	1 / 497 (0.20%)	0 / 504 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			
subjects affected / exposed	1 / 497 (0.20%)	1 / 504 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	1 / 497 (0.20%)	2 / 504 (0.40%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 497 (0.00%)	1 / 504 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypersensitivity			
subjects affected / exposed	1 / 497 (0.20%)	1 / 504 (0.20%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Haemoptysis			
subjects affected / exposed	1 / 497 (0.20%)	1 / 504 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	0 / 497 (0.00%)	1 / 504 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	1 / 497 (0.20%)	0 / 504 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 497 (0.00%)	2 / 504 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Psychiatric disorders			
Mental status changes			
subjects affected / exposed	0 / 497 (0.00%)	1 / 504 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood glucose increased			

subjects affected / exposed	0 / 497 (0.00%)	1 / 504 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoglobin decreased			
subjects affected / exposed	1 / 497 (0.20%)	0 / 504 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Fracture			
subjects affected / exposed	0 / 497 (0.00%)	1 / 504 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxicity to various agents			
subjects affected / exposed	0 / 497 (0.00%)	1 / 504 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 497 (0.20%)	0 / 504 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	1 / 497 (0.20%)	1 / 504 (0.20%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	0 / 497 (0.00%)	1 / 504 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiac disorder			
subjects affected / exposed	1 / 497 (0.20%)	0 / 504 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	

Supraventricular tachycardia			
subjects affected / exposed	1 / 497 (0.20%)	0 / 504 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebral infarction			
subjects affected / exposed	1 / 497 (0.20%)	0 / 504 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epilepsy			
subjects affected / exposed	0 / 497 (0.00%)	1 / 504 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	0 / 497 (0.00%)	1 / 504 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	1 / 497 (0.20%)	0 / 504 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Abdominal lymphadenopathy			
subjects affected / exposed	0 / 497 (0.00%)	1 / 504 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia			
subjects affected / exposed	1 / 497 (0.20%)	0 / 504 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	5 / 497 (1.01%)	8 / 504 (1.59%)	
occurrences causally related to treatment / all	0 / 5	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	

Leukocytosis			
subjects affected / exposed	0 / 497 (0.00%)	1 / 504 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukopenia			
subjects affected / exposed	1 / 497 (0.20%)	0 / 504 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	4 / 497 (0.80%)	3 / 504 (0.60%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 497 (0.00%)	1 / 504 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	0 / 497 (0.00%)	1 / 504 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	1 / 497 (0.20%)	0 / 504 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	1 / 497 (0.20%)	1 / 504 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorder			
subjects affected / exposed	0 / 497 (0.00%)	1 / 504 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrooesophageal reflux disease			

subjects affected / exposed	0 / 497 (0.00%)	1 / 504 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	1 / 497 (0.20%)	0 / 504 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenic colitis			
subjects affected / exposed	0 / 497 (0.00%)	1 / 504 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pancreatitis			
subjects affected / exposed	1 / 497 (0.20%)	0 / 504 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	1 / 497 (0.20%)	1 / 504 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hepatorenal failure			
subjects affected / exposed	0 / 497 (0.00%)	1 / 504 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	2 / 497 (0.40%)	1 / 504 (0.20%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myalgia			
subjects affected / exposed	0 / 497 (0.00%)	1 / 504 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Infections and infestations			
Diverticulitis			
subjects affected / exposed	2 / 497 (0.40%)	0 / 504 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	1 / 497 (0.20%)	0 / 504 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	1 / 497 (0.20%)	0 / 504 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oral candidiasis			
subjects affected / exposed	0 / 497 (0.00%)	1 / 504 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	3 / 497 (0.60%)	1 / 504 (0.20%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Respiratory tract infection			
subjects affected / exposed	1 / 497 (0.20%)	0 / 504 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 497 (0.00%)	2 / 504 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 497 (0.00%)	1 / 504 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Dehydration			
subjects affected / exposed	1 / 497 (0.20%)	0 / 504 (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	Control Regimen	Fosaprepitant Regimen	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	193 / 497 (38.83%)	190 / 504 (37.70%)	
Nervous system disorders			
Headache			
subjects affected / exposed	35 / 497 (7.04%)	30 / 504 (5.95%)	
occurrences (all)	37	32	
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	33 / 497 (6.64%)	38 / 504 (7.54%)	
occurrences (all)	33	38	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	64 / 497 (12.88%)	75 / 504 (14.88%)	
occurrences (all)	64	78	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	51 / 497 (10.26%)	47 / 504 (9.33%)	
occurrences (all)	53	48	
Diarrhoea			
subjects affected / exposed	55 / 497 (11.07%)	63 / 504 (12.50%)	
occurrences (all)	57	66	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	26 / 497 (5.23%)	11 / 504 (2.18%)	
occurrences (all)	26	11	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	32 / 497 (6.44%)	26 / 504 (5.16%)	
occurrences (all)	32	27	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 March 2013	Amendment 04: This amendment provided important clarifications related to the targeted participant population and study procedures, including use of multiday chemotherapy, concomitant radiotherapy, contraception, and overdose. Several other operational clarifications were included such as dosing and administration details and specifying the documenting investigator review of laboratory tests and electrocardiograms prior to randomization.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported