



Clinical trial results:

A Phase IIb, Partially-Blinded Randomized, Active Comparator-Controlled Study to Evaluate the Pharmacokinetics/Pharmacodynamics, Safety, and Tolerability of Fosaprepitant in Pediatric Patients for the Prevention of Chemotherapy-Induced Nausea and Vomiting (CINV) Associated with Emetogenic Chemotherapy

Subtitle:

Open-Label Cohort to Further Evaluate the Pharmacokinetics/Pharmacodynamics, Safety, and Tolerability of Fosaprepitant in Pediatric Patients Birth to <12 Years Old

Summary

EudraCT number	2012-002340-24
Trial protocol	ES PT DE AT HU EE GB LT GR IT RO Outside EU/EEA
Global end of trial date	21 November 2016

Results information

Result version number	v1
This version publication date	18 May 2017
First version publication date	18 May 2017

Trial information

Trial identification

Sponsor protocol code	0517-029
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01697579
WHO universal trial number (UTN)	-
Other trial identifiers	Merck Registration Number: MK-0517-029

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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	21 November 2016
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	21 November 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study was to determine the appropriate dosing regimen of fosaprepitant, when administered with ondansetron (with or without dexamethasone), for the prevention of CINV in children from birth to <17 years of age. Fosaprepitant is a prodrug to aprepitant. All participants who completed the randomized Cycle 1 could elect to receive open-label fosaprepitant during optional Cycles 2-6.

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: Participants will be permitted to take "rescue medication" for established (not anticipated) nausea and vomiting throughout the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 December 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: 3
Country: Number of subjects enrolled	Austria: 16
Country: Number of subjects enrolled	Brazil: 10
Country: Number of subjects enrolled	Canada: 2
Country: Number of subjects enrolled	Chile: 28
Country: Number of subjects enrolled	Estonia: 4
Country: Number of subjects enrolled	Germany: 6

Country: Number of subjects enrolled	Greece: 10
Country: Number of subjects enrolled	Hungary: 13
Country: Number of subjects enrolled	Italy: 12
Country: Number of subjects enrolled	Korea, Republic of: 20
Country: Number of subjects enrolled	Lithuania: 2
Country: Number of subjects enrolled	Peru: 7
Country: Number of subjects enrolled	Portugal: 8
Country: Number of subjects enrolled	Ukraine: 6
Country: Number of subjects enrolled	United Kingdom: 16
Country: Number of subjects enrolled	United States: 6
Country: Number of subjects enrolled	Romania: 22
Country: Number of subjects enrolled	Russian Federation: 7
Country: Number of subjects enrolled	South Africa: 8
Country: Number of subjects enrolled	Spain: 21
Country: Number of subjects enrolled	Turkey: 13
Worldwide total number of subjects	240
EEA total number of subjects	130

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)	23
Children (2-11 years)	149
Adolescents (12-17 years)	68
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study enrolled participants scheduled to receive chemotherapeutic agent(s) associated with moderate, high, or very high risk of emetogenicity for no more than 5 consecutive days and was expected to receive ondansetron as part of their antiemetic regimen. Additional inclusion and exclusion criteria applied.

Pre-assignment

Screening details:

Participants (2 to <6, 6 to <12 and 12 to 17 years-old) were enrolled in a randomized, partially-blinded, study of 4 doses of fosaprepitant and a control in Cycle 1. Participants (0 to <2, 2 to <6 and 6 to <12 years-old) were invited to participate in optional Cycles 2-6 which was an open-label study of 2 doses of fosaprepitant.

Period 1

Period 1 title	Base Study-Cycle 1
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 5 mg/kg-Cycle 1

Arm description:

Participants were administered intravenous (IV) Fosaprepitant at the following weight-adjusted doses: Participants 4 months to <12 years old were administered 5 mg/kg (not to exceed 150 mg), Participants 1 to <4 months old were administered 2.5 mg/kg; Participants 0 to <1 month old were administered 1.25 mg/kg. Participants were also administered IV ondansetron (0.15 mg/kg x 3 doses for children 6 months to 17 years of age or per local standard of care for children <6 months of age), with or without dexamethasone.

Arm type	Experimental
Investigational medicinal product name	Fosaprepitant
Investigational medicinal product code	
Other name	Emend® for injection Fosaprepitant dimeglumine MK-0517
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Fosaprepitant 5 mg/kg administered IV as a single dose.

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

Dosage and administration details:

Administered as specified by local labeling and/or local standard of care

Investigational medicinal product name	Ondansetron
Investigational medicinal product code	
Other name	Ondansetron hydrochloride Zofran® Injection
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered IV

Arm title	Fosaprepitant 3 mg/kg-Cycle 1
Arm description:	
Participants 12 to 17 years old were administered 150 mg IV Fosaprepitant. Participants 2 to <12 years old were administered a weight-adjusted dose of 3 mg/kg (not to exceed 150 mg). Participants were also administered IV ondansetron (0.15 mg/kg x 3 doses for children 6 months to 17 years of age or per local standard of care for children <6 months of age), with or without dexamethasone.	
Arm type	Experimental
Investigational medicinal product name	Fosaprepitant
Investigational medicinal product code	
Other name	Emend® for injection Fosaprepitant dimeglumine MK-0517
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use
Dosage and administration details:	
Fosaprepitant 3 mg/kg administered IV as a single dose.	
Investigational medicinal product name	Ondansetron
Investigational medicinal product code	
Other name	Ondansetron hydrochloride Zofran® Injection
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use
Dosage and administration details:	
Administered IV	
Investigational medicinal product name	Dexamethasone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use
Dosage and administration details:	
Administered as specified by local labeling and/or local standard of care	
Arm title	Fosaprepitant 1.2 mg/kg-Cycle 1
Arm description:	
Participants 12 to 17 years old were administered 60 mg IV Fosaprepitant. Participants 2 to <12 years old were administered a weight-adjusted dose of 1.2 mg/kg (not to exceed 60 mg). Participants were also administered IV ondansetron (0.15 mg/kg x 3 doses for children 6 months to 17 years of age or per local standard of care for children <6 months of age), with or without dexamethasone.	
Arm type	Experimental
Investigational medicinal product name	Fosaprepitant
Investigational medicinal product code	
Other name	Emend® for injection Fosaprepitant dimeglumine MK-0517
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use
Dosage and administration details:	
Fosaprepitant 1.2 mg/kg administered IV as a single dose.	
Investigational medicinal product name	Ondansetron
Investigational medicinal product code	
Other name	Ondansetron hydrochloride Zofran® Injection
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use
Dosage and administration details:	
Administered IV	
Investigational medicinal product name	Dexamethasone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion

Routes of administration	Intravenous use
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Dosage and administration details:

Administered as specified by local labeling and/or local standard of care

Arm title	Fosaprepitant 0.4 mg/kg-Cycle 1
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Arm description:

Participants 12 to 17 years old were administered 20 mg IV Fosaprepitant. Participants 2 to <12 years old were administered a weight-adjusted dose of 0.4 mg/kg (not to exceed 20 mg). Participants were also administered IV ondansetron (0.15 mg/kg x 3 doses for children 6 months to 17 years of age or per local standard of care for children <6 months of age), with or without dexamethasone.

Arm type	Experimental
Investigational medicinal product name	Fosaprepitant
Investigational medicinal product code	
Other name	Emend® for injection Fosaprepitant dimeglumine MK-0517
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Fosaprepitant 0.4 mg/kg administered IV as a single dose.

Investigational medicinal product name	Ondansetron
Investigational medicinal product code	
Other name	Ondansetron hydrochloride Zofran® Injection
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered IV

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

Dosage and administration details:

Administered as specified by local labeling and/or local standard of care

Arm title	Placebo Control-Cycle 1
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Arm description:

Participants were administered IV normal saline at volume to match age and weight specific doses of Fosaprepitant. Participants were also administered IV ondansetron (0.15 mg/kg x 3 doses for children 6 months to 17 years of age or per local standard of care for children <6 months of age), with or without dexamethasone.

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

Dosage and administration details:

Placebo Fosaprepitant administered IV as a single dose.

Investigational medicinal product name	Ondansetron
Investigational medicinal product code	
Other name	Ondansetron hydrochloride Zofran® Injection
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered IV

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

Dosage and administration details:

Administered as specified by local labeling and/or local standard of care

Number of subjects in period 1	Fosaprepitant 5 mg/kg-Cycle 1	Fosaprepitant 3 mg/kg-Cycle 1	Fosaprepitant 1.2 mg/kg-Cycle 1
Started	74	43	44
Completed	72	42	43
Not completed	2	1	1
Consent withdrawn by subject	-	1	-
Adverse event, non-fatal	1	-	-
Technical problems	-	-	1
Withdrawal by parent/guardian	1	-	-
Protocol deviation	-	-	-

Number of subjects in period 1	Fosaprepitant 0.4 mg/kg-Cycle 1	Placebo Control-Cycle 1
Started	41	38
Completed	40	35
Not completed	1	3
Consent withdrawn by subject	-	-
Adverse event, non-fatal	-	-
Technical problems	1	-
Withdrawal by parent/guardian	-	-
Protocol deviation	-	3

Period 2

Period 2 title	Optional Extension-Cycles 2-6
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
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Arm title	Fosaprepitant 5 mg/kg Cycle 2-6
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Arm description:

For optional Cycles 2-6, participants from the 5 mg/kg Fosaprepitant arm in Cycle 1 were administered Fosaprepitant 5 mg/kg IV (or age-adjusted equivalent). For Cycle 2, Fosaprepitant was administered IV plus ondansetron with or without dexamethasone. For Cycles 3-6, Fosaprepitant was administered IV plus a 5-hydroxytryptamine 3 (5-HT3) antagonist with or without dexamethasone. Participants 1 year or less were required to receive ondansetron in all cycles as the 5-HT3 antagonist.

Arm type	Experimental
Investigational medicinal product name	Fosaprepitant
Investigational medicinal product code	
Other name	Emend® for injection Fosaprepitant dimeglumine MK-0517
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Fosaprepitant 5 mg/kg administered IV as a single dose.

Investigational medicinal product name	5-hydroxytryptamine 3 antagonist
Investigational medicinal product code	
Other name	5-HT3
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered as specified by local labeling and/or local standard of care

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

Dosage and administration details:

Administered as specified by local labeling and/or local standard of care

Investigational medicinal product name	Ondansetron
Investigational medicinal product code	
Other name	Ondansetron hydrochloride Zofran® Injection
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered IV

Arm title	Fosaprepitant 3 mg/kg Cycle 2-6
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Arm description:

For optional Cycles 2-6, participants from Cycle 1 Fosaprepitant arms (3, 1.2, or 0.4 mg/kg) or Cycle 1 Control arm were administered Fosaprepitant 3 mg/kg IV (or age-adjusted equivalent). For Cycle 2, Fosaprepitant was administered IV plus ondansetron with or without dexamethasone. For Cycles 3-6, Fosaprepitant was administered IV plus a 5-HT3 antagonist with or without dexamethasone.

Arm type	Experimental
Investigational medicinal product name	Fosaprepitant
Investigational medicinal product code	
Other name	Emend® for injection Fosaprepitant dimeglumine MK-0517
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Fosaprepitant 3 mg/kg administered IV as a single dose.

Investigational medicinal product name	5-hydroxytryptamine 3 antagonist
Investigational medicinal product code	
Other name	5-HT3

Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use
Dosage and administration details:	
Administered as specified by local labeling and/or local standard of care	
Investigational medicinal product name	Dexamethasone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use
Dosage and administration details:	
Administered as specified by local labeling and/or local standard of care	
Investigational medicinal product name	Ondansetron
Investigational medicinal product code	
Other name	Ondansetron hydrochloride Zofran® Injection
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use
Dosage and administration details:	
Administered IV	

Number of subjects in period 2 ^[1]	Fosaprepitant 5 mg/kg Cycle 2-6	Fosaprepitant 3 mg/kg Cycle 2-6
	Started	47
Completed	12	37
Not completed	35	69
Participant moved	-	2
Physician decision	7	11
Technical problems	-	1
Excluded medication	1	2
Additional cycle inclusion/exclusion criteria	4	11
Did not respond to chemotherapy regimen	1	-
Withdrawal by parent/guardian	1	5
Consent withdrawn by subject	-	2
Completed chemotherapy regimen	15	24
Death	-	2
Lost to follow-up	-	1
Non compliance with protocol	6	4
Protocol deviation	-	4

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Participants completing Cycle 1 were invited to participate in optional Cycles 2-6 and received 1 of the 2 dose regimens studied in optional Cycles 2-6.

Baseline characteristics

Reporting groups

Reporting group title	Fosaprepitant 5 mg/kg-Cycle 1
Reporting group description: Participants were administered intravenous (IV) Fosaprepitant at the following weight-adjusted doses: Participants 4 months to <12 years old were administered 5 mg/kg (not to exceed 150 mg), Participants 1 to <4 months old were administered 2.5 mg/kg; Participants 0 to <1 month old were administered 1.25 mg/kg. Participants were also administered IV ondansetron (0.15 mg/kg x 3 doses for children 6 months to 17 years of age or per local standard of care for children <6 months of age), with or without dexamethasone.	
Reporting group title	Fosaprepitant 3 mg/kg-Cycle 1
Reporting group description: Participants 12 to 17 years old were administered 150 mg IV Fosaprepitant. Participants 2 to <12 years old were administered a weight-adjusted dose of 3 mg/kg (not to exceed 150 mg). Participants were also administered IV ondansetron (0.15 mg/kg x 3 doses for children 6 months to 17 years of age or per local standard of care for children <6 months of age), with or without dexamethasone.	
Reporting group title	Fosaprepitant 1.2 mg/kg-Cycle 1
Reporting group description: Participants 12 to 17 years old were administered 60 mg IV Fosaprepitant. Participants 2 to <12 years old were administered a weight-adjusted dose of 1.2 mg/kg (not to exceed 60 mg). Participants were also administered IV ondansetron (0.15 mg/kg x 3 doses for children 6 months to 17 years of age or per local standard of care for children <6 months of age), with or without dexamethasone.	
Reporting group title	Fosaprepitant 0.4 mg/kg-Cycle 1
Reporting group description: Participants 12 to 17 years old were administered 20 mg IV Fosaprepitant. Participants 2 to <12 years old were administered a weight-adjusted dose of 0.4 mg/kg (not to exceed 20 mg). Participants were also administered IV ondansetron (0.15 mg/kg x 3 doses for children 6 months to 17 years of age or per local standard of care for children <6 months of age), with or without dexamethasone.	
Reporting group title	Placebo Control-Cycle 1
Reporting group description: Participants were administered IV normal saline at volume to match age and weight specific doses of Fosaprepitant. Participants were also administered IV ondansetron (0.15 mg/kg x 3 doses for children 6 months to 17 years of age or per local standard of care for children <6 months of age), with or without dexamethasone.	

Reporting group values	Fosaprepitant 5 mg/kg-Cycle 1	Fosaprepitant 3 mg/kg-Cycle 1	Fosaprepitant 1.2 mg/kg-Cycle 1
Number of subjects	74	43	44
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)	23	0	0
Children (2-11 years)	51	26	27
Adolescents (12-17 years)	0	17	17
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous Units: months arithmetic mean	60.2	123.8	119.4

standard deviation	± 42.3	± 51.3	± 52.7
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Gender Categorical Units: Subjects			
Female	32	18	23
Male	42	25	21

Reporting group values	Fosaprepitant 0.4 mg/kg-Cycle 1	Placebo Control- Cycle 1	Total
Number of subjects	41	38	240
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	23
Children (2-11 years)	24	21	149
Adolescents (12-17 years)	17	17	68
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous Units: months			
arithmetic mean	119.2	122.5	
standard deviation	± 54.3	± 54	-
Gender Categorical Units: Subjects			
Female	19	19	111
Male	22	19	129

End points

End points reporting groups

Reporting group title	Fosaprepitant 5 mg/kg-Cycle 1
Reporting group description: Participants were administered intravenous (IV) Fosaprepitant at the following weight-adjusted doses: Participants 4 months to <12 years old were administered 5 mg/kg (not to exceed 150 mg), Participants 1 to <4 months old were administered 2.5 mg/kg; Participants 0 to <1 month old were administered 1.25 mg/kg. Participants were also administered IV ondansetron (0.15 mg/kg x 3 doses for children 6 months to 17 years of age or per local standard of care for children <6 months of age), with or without dexamethasone.	
Reporting group title	Fosaprepitant 3 mg/kg-Cycle 1
Reporting group description: Participants 12 to 17 years old were administered 150 mg IV Fosaprepitant. Participants 2 to <12 years old were administered a weight-adjusted dose of 3 mg/kg (not to exceed 150 mg). Participants were also administered IV ondansetron (0.15 mg/kg x 3 doses for children 6 months to 17 years of age or per local standard of care for children <6 months of age), with or without dexamethasone.	
Reporting group title	Fosaprepitant 1.2 mg/kg-Cycle 1
Reporting group description: Participants 12 to 17 years old were administered 60 mg IV Fosaprepitant. Participants 2 to <12 years old were administered a weight-adjusted dose of 1.2 mg/kg (not to exceed 60 mg). Participants were also administered IV ondansetron (0.15 mg/kg x 3 doses for children 6 months to 17 years of age or per local standard of care for children <6 months of age), with or without dexamethasone.	
Reporting group title	Fosaprepitant 0.4 mg/kg-Cycle 1
Reporting group description: Participants 12 to 17 years old were administered 20 mg IV Fosaprepitant. Participants 2 to <12 years old were administered a weight-adjusted dose of 0.4 mg/kg (not to exceed 20 mg). Participants were also administered IV ondansetron (0.15 mg/kg x 3 doses for children 6 months to 17 years of age or per local standard of care for children <6 months of age), with or without dexamethasone.	
Reporting group title	Placebo Control-Cycle 1
Reporting group description: Participants were administered IV normal saline at volume to match age and weight specific doses of Fosaprepitant. Participants were also administered IV ondansetron (0.15 mg/kg x 3 doses for children 6 months to 17 years of age or per local standard of care for children <6 months of age), with or without dexamethasone.	
Reporting group title	Fosaprepitant 5 mg/kg Cycle 2-6
Reporting group description: For optional Cycles 2-6, participants from the 5 mg/kg Fosaprepitant arm in Cycle 1 were administered Fosaprepitant 5 mg/kg IV (or age-adjusted equivalent). For Cycle 2, Fosaprepitant was administered IV plus ondansetron with or without dexamethasone. For Cycles 3-6, Fosaprepitant was administered IV plus a 5-hydroxytryptamine 3 (5-HT ₃) antagonist with or without dexamethasone. Participants 1 year or less were required to receive ondansetron in all cycles as the 5-HT ₃ antagonist.	
Reporting group title	Fosaprepitant 3 mg/kg Cycle 2-6
Reporting group description: For optional Cycles 2-6, participants from Cycle 1 Fosaprepitant arms (3, 1.2, or 0.4 mg/kg) or Cycle 1 Control arm were administered Fosaprepitant 3 mg/kg IV (or age-adjusted equivalent). For Cycle 2, Fosaprepitant was administered IV plus ondansetron with or without dexamethasone. For Cycles 3-6, Fosaprepitant was administered IV plus a 5-HT ₃ antagonist with or without dexamethasone.	
Subject analysis set title	Fosaprepitant 5 mg/kg-Cycle 1
Subject analysis set type	Per protocol
Subject analysis set description: Participants were administered IV Fosaprepitant at the following weight-adjusted doses: Participants 4 months to <12 years old were administered 5 mg/kg (not to exceed 150 mg), Participants 1 to <4 months old were administered 2.5 mg/kg; Participants 0 to <1 month old were administered 1.25 mg/kg. Participants were also administered IV ondansetron (0.15 mg/kg x 3 doses for children 6 months to 17 years of age or per local standard of care for children <6 months of age), with or without dexamethasone. Analysis was in the per-protocol (PP) population which includes all participants that received one dose of study therapy and did not have important deviations from the study protocol.	
Subject analysis set title	Fosaprepitant 3 mg/kg-Cycle 1

Subject analysis set type	Per protocol
Subject analysis set description:	
Participants 12 to 17 years old were administered 150 mg IV Fosaprepitant. Participants 2 to <12 years old were administered a weight-adjusted dose of 3 mg/kg (not to exceed 150 mg). Participants were also administered IV ondansetron (0.15 mg/kg x 3 doses for children 6 months to 17 years of age or per local standard of care for children <6 months of age), with or without dexamethasone. Analysis was in the PP population which includes all participants that received one dose of study therapy and did not have important deviations from the study protocol.	
Subject analysis set title	Fosaprepitant 1.2 mg/kg-Cycle 1
Subject analysis set type	Per protocol
Subject analysis set description:	
Participants 12 to 17 years old were administered 60 mg IV Fosaprepitant. Participants 2 to <12 years old were administered a weight-adjusted dose of 1.2 mg/kg (not to exceed 60 mg). Participants were also administered IV ondansetron (0.15 mg/kg x 3 doses for children 6 months to 17 years of age or per local standard of care for children <6 months of age), with or without dexamethasone. Analysis was in the PP population which includes all participants that received one dose of study therapy and did not have important deviations from the study protocol.	
Subject analysis set title	Fosaprepitant 0.4 mg/kg-Cycle 1
Subject analysis set type	Per protocol
Subject analysis set description:	
Participants 12 to 17 years old were administered 20 mg IV Fosaprepitant. Participants 2 to <12 years old were administered a weight-adjusted dose of 0.4 mg/kg (not to exceed 20 mg). Participants were also administered IV ondansetron (0.15 mg/kg x 3 doses for children 6 months to 17 years of age or per local standard of care for children <6 months of age), with or without dexamethasone. Analysis was in the PP population which includes all participants that received one dose of study therapy and did not have important deviations from the study protocol.	
Subject analysis set title	Placebo Control-Cycle 1
Subject analysis set type	Per protocol
Subject analysis set description:	
Participants were administered IV normal saline at volume to match age and weight specific doses of Fosaprepitant. Participants were also administered IV ondansetron (0.15 mg/kg x 3 doses for children 6 months to 17 years of age or per local standard of care for children <6 months of age), with or without dexamethasone. Analysis was in the PP population which includes all participants that received one dose of placebo control and did not have important deviations from the study protocol.	
Subject analysis set title	Fosaprepitant 5 mg/kg: 0 to <2 Years-Cycle 1
Subject analysis set type	Per protocol
Subject analysis set description:	
Participants were administered IV Fosaprepitant at the following weight-adjusted doses: Participants 4 months to <12 years old were administered 5 mg/kg (not to exceed 150 mg), Participants 1 to <4 months old were administered 2.5 mg/kg; Participants 0 to <1 month old were administered 1.25 mg/kg. Participants were also administered IV ondansetron (0.15 mg/kg x 3 doses for children 6 months to 17 years of age or per local standard of care for children <6 months of age), with or without dexamethasone. Analysis was in the PP population which includes all participants that received one dose of study therapy and did not have important deviations from the study protocol.	
Subject analysis set title	Fosaprepitant 5 mg/kg: 2 to <6 Years-Cycle 1
Subject analysis set type	Per protocol
Subject analysis set description:	
Participants were administered IV Fosaprepitant at the weight-adjusted dose of 5 mg/kg (not to exceed 150 mg). Participants also were administered IV ondansetron at 0.15 mg/kg x 3 doses with or without dexamethasone. Analysis was in the PP population which includes all participants that received one dose of study therapy and did not have important deviations from the study protocol.	
Subject analysis set title	Fosaprepitant 5 mg/kg: 6 to <12 Years-Cycle 1
Subject analysis set type	Per protocol
Subject analysis set description:	
Participants were administered IV Fosaprepitant at the weight-adjusted dose of 5 mg/kg (not to exceed 150 mg). Participants also were administered IV ondansetron at 0.15 mg/kg x 3 doses with or without dexamethasone. Analysis was in the PP population which includes all participants that received one dose of study therapy and did not have important deviations from the study protocol.	
Subject analysis set title	Fosaprepitant 3 mg/kg: 2 to <6 Years-Cycle 1
Subject analysis set type	Per protocol

Subject analysis set description:

Participants 2 to <12 years old were administered a weight-adjusted dose of 3 mg/kg Fosaprepitant IV (not to exceed 150 mg). Participants were also administered IV ondansetron at 0.15 mg/kg x 3 doses for children 6 months to 17 years of age with or without dexamethasone. Analysis was in the PP population which includes all participants that received one dose of study therapy and did not have important deviations from the study protocol.

Subject analysis set title	Fosaprepitant 3 mg/kg: 6 to <12 Years-Cycle 1
Subject analysis set type	Per protocol

Subject analysis set description:

Participants 2 to <12 years old were administered a weight-adjusted dose of 3 mg/kg Fosaprepitant IV (not to exceed 150 mg). Participants were also administered IV ondansetron at 0.15 mg/kg x 3 doses for children 6 months to 17 years of age with or without dexamethasone. Analysis was in the PP population which includes all participants that received one dose of study therapy and did not have important deviations from the study protocol.

Subject analysis set title	Fosaprepitant 3 mg/kg: 12 to 17 Years-Cycle 1
Subject analysis set type	Per protocol

Subject analysis set description:

Participants 12 to 17 years old were administered 150 mg IV Fosaprepitant. Participants were also administered IV ondansetron at 0.15 mg/kg x 3 doses for children 6 months to 17 years of age with or without dexamethasone. Analysis was in the PP population which includes all participants that received one dose of study therapy and did not have important deviations from the study protocol.

Subject analysis set title	Fosaprepitant 1.2 mg/kg: 2 to <6 Years-Cycle 1
Subject analysis set type	Per protocol

Subject analysis set description:

Participants 2 to <12 years old were administered a weight-adjusted dose of 1.2 mg/kg of Fosaprepitant IV (not to exceed 60 mg). Participants were also administered IV ondansetron at 0.15 mg/kg x 3 doses for children 6 months to 17 years of age with or without dexamethasone. Analysis was in the PP population which includes all participants that received one dose of study therapy and did not have important deviations from the study protocol.

Subject analysis set title	Fosaprepitant 1.2 mg/kg: 6 to <12 Years-Cycle 1
Subject analysis set type	Per protocol

Subject analysis set description:

Participants 2 to <12 years old were administered a weight-adjusted dose of 1.2 mg/kg of Fosaprepitant IV (not to exceed 60 mg). Participants were also administered IV ondansetron at 0.15 mg/kg x 3 doses for children 6 months to 17 years of age with or without dexamethasone. Analysis was in the PP population which includes all participants that received one dose of study therapy and did not have important deviations from the study protocol.

Subject analysis set title	Fosaprepitant 1.2 mg/kg: 12 to 17 Years-Cycle 1
Subject analysis set type	Per protocol

Subject analysis set description:

Participants 12 to 17 years old were administered 60 mg IV Fosaprepitant. Participants were also administered IV ondansetron at 0.15 mg/kg x 3 doses for children 6 months to 17 years of age with or without dexamethasone. Analysis was in the PP population which includes all participants that received one dose of study therapy and did not have important deviations from the study protocol.

Subject analysis set title	Fosaprepitant 0.4 mg/kg: 2 to <6 Years-Cycle 1
Subject analysis set type	Per protocol

Subject analysis set description:

Participants 2 to <12 years old were administered a weight-adjusted dose of 0.4 mg/kg Fosaprepitant IV (not to exceed 20 mg). Participants were also administered IV ondansetron at 0.15 mg/kg x 3 doses for children 6 months to 17 years of age with or without dexamethasone. Analysis was in the PP population which includes all participants that received one dose of study therapy and did not have important deviations from the study protocol.

Subject analysis set title	Fosaprepitant 0.4 mg/kg: 6 to <12 Years-Cycle 1
Subject analysis set type	Per protocol

Subject analysis set description:

Participants 2 to <12 years old were administered a weight-adjusted dose of 0.4 mg/kg Fosaprepitant IV (not to exceed 20 mg). Participants were also administered IV ondansetron at 0.15 mg/kg x 3 doses for children 6 months to 17 years of age with or without dexamethasone. Analysis was in the PP population which includes all participants that received one dose of study therapy and did not have important deviations from the study protocol.

Subject analysis set title	Fosaprepitant 0.4 mg/kg: 12 to 17 Years-Cycle 1
Subject analysis set type	Per protocol

Subject analysis set description:

Participants 12 to 17 years old administered 20 mg IV Fosaprepitant. Participants were also administered IV ondansetron at 0.15 mg/kg x 3 doses for children 6 months to 17 years of age with or without dexamethasone. Analysis was in the PP population which includes all participants that received one dose of study therapy and did not have important deviations from the study protocol.

Subject analysis set title	Fosaprepitant 5 mg/kg Cycles 2-6
Subject analysis set type	Safety analysis

Subject analysis set description:

For optional Cycles 2-6, participants from the 5 mg/kg Fosaprepitant arm in Cycle 1 were administered Fosaprepitant 5 mg/kg IV (or age-adjusted equivalent). For Cycle 2, Fosaprepitant was administered IV plus ondansetron with or without dexamethasone. For Cycles 3-6, Fosaprepitant was administered IV plus a 5-hydroxytryptamine 3 (5-HT3) antagonist with or without dexamethasone. Participants 1 year or less were required to receive ondansetron in all cycles as the 5-HT3 antagonist. Analysis was in the All Patients as Treated Population that included all randomized participants who received at least one dose of study treatment.

Subject analysis set title	Fosaprepitant 3 mg/kg Cycles 2-6
Subject analysis set type	Safety analysis

Subject analysis set description:

For optional Cycles 2-6, participants from Cycle 1 Fosaprepitant arms (3, 1.2, or 0.4 mg/kg) or Cycle 1 Control arm were administered Fosaprepitant 3 mg/kg IV (or age-adjusted equivalent). For Cycle 2, Fosaprepitant was administered IV plus ondansetron with or without dexamethasone. For Cycles 3-6, Fosaprepitant was administered IV plus a 5-HT3 antagonist with or without dexamethasone. Analysis was in the All Patients as Treated Population that included all randomized participants who received at least one dose of study treatment.

Primary: Maximum concentration (Cmax) of aprepitant in participants 0 to <2 years of age

End point title	Maximum concentration (Cmax) of aprepitant in participants 0 to <2 years of age ^[1]
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End point description:

Fosaprepitant is a pro-drug that is rapidly converted to aprepitant. Because of this rapid conversion to aprepitant, Fosaprepitant cannot be assessed directly. The pharmacokinetics for each Fosaprepitant dose were determined by analyzing aprepitant in plasma. The Cmax for aprepitant was determined by measuring aprepitant levels at pre-infusion, immediately after infusion, and 2-4, 5-7, 8-10, 23-25, and 46-50 hours post-infusion.

End point type	Primary
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End point timeframe:

Pre-infusion, immediately after infusion, and 2-4, 5-7, 8-10, 23-25, and 46-50 hours post-infusion

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: No statistical analyses for group comparisons were planned for this endpoint.

End point values	Fosaprepitant 5 mg/kg: 0 to <2 Years-Cycle 1			
Subject group type	Subject analysis set			
Number of subjects analysed	22			
Units: ng/mL				
arithmetic mean (standard deviation)	3550 (± 1500)			

Statistical analyses

No statistical analyses for this end point

Primary: Time to maximum concentration (Tmax) of Aprepitant in participants 0 to <2 years of age

End point title	Time to maximum concentration (Tmax) of Aprepitant in participants 0 to <2 years of age ^[2]
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End point description:

Fosaprepitant is a pro-drug that is rapidly converted to Aprepitant. Because of this rapid conversion to Aprepitant, Fosaprepitant cannot be assessed directly. The pharmacokinetics for each Fosaprepitant dose were determined by analyzing Aprepitant in plasma. The Tmax for Aprepitant was determined by measuring Aprepitant levels at pre-infusion, immediately after infusion, and 2-4, 5-7, 8-10, 23-25, and 46-50 hours post-infusion.

End point type	Primary
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End point timeframe:

Pre-infusion, immediately after infusion, and 2-4, 5-7, 8-10, 23-25, and 46-50 hours post-infusion

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: No statistical analyses for group comparisons were planned for this endpoint.

End point values	Fosaprepitant 5 mg/kg: 0 to <2 Years-Cycle 1			
Subject group type	Subject analysis set			
Number of subjects analysed	22			
Units: hours				
arithmetic mean (standard deviation)	2.01 (± 2.1)			

Statistical analyses

No statistical analyses for this end point

Primary: Area under the concentration-time curve of Aprepitant from time 0 to infinity (AUC 0-∞) in participants 0 to <2 years of age

End point title	Area under the concentration-time curve of Aprepitant from time 0 to infinity (AUC 0-∞) in participants 0 to <2 years of age ^[3]
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End point description:

Fosaprepitant is a pro-drug that is rapidly converted to Aprepitant. Because of this rapid conversion to Aprepitant, Fosaprepitant cannot be assessed directly. The pharmacokinetics for each Fosaprepitant dose were determined by analyzing Aprepitant in plasma. The AUC 0-∞ for Aprepitant was determined by measuring Aprepitant levels at pre-infusion, immediately after infusion, and 2-4, 5-7, 8-10, 23-25, and 46-50 hours post-infusion.

End point type	Primary
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End point timeframe:

Pre-infusion, immediately after infusion, and 2-4, 5-7, 8-10, 23-25, and 46-50 hours post-infusion

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 statistical analyses for group comparisons were planned for this endpoint.

End point values	Fosaprepitant 5 mg/kg: 0 to <2 Years-Cycle 1			
Subject group type	Subject analysis set			
Number of subjects analysed	16			
Units: hr•ng/mL				
arithmetic mean (standard deviation)	37200 (± 15800)			

Statistical analyses

No statistical analyses for this end point

Primary: Area under the concentration-time curve of aprepitant from time 0 to 24 hours (AUC 0-24hr) in participants 0 to <2 years of age

End point title	Area under the concentration-time curve of aprepitant from time 0 to 24 hours (AUC 0-24hr) in participants 0 to <2 years of age ^[4]
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End point description:

Fosaprepitant is a pro-drug that is rapidly converted to aprepitant. Because of this rapid conversion to aprepitant, Fosaprepitant cannot be assessed directly. The pharmacokinetics for each Fosaprepitant dose were determined by analyzing aprepitant in plasma. The AUC 0-24hr for aprepitant was determined by measuring aprepitant levels at pre-infusion, immediately after infusion, and 2-4, 5-7, 8-10, 23-25, and 46-50 hours post-infusion.

End point type	Primary
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End point timeframe:

Pre-infusion, immediately after infusion, and 2-4, 5-7, 8-10, 23-25, and 46-50 hours post-infusion

Notes:

[4] - 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 statistical analyses for group comparisons were planned for this endpoint.

End point values	Fosaprepitant 5 mg/kg: 0 to <2 Years-Cycle 1			
Subject group type	Subject analysis set			
Number of subjects analysed	21			
Units: hr•ng/mL				
arithmetic mean (standard deviation)	36800 (± 21800)			

Statistical analyses

No statistical analyses for this end point

Primary: Apparent terminal half-life (t_{1/2}) of aprepitant in participants 0 to <2 years of age

End point title	Apparent terminal half-life (t _{1/2}) of aprepitant in participants 0 to <2 years of age ^[5]
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End point description:

Fosaprepitant is a pro-drug that is rapidly converted to aprepitant. Because of this rapid conversion to aprepitant, Fosaprepitant cannot be assessed directly. The pharmacokinetics for each Fosaprepitant

dose were determined by analyzing aprepitant in plasma. The t1/2 for aprepitant was determined by measuring aprepitant levels at pre-infusion, immediately after infusion, and 2-4, 5-7, 8-10, 23-25, and 46-50 hours post-infusion.

End point type	Primary
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End point timeframe:

Pre-infusion, immediately after infusion, and 2-4, 5-7, 8-10, 23-25, and 46-50 hours post-infusion

Notes:

[5] - 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 statistical analyses for group comparisons were planned for this endpoint.

End point values	Fosaprepitant 5 mg/kg: 0 to <2 Years-Cycle 1			
Subject group type	Subject analysis set			
Number of subjects analysed	16			
Units: hours				
arithmetic mean (standard deviation)	7.94 (± 2.86)			

Statistical analyses

No statistical analyses for this end point

Primary: Concentration of aprepitant after 24 hours (C24hr) in participants 0 to <2 years of age

End point title	Concentration of aprepitant after 24 hours (C24hr) in participants 0 to <2 years of age ^[6]
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End point description:

Fosaprepitant is a pro-drug that is rapidly converted to aprepitant. Because of this rapid conversion to aprepitant, Fosaprepitant cannot be assessed directly. The pharmacokinetics for each Fosaprepitant dose were determined by analyzing aprepitant in plasma. The C24hr for aprepitant was determined by measuring aprepitant levels at pre-infusion, immediately after infusion, and 2-4, 5-7, 8-10, 23-25, and 46-50 hours post-infusion.

End point type	Primary
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End point timeframe:

Pre-infusion, immediately after infusion, and 2-4, 5-7, 8-10, 23-25, and 46-50 hours post-infusion

Notes:

[6] - 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 statistical analyses for group comparisons were planned for this endpoint.

End point values	Fosaprepitant 5 mg/kg: 0 to <2 Years-Cycle 1			
Subject group type	Subject analysis set			
Number of subjects analysed	21			
Units: ng/mL				
arithmetic mean (standard deviation)	691 (± 852)			

Statistical analyses

No statistical analyses for this end point

Primary: Concentration of aprepitant after 48 hours (C48hr) in participants 0 to <2 years of age

End point title	Concentration of aprepitant after 48 hours (C48hr) in participants 0 to <2 years of age ^[7]
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End point description:

Fosaprepitant is a pro-drug that is rapidly converted to aprepitant. Because of this rapid conversion to aprepitant, Fosaprepitant cannot be assessed directly. The pharmacokinetics for each Fosaprepitant dose were determined by analyzing aprepitant in plasma. The C48hr for aprepitant was determined by measuring aprepitant levels at pre-infusion, immediately after infusion, and 2-4, 5-7, 8-10, 23-25, and 46-50 hours post-infusion.

End point type	Primary
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End point timeframe:

Pre-infusion, immediately after infusion, and 2-4, 5-7, 8-10, 23-25, and 46-50 hours post-infusion

Notes:

[7] - 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 statistical analyses for group comparisons were planned for this endpoint.

End point values	Fosaprepitant 5 mg/kg: 0 to <2 Years-Cycle 1			
Subject group type	Subject analysis set			
Number of subjects analysed	10			
Units: ng/mL				
arithmetic mean (standard deviation)	352 (± 929)			

Statistical analyses

No statistical analyses for this end point

Primary: Apparent total body clearance (CL/F) of aprepitant in participants 0 to <2 years of age

End point title	Apparent total body clearance (CL/F) of aprepitant in participants 0 to <2 years of age ^[8]
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End point description:

Fosaprepitant is a pro-drug that is rapidly converted to aprepitant. Because of this rapid conversion to aprepitant, Fosaprepitant cannot be assessed directly. The pharmacokinetics for each Fosaprepitant dose were determined by analyzing aprepitant in plasma. The CL/F for aprepitant was determined by measuring aprepitant levels at pre-infusion, immediately after infusion, and 2-4, 5-7, 8-10, 23-25, and 46-50 hours post-infusion.

End point type	Primary
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End point timeframe:

Pre-infusion, immediately after infusion, and 2-4, 5-7, 8-10, 23-25, and 46-50 hours post-infusion

Notes:

[8] - 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 statistical analyses for group comparisons were planned for this endpoint.

End point values	Fosaprepitant 5 mg/kg: 0 to <2 Years-Cycle 1			
Subject group type	Subject analysis set			
Number of subjects analysed	16			
Units: mL/min				
arithmetic mean (standard deviation)	24.2 (± 11.9)			

Statistical analyses

No statistical analyses for this end point

Primary: Cmax of aprepitant in participants 2 to <6 years of age

End point title	Cmax of aprepitant in participants 2 to <6 years of age ^[9]
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End point description:

Fosaprepitant is a pro-drug that is rapidly converted to aprepitant. Because of this rapid conversion to aprepitant, Fosaprepitant cannot be assessed directly. The pharmacokinetics for each Fosaprepitant dose were determined by analyzing aprepitant in plasma. The Cmax for aprepitant was determined by measuring aprepitant levels at pre-infusion, immediately after infusion, and 2-4, 5-7, 8-10, 23-25, and 46-50 hours post-infusion.

End point type	Primary
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End point timeframe:

Pre-infusion, immediately after infusion, and 2-4, 5-7, 8-10, 23-25, and 46-50 hours post-infusion

Notes:

[9] - 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 statistical analyses for group comparisons were planned for this endpoint.

End point values	Fosaprepitant 5 mg/kg: 2 to <6 Years-Cycle 1	Fosaprepitant 3 mg/kg: 2 to <6 Years-Cycle 1	Fosaprepitant 1.2 mg/kg: 2 to <6 Years-Cycle 1	Fosaprepitant 0.4 mg/kg: 2 to <6 Years-Cycle 1
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	25	6	8	6
Units: ng/mL				
arithmetic mean (standard deviation)	4270 (± 2370)	2320 (± 1540)	2030 (± 1780)	323 (± 103)

Statistical analyses

No statistical analyses for this end point

Primary: Tmax of aprepitant in participants 2 to <6 years of age

End point title	Tmax of aprepitant in participants 2 to <6 years of age ^[10]
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End point description:

Fosaprepitant is a pro-drug that is rapidly converted to aprepitant. Because of this rapid conversion to aprepitant, Fosaprepitant cannot be assessed directly. The pharmacokinetics for each Fosaprepitant dose were determined by analyzing aprepitant in plasma. The Tmax for aprepitant was determined by measuring aprepitant levels at pre-infusion, immediately after infusion, and 2-4, 5-7, 8-10, 23-25, and 46-50 hours post-infusion.

End point type	Primary
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End point timeframe:

Pre-infusion, immediately after infusion, and 2-4, 5-7, 8-10, 23-25, and 46-50 hours post-infusion

Notes:

[10] - 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 statistical analyses for group comparisons were planned for this endpoint.

End point values	Fosaprepitant 5 mg/kg: 2 to <6 Years-Cycle 1	Fosaprepitant 3 mg/kg: 2 to <6 Years-Cycle 1	Fosaprepitant 1.2 mg/kg: 2 to <6 Years-Cycle 1	Fosaprepitant 0.4 mg/kg: 2 to <6 Years-Cycle 1
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	25	6	8	6
Units: hours				
arithmetic mean (standard deviation)	1.9 (± 2.16)	2.29 (± 2.14)	1.36 (± 0.868)	1.34 (± 0.771)

Statistical analyses

No statistical analyses for this end point

Primary: AUC 0-∞ of aprepitant in participants 2 to <6 years of age

End point title | AUC 0-∞ of aprepitant in participants 2 to <6 years of age^[11]

End point description:

Fosaprepitant is a pro-drug that is rapidly converted to aprepitant. Because of this rapid conversion to aprepitant, Fosaprepitant cannot be assessed directly. The pharmacokinetics for each Fosaprepitant dose were determined by analyzing aprepitant in plasma. The AUC 0-∞ for aprepitant was determined by measuring aprepitant levels at pre-infusion, immediately after infusion, and 2-4, 5-7, 8-10, 23-25, and 46-50 hours post-infusion.

End point type | Primary

End point timeframe:

Pre-infusion, immediately after infusion, and 2-4, 5-7, 8-10, 23-25, and 46-50 hours post-infusion

Notes:

[11] - 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 statistical analyses for group comparisons were planned for this endpoint.

End point values	Fosaprepitant 5 mg/kg: 2 to <6 Years-Cycle 1	Fosaprepitant 3 mg/kg: 2 to <6 Years-Cycle 1	Fosaprepitant 1.2 mg/kg: 2 to <6 Years-Cycle 1	Fosaprepitant 0.4 mg/kg: 2 to <6 Years-Cycle 1
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	20	5	5	4
Units: hr•ng/mL				
arithmetic mean (standard deviation)	46400 (± 18600)	15300 (± 11100)	16000 (± 9680)	2070 (± 992)

Statistical analyses

No statistical analyses for this end point

Primary: AUC 0-24hr of aprepitant in participants 2 to <6 years of age

End point title	AUC 0-24hr of aprepitant in participants 2 to <6 years of
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End point description:

Fosaprepitant is a pro-drug that is rapidly converted to aprepitant. Because of this rapid conversion to aprepitant, Fosaprepitant cannot be assessed directly. The pharmacokinetics for each Fosaprepitant dose were determined by analyzing aprepitant in plasma. The AUC 0-24hr for aprepitant was determined by measuring aprepitant levels at pre-infusion, immediately after infusion, and 2-4, 5-7, 8-10, 23-25, and 46-50 hours post-infusion.

End point type	Primary
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End point timeframe:

Pre-infusion, immediately after infusion, and 2-4, 5-7, 8-10, 23-25, and 46-50 hours post-infusion

Notes:

[12] - 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 statistical analyses for group comparisons were planned for this endpoint.

End point values	Fosaprepitant 5 mg/kg: 2 to <6 Years-Cycle 1	Fosaprepitant 3 mg/kg: 2 to <6 Years-Cycle 1	Fosaprepitant 1.2 mg/kg: 2 to <6 Years-Cycle 1	Fosaprepitant 0.4 mg/kg: 2 to <6 Years-Cycle 1
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	25	6	8	5
Units: hr•ng/mL				
arithmetic mean (standard deviation)	45000 (± 23800)	21800 (± 22200)	19700 (± 18500)	1840 (± 742)

Statistical analyses

No statistical analyses for this end point

Primary: t1/2 of aprepitant in participants 2 to <6 years of age

End point title	t1/2 of aprepitant in participants 2 to <6 years of age ^[13]
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End point description:

Fosaprepitant is a pro-drug that is rapidly converted to aprepitant. Because of this rapid conversion to aprepitant, Fosaprepitant cannot be assessed directly. The pharmacokinetics for each Fosaprepitant dose were determined by analyzing aprepitant in plasma. The t1/2 for aprepitant was determined by measuring aprepitant levels at pre-infusion, immediately after infusion, and 2-4, 5-7, 8-10, 23-25, and 46-50 hours post-infusion.

End point type	Primary
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End point timeframe:

Pre-infusion, immediately after infusion, and 2-4, 5-7, 8-10, 23-25, and 46-50 hours post-infusion

Notes:

[13] - 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 statistical analyses for group comparisons were planned for this endpoint.

End point values	Fosaprepitant 5 mg/kg: 2 to <6 Years-Cycle 1	Fosaprepitant 3 mg/kg: 2 to <6 Years-Cycle 1	Fosaprepitant 1.2 mg/kg: 2 to <6 Years-Cycle 1	Fosaprepitant 0.4 mg/kg: 2 to <6 Years-Cycle 1
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	20	5	5	4
Units: hours				

arithmetic mean (standard deviation)	9.27 (± 4.17)	6.55 (± 3.62)	7.27 (± 3.47)	6.18 (± 3.51)
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Statistical analyses

No statistical analyses for this end point

Primary: C24hr of aprepitant in participants 2 to <6 years of age

End point title	C24hr of aprepitant in participants 2 to <6 years of age ^[14]
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End point description:

Fosaprepitant is a pro-drug that is rapidly converted to aprepitant. Because of this rapid conversion to aprepitant, Fosaprepitant cannot be assessed directly. The pharmacokinetics for each Fosaprepitant dose were determined by analyzing aprepitant in plasma. The C24hr for aprepitant was determined by measuring aprepitant levels at pre-infusion, immediately after infusion, and 2-4, 5-7, 8-10, 23-25, and 46-50 hours post-infusion.

End point type	Primary
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End point timeframe:

Pre-infusion, immediately after infusion, and 2-4, 5-7, 8-10, 23-25, and 46-50 hours post-infusion

Notes:

[14] - 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 statistical analyses for group comparisons were planned for this endpoint.

End point values	Fosaprepitant 5 mg/kg: 2 to <6 Years-Cycle 1	Fosaprepitant 3 mg/kg: 2 to <6 Years-Cycle 1	Fosaprepitant 1.2 mg/kg: 2 to <6 Years-Cycle 1	Fosaprepitant 0.4 mg/kg: 2 to <6 Years-Cycle 1
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	25	6	8	6
Units: ng/mL				
arithmetic mean (standard deviation)	1060 (± 1020)	278 (± 398)	332 (± 430)	9.23 (± 14.8)

Statistical analyses

No statistical analyses for this end point

Primary: C48hr of aprepitant in participants 2 to <6 years of age

End point title	C48hr of aprepitant in participants 2 to <6 years of age ^[15]
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End point description:

Fosaprepitant is a pro-drug that is rapidly converted to aprepitant. Because of this rapid conversion to aprepitant, Fosaprepitant cannot be assessed directly. The pharmacokinetics for each Fosaprepitant dose were determined by analyzing aprepitant in plasma. The C48hr for aprepitant was determined by measuring aprepitant levels at pre-infusion, immediately after infusion, and 2-4, 5-7, 8-10, 23-25, and 46-50 hours post-infusion.

End point type	Primary
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End point timeframe:

Pre-infusion, immediately after infusion, and 2-4, 5-7, 8-10, 23-25, and 46-50 hours post-infusion

Notes:

[15] - 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 statistical analyses for group comparisons were planned for this endpoint.

End point values	Fosaprepitant 5 mg/kg: 2 to <6 Years-Cycle 1	Fosaprepitant 3 mg/kg: 2 to <6 Years-Cycle 1	Fosaprepitant 1.2 mg/kg: 2 to <6 Years-Cycle 1	Fosaprepitant 0.4 mg/kg: 2 to <6 Years-Cycle 1
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	20	0 ^[16]	0 ^[17]	0 ^[18]
Units: ng/mL				
arithmetic mean (standard deviation)	232 (± 471)	()	()	()

Notes:

[16] - Endpoint not calculated

[17] - Endpoint not calculated

[18] - Endpoint not calculated

Statistical analyses

No statistical analyses for this end point

Primary: CL/F of aprepitant in participants 2 to <6 years of age

End point title	CL/F of aprepitant in participants 2 to <6 years of age ^[19]
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End point description:

Fosaprepitant is a pro-drug that is rapidly converted to aprepitant. Because of this rapid conversion to aprepitant, Fosaprepitant cannot be assessed directly. The pharmacokinetics for each Fosaprepitant dose were determined by analyzing aprepitant in plasma. The CL/F for aprepitant was determined by measuring aprepitant levels at pre-infusion, immediately after infusion, and 2-4, 5-7, 8-10, 23-25, and 46-50 hours post-infusion.

End point type	Primary
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End point timeframe:

Pre-infusion, immediately after infusion, and 2-4, 5-7, 8-10, 23-25, and 46-50 hours post-infusion

Notes:

[19] - 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 statistical analyses for group comparisons were planned for this endpoint.

End point values	Fosaprepitant 5 mg/kg: 2 to <6 Years-Cycle 1	Fosaprepitant 3 mg/kg: 2 to <6 Years-Cycle 1	Fosaprepitant 1.2 mg/kg: 2 to <6 Years-Cycle 1	Fosaprepitant 0.4 mg/kg: 2 to <6 Years-Cycle 1
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	20	5	5	4
Units: mL/min				
arithmetic mean (standard deviation)	31.8 (± 13.8)	66.2 (± 25.5)	29.6 (± 22.1)	48.5 (± 28.4)

Statistical analyses

No statistical analyses for this end point

Primary: Cmax of aprepitant in participants 6 to <12 years of age

End point title	Cmax of aprepitant in participants 6 to <12 years of age ^[20]
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End point description:

Fosaprepitant is a pro-drug that is rapidly converted to aprepitant. Because of this rapid conversion to aprepitant, Fosaprepitant cannot be assessed directly. The pharmacokinetics for each Fosaprepitant dose were determined by analyzing aprepitant in plasma. The C_{max} for aprepitant was determined by measuring aprepitant levels at pre-infusion, immediately after infusion, and 2-4, 5-7, 8-10, 23-25, and 46-50 hours post-infusion.

End point type Primary

End point timeframe:

Pre-infusion, immediately after infusion, and 2-4, 5-7, 8-10, 23-25, and 46-50 hours post-infusion

Notes:

[20] - 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 statistical analyses for group comparisons were planned for this endpoint.

End point values	Fosaprepitant 5 mg/kg: 6 to <12 Years-Cycle 1	Fosaprepitant 3 mg/kg: 6 to <12 Years-Cycle 1	Fosaprepitant 1.2 mg/kg: 6 to <12 Years-Cycle 1	Fosaprepitant 0.4 mg/kg: 6 to <12 Years-Cycle 1
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	24	14	13	12
Units: ng/mL				
arithmetic mean (standard deviation)	4400 (± 1910)	3550 (± 2460)	1360 (± 903)	507 (± 443)

Statistical analyses

No statistical analyses for this end point

Primary: T_{max} of aprepitant in participants 6 to <12 years of age

End point title T_{max} of aprepitant in participants 6 to <12 years of age^[21]

End point description:

Fosaprepitant is a pro-drug that is rapidly converted to aprepitant. Because of this rapid conversion to aprepitant, Fosaprepitant cannot be assessed directly. The pharmacokinetics for each Fosaprepitant dose were determined by analyzing aprepitant in plasma. The T_{max} for aprepitant was determined by measuring aprepitant levels at pre-infusion, immediately after infusion, and 2-4, 5-7, 8-10, 23-25, and 46-50 hours post-infusion.

End point type Primary

End point timeframe:

Pre-infusion, immediately after infusion, and 2-4, 5-7, 8-10, 23-25, and 46-50 hours post-infusion

Notes:

[21] - 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 statistical analyses for group comparisons were planned for this endpoint.

End point values	Fosaprepitant 5 mg/kg: 6 to <12 Years-Cycle 1	Fosaprepitant 3 mg/kg: 6 to <12 Years-Cycle 1	Fosaprepitant 1.2 mg/kg: 6 to <12 Years-Cycle 1	Fosaprepitant 0.4 mg/kg: 6 to <12 Years-Cycle 1
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	24	14	13	12
Units: hours				
arithmetic mean (standard deviation)	2.92 (± 5.09)	1.99 (± 1.62)	2.14 (± 1.96)	1.68 (± 2.46)

Statistical analyses

No statistical analyses for this end point

Primary: AUC 0-∞ of aprepitant in participants 6 to <12 years of age

End point title	AUC 0-∞ of aprepitant in participants 6 to <12 years of age ^[22]
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End point description:

Fosaprepitant is a pro-drug that is rapidly converted to aprepitant. Because of this rapid conversion to aprepitant, Fosaprepitant cannot be assessed directly. The pharmacokinetics for each Fosaprepitant dose were determined by analyzing aprepitant in plasma. The AUC 0-∞ for aprepitant was determined by measuring aprepitant levels at pre-infusion, immediately after infusion, and 2-4, 5-7, 8-10, 23-25, and 46-50 hours post-infusion.

End point type	Primary
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End point timeframe:

Pre-infusion, immediately after infusion, and 2-4, 5-7, 8-10, 23-25, and 46-50 hours post-infusion

Notes:

[22] - 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 statistical analyses for group comparisons were planned for this endpoint.

End point values	Fosaprepitant 5 mg/kg: 6 to <12 Years-Cycle 1	Fosaprepitant 3 mg/kg: 6 to <12 Years-Cycle 1	Fosaprepitant 1.2 mg/kg: 6 to <12 Years-Cycle 1	Fosaprepitant 0.4 mg/kg: 6 to <12 Years-Cycle 1
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	13	8	9	8
Units: hr•ng/mL				
arithmetic mean (standard deviation)	55300 (± 11900)	34300 (± 20300)	10700 (± 5440)	2860 (± 1120)

Statistical analyses

No statistical analyses for this end point

Primary: AUC 0-24hr of aprepitant in participants 6 to <12 years of age

End point title	AUC 0-24hr of aprepitant in participants 6 to <12 years of
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End point description:

Fosaprepitant is a pro-drug that is rapidly converted to aprepitant. Because of this rapid conversion to aprepitant, Fosaprepitant cannot be assessed directly. The pharmacokinetics for each Fosaprepitant dose were determined by analyzing aprepitant in plasma. The AUC 0-24hr for aprepitant was determined by measuring aprepitant levels at pre-infusion, immediately after infusion, and 2-4, 5-7, 8-10, 23-25, and 46-50 hours post-infusion.

End point type	Primary
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End point timeframe:

Pre-infusion, immediately after infusion, and 2-4, 5-7, 8-10, 23-25, and 46-50 hours post-infusion

Notes:

[23] - 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 statistical analyses for group comparisons were planned for this endpoint.

End point values	Fosaprepitant 5 mg/kg: 6 to <12 Years-Cycle 1	Fosaprepitant 3 mg/kg: 6 to <12 Years-Cycle 1	Fosaprepitant 1.2 mg/kg: 6 to <12 Years-Cycle 1	Fosaprepitant 0.4 mg/kg: 6 to <12 Years-Cycle 1
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	23	14	13	12
Units: hr•ng/mL				
arithmetic mean (standard deviation)	47400 (± 17300)	29200 (± 14300)	12000 (± 11000)	4260 (± 5040)

Statistical analyses

No statistical analyses for this end point

Primary: t1/2 of aprepitant in participants 6 to <12 years of age

End point title | t1/2 of aprepitant in participants 6 to <12 years of age^[24]

End point description:

Fosaprepitant is a pro-drug that is rapidly converted to aprepitant. Because of this rapid conversion to aprepitant, Fosaprepitant cannot be assessed directly. The pharmacokinetics for each Fosaprepitant dose were determined by analyzing aprepitant in plasma. The t1/2 for aprepitant was determined by measuring aprepitant levels at pre-infusion, immediately after infusion, and 2-4, 5-7, 8-10, 23-25, and 46-50 hours post-infusion.

End point type | Primary

End point timeframe:

Pre-infusion, immediately after infusion, and 2-4, 5-7, 8-10, 23-25, and 46-50 hours post-infusion

Notes:

[24] - 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 statistical analyses for group comparisons were planned for this endpoint.

End point values	Fosaprepitant 5 mg/kg: 6 to <12 Years-Cycle 1	Fosaprepitant 3 mg/kg: 6 to <12 Years-Cycle 1	Fosaprepitant 1.2 mg/kg: 6 to <12 Years-Cycle 1	Fosaprepitant 0.4 mg/kg: 6 to <12 Years-Cycle 1
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	13	8	9	8
Units: hours				
arithmetic mean (standard deviation)	9.77 (± 2.49)	7.69 (± 2.09)	8.23 (± 1.83)	6.58 (± 2.36)

Statistical analyses

No statistical analyses for this end point

Primary: C24hr of aprepitant in participants 6 to <12 years of age

End point title | C24hr of aprepitant in participants 6 to <12 years of age^[25]

End point description:

Fosaprepitant is a pro-drug that is rapidly converted to aprepitant. Because of this rapid conversion to aprepitant, Fosaprepitant cannot be assessed directly. The pharmacokinetics for each Fosaprepitant dose were determined by analyzing aprepitant in plasma. The C24hr for aprepitant was determined by measuring aprepitant levels at pre-infusion, immediately after infusion, and 2-4, 5-7, 8-10, 23-25, and 46-50 hours post-infusion.

End point type Primary

End point timeframe:

Pre-infusion, immediately after infusion, and 2-4, 5-7, 8-10, 23-25, and 46-50 hours post-infusion

Notes:

[25] - 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 statistical analyses for group comparisons were planned for this endpoint.

End point values	Fosaprepitant 5 mg/kg: 6 to <12 Years-Cycle 1	Fosaprepitant 3 mg/kg: 6 to <12 Years-Cycle 1	Fosaprepitant 1.2 mg/kg: 6 to <12 Years-Cycle 1	Fosaprepitant 0.4 mg/kg: 6 to <12 Years-Cycle 1
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	24	14	13	12
Units: ng/mL				
arithmetic mean (standard deviation)	1210 (\pm 1000)	589 (\pm 433)	219 (\pm 379)	70.4 (\pm 136)

Statistical analyses

No statistical analyses for this end point

Primary: C48hr of aprepitant in participants 6 to <12 years of age

End point title C48hr of aprepitant in participants 6 to <12 years of age^[26]

End point description:

Fosaprepitant is a pro-drug that is rapidly converted to aprepitant. Because of this rapid conversion to aprepitant, Fosaprepitant cannot be assessed directly. The pharmacokinetics for each Fosaprepitant dose were determined by analyzing aprepitant in plasma. The C48hr for aprepitant was determined by measuring aprepitant levels at pre-infusion, immediately after infusion, and 2-4, 5-7, 8-10, 23-25, and 46-50 hours post-infusion.

End point type Primary

End point timeframe:

Pre-infusion, immediately after infusion, and 2-4, 5-7, 8-10, 23-25, and 46-50 hours post-infusion

Notes:

[26] - 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 statistical analyses for group comparisons were planned for this endpoint.

End point values	Fosaprepitant 5 mg/kg: 6 to <12 Years-Cycle 1	Fosaprepitant 3 mg/kg: 6 to <12 Years-Cycle 1	Fosaprepitant 1.2 mg/kg: 6 to <12 Years-Cycle 1	Fosaprepitant 0.4 mg/kg: 6 to <12 Years-Cycle 1
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	11	0 ^[27]	0 ^[28]	0 ^[29]
Units: ng/mL				
arithmetic mean (standard deviation)	164 (\pm 124)	()	()	()

Notes:

[27] - Endpoint not calculated

[28] - Endpoint not calculated

[29] - Endpoint not calculated

Statistical analyses

No statistical analyses for this end point

Primary: CL/F of aprepitant in participants 6 to <12 years of age

End point title | CL/F of aprepitant in participants 6 to <12 years of age^[30]

End point description:

Fosaprepitant is a pro-drug that is rapidly converted to aprepitant. Because of this rapid conversion to aprepitant, Fosaprepitant cannot be assessed directly. The pharmacokinetics for each Fosaprepitant dose were determined by analyzing aprepitant in plasma. The CL/F for aprepitant was determined by measuring aprepitant levels at pre-infusion, immediately after infusion, and 2-4, 5-7, 8-10, 23-25, and 46-50 hours post-infusion.

End point type | Primary

End point timeframe:

Pre-infusion, immediately after infusion, and 2-4, 5-7, 8-10, 23-25, and 46-50 hours post-infusion

Notes:

[30] - 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 statistical analyses for group comparisons were planned for this endpoint.

End point values	Fosaprepitant 5 mg/kg: 6 to <12 Years-Cycle 1	Fosaprepitant 3 mg/kg: 6 to <12 Years-Cycle 1	Fosaprepitant 1.2 mg/kg: 6 to <12 Years-Cycle 1	Fosaprepitant 0.4 mg/kg: 6 to <12 Years-Cycle 1
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	13	8	9	8
Units: mL/min				
arithmetic mean (standard deviation)	42.1 (± 12.7)	69.2 (± 66.4)	78.8 (± 39.1)	89.6 (± 40.9)

Statistical analyses

No statistical analyses for this end point

Primary: Cmax of aprepitant in participants 12 to 17 years of age

End point title | Cmax of aprepitant in participants 12 to 17 years of age^[31]

End point description:

Fosaprepitant is a pro-drug that is rapidly converted to aprepitant. Because of this rapid conversion to aprepitant, Fosaprepitant cannot be assessed directly. The pharmacokinetics for each Fosaprepitant dose were determined by analyzing aprepitant in plasma. The Cmax for aprepitant was determined by measuring aprepitant levels at pre-infusion, immediately after infusion, and 2-4, 5-7, 8-10, 23-25, and 46-50 hours post-infusion.

End point type | Primary

End point timeframe:

Pre-infusion, immediately after infusion, and 2-4, 5-7, 8-10, 23-25, and 46-50 hours post-infusion

Notes:

[31] - 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 statistical analyses for group comparisons were planned for this endpoint.

End point values	Fosaprepitant 3 mg/kg: 12 to 17 Years-Cycle 1	Fosaprepitant 1.2 mg/kg: 12 to 17 Years-Cycle 1	Fosaprepitant 0.4 mg/kg: 12 to 17 Years-Cycle 1	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	12	12	13	
Units: ng/mL				
arithmetic mean (standard deviation)	3500 (± 972)	1180 (± 408)	582 (± 437)	

Statistical analyses

No statistical analyses for this end point

Primary: Tmax of aprepitant in participants 12 to 17 years of age

End point title | Tmax of aprepitant in participants 12 to 17 years of age^[32]

End point description:

Fosaprepitant is a pro-drug that is rapidly converted to aprepitant. Because of this rapid conversion to aprepitant, Fosaprepitant cannot be assessed directly. The pharmacokinetics for each Fosaprepitant dose were determined by analyzing aprepitant in plasma. The Tmax for aprepitant was determined by measuring aprepitant levels at pre-infusion, immediately after infusion, and 2-4, 5-7, 8-10, 23-25, and 46-50 hours post-infusion.

End point type | Primary

End point timeframe:

Pre-infusion, immediately after infusion, and 2-4, 5-7, 8-10, 23-25, and 46-50 hours post-infusion

Notes:

[32] - 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 statistical analyses for group comparisons were planned for this endpoint.

End point values	Fosaprepitant 3 mg/kg: 12 to 17 Years-Cycle 1	Fosaprepitant 1.2 mg/kg: 12 to 17 Years-Cycle 1	Fosaprepitant 0.4 mg/kg: 12 to 17 Years-Cycle 1	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	12	12	13	
Units: hours				
arithmetic mean (standard deviation)	0.546 (± 0.144)	0.722 (± 0.608)	0.736 (± 0.561)	

Statistical analyses

No statistical analyses for this end point

Primary: AUC 0-∞ of aprepitant in participants 12 to 17 years of age

End point title | AUC 0-∞ of aprepitant in participants 12 to 17 years of age^[33]

End point description:

Fosaprepitant is a pro-drug that is rapidly converted to aprepitant. Because of this rapid conversion to aprepitant, Fosaprepitant cannot be assessed directly. The pharmacokinetics for each Fosaprepitant dose were determined by analyzing aprepitant in plasma. The AUC 0-∞ for aprepitant was determined by measuring aprepitant levels at pre-infusion, immediately after infusion, and 2-4, 5-7, 8-10, 23-25, and 46-50 hours post-infusion.

End point type Primary

End point timeframe:

Pre-infusion, immediately after infusion, and 2-4, 5-7, 8-10, 23-25, and 46-50 hours post-infusion

Notes:

[33] - 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 statistical analyses for group comparisons were planned for this endpoint.

End point values	Fosaprepitant 3 mg/kg: 12 to 17 Years-Cycle 1	Fosaprepitant 1.2 mg/kg: 12 to 17 Years-Cycle 1	Fosaprepitant 0.4 mg/kg: 12 to 17 Years-Cycle 1	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	3	8	9	
Units: hr•ng/mL				
arithmetic mean (standard deviation)	33800 (± 7180)	12300 (± 4660)	3500 (± 1430)	

Statistical analyses

No statistical analyses for this end point

Primary: AUC 0-24hr of aprepitant in participants 12 to 17 years of age

End point title AUC 0-24hr of aprepitant in participants 12 to 17 years of

End point description:

Fosaprepitant is a pro-drug that is rapidly converted to aprepitant. Because of this rapid conversion to aprepitant, Fosaprepitant cannot be assessed directly. The pharmacokinetics for each Fosaprepitant dose were determined by analyzing aprepitant in plasma. The AUC 0-24hr for aprepitant was determined by measuring aprepitant levels at pre-infusion, immediately after infusion, and 2-4, 5-7, 8-10, 23-25, and 46-50 hours post-infusion.

End point type Primary

End point timeframe:

Pre-infusion, immediately after infusion, and 2-4, 5-7, 8-10, 23-25, and 46-50 hours post-infusion

Notes:

[34] - 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 statistical analyses for group comparisons were planned for this endpoint.

End point values	Fosaprepitant 3 mg/kg: 12 to 17 Years-Cycle 1	Fosaprepitant 1.2 mg/kg: 12 to 17 Years-Cycle 1	Fosaprepitant 0.4 mg/kg: 12 to 17 Years-Cycle 1	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	12	12	13	
Units: hr•ng/mL				
arithmetic mean (standard deviation)	30400 (± 8290)	9700 (± 4200)	4820 (± 7240)	

Statistical analyses

No statistical analyses for this end point

Primary: t1/2 of aprepitant in participants 12 to 17 years of age

End point title | t1/2 of aprepitant in participants 12 to 17 years of age^[35]

End point description:

Fosaprepitant is a pro-drug that is rapidly converted to aprepitant. Because of this rapid conversion to aprepitant, Fosaprepitant cannot be assessed directly. The pharmacokinetics for each Fosaprepitant dose were determined by analyzing aprepitant in plasma. The t1/2 for aprepitant was determined by measuring aprepitant levels at pre-infusion, immediately after infusion, and 2-4, 5-7, 8-10, 23-25, and 46-50 hours post-infusion.

End point type | Primary

End point timeframe:

Pre-infusion, immediately after infusion, and 2-4, 5-7, 8-10, 23-25, and 46-50 hours post-infusion

Notes:

[35] - 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 statistical analyses for group comparisons were planned for this endpoint.

End point values	Fosaprepitant 3 mg/kg: 12 to 17 Years-Cycle 1	Fosaprepitant 1.2 mg/kg: 12 to 17 Years-Cycle 1	Fosaprepitant 0.4 mg/kg: 12 to 17 Years-Cycle 1	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	3	8	9	
Units: hours				
arithmetic mean (standard deviation)	10.5 (± 1)	7.92 (± 1.38)	8.27 (± 1.2)	

Statistical analyses

No statistical analyses for this end point

Primary: C24hr of aprepitant in participants 12 to 17 years of age

End point title | C24hr of aprepitant in participants 12 to 17 years of age^[36]

End point description:

Fosaprepitant is a pro-drug that is rapidly converted to aprepitant. Because of this rapid conversion to aprepitant, Fosaprepitant cannot be assessed directly. The pharmacokinetics for each Fosaprepitant dose were determined by analyzing aprepitant in plasma. The C24hr for aprepitant was determined by measuring aprepitant levels at pre-infusion, immediately after infusion, and 2-4, 5-7, 8-10, 23-25, and 46-50 hours post-infusion.

End point type | Primary

End point timeframe:

Pre-infusion, immediately after infusion, and 2-4, 5-7, 8-10, 23-25, and 46-50 hours post-infusion

Notes:

[36] - 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 statistical analyses for group comparisons were planned for this endpoint.

End point values	Fosaprepitant 3 mg/kg: 12 to 17 Years-Cycle 1	Fosaprepitant 1.2 mg/kg: 12 to 17 Years-Cycle 1	Fosaprepitant 0.4 mg/kg: 12 to 17 Years-Cycle 1	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	12	12	13	
Units: ng/mL				
arithmetic mean (standard deviation)	735 (± 310)	142 (± 86.4)	101 (± 247)	

Statistical analyses

No statistical analyses for this end point

Primary: C48hr of aprepitant in participants 12 to 17 years of age

End point title | C48hr of aprepitant in participants 12 to 17 years of age^[37]

End point description:

Fosaprepitant is a pro-drug that is rapidly converted to aprepitant. Because of this rapid conversion to aprepitant, Fosaprepitant cannot be assessed directly. The pharmacokinetics for each Fosaprepitant dose were determined by analyzing aprepitant in plasma. The C48hr for aprepitant was determined by measuring aprepitant levels at pre-infusion, immediately after infusion, and 2-4, 5-7, 8-10, 23-25, and 46-50 hours post-infusion.

End point type | Primary

End point timeframe:

Pre-infusion, immediately after infusion, and 2-4, 5-7, 8-10, 23-25, and 46-50 hours post-infusion

Notes:

[37] - 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 statistical analyses for group comparisons were planned for this endpoint.

End point values	Fosaprepitant 3 mg/kg: 12 to 17 Years-Cycle 1	Fosaprepitant 1.2 mg/kg: 12 to 17 Years-Cycle 1	Fosaprepitant 0.4 mg/kg: 12 to 17 Years-Cycle 1	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	0 ^[38]	0 ^[39]	0 ^[40]	
Units: ng/mL				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[38] - Endpoint not calculated

[39] - Endpoint not calculated

[40] - Endpoint not calculated

Statistical analyses

No statistical analyses for this end point

Primary: CL/F of aprepitant in participants 12 to 17 years of age

End point title | CL/F of aprepitant in participants 12 to 17 years of age^[41]

End point description:

Fosaprepitant is a pro-drug that is rapidly converted to aprepitant. Because of this rapid conversion to aprepitant, Fosaprepitant cannot be assessed directly. The pharmacokinetics for each Fosaprepitant dose were determined by analyzing aprepitant in plasma. The CL/F for aprepitant was determined by measuring aprepitant levels at pre-infusion, immediately after infusion, and 2-4, 5-7, 8-10, 23-25, and 46-50 hours post-infusion.

End point type Primary

End point timeframe:

Pre-infusion, immediately after infusion, and 2-4, 5-7, 8-10, 23-25, and 46-50 hours post-infusion

Notes:

[41] - 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 statistical analyses for group comparisons were planned for this endpoint.

End point values	Fosaprepitant 3 mg/kg: 12 to 17 Years-Cycle 1	Fosaprepitant 1.2 mg/kg: 12 to 17 Years-Cycle 1	Fosaprepitant 0.4 mg/kg: 12 to 17 Years-Cycle 1	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	3	8	9	
Units: mL/min				
arithmetic mean (standard deviation)	76.2 (± 16.2)	91.7 (± 32.5)	105 (± 29)	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of participants who experienced at least one adverse event (AE) in Cycle 1

End point title Percentage of participants who experienced at least one adverse event (AE) in Cycle 1^[42]

End point description:

AE was defined as any untoward medical occurrence in a participant administered a pharmaceutical product and which did not necessarily have to have a causal relationship with this treatment. An AE could therefore be any unfavorable and unintended sign, symptom, or disease temporally associated with the use of a medicinal product/protocol specified procedure, whether or not considered related to the medicinal product/protocol specified procedure. Any worsening of a preexisting condition temporally associated with the use of the product was also an AE.

End point type Primary

End point timeframe:

Up to 14 days postdose

Notes:

[42] - 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 statistical analyses for group comparisons were planned for this endpoint.

End point values	Fosaprepitant 5 mg/kg-Cycle 1	Fosaprepitant 3 mg/kg-Cycle 1	Fosaprepitant 1.2 mg/kg-Cycle 1	Fosaprepitant 0.4 mg/kg-Cycle 1
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	74	42	43	40
Units: Percentage of participants				
number (not applicable)	87.8	83.3	90.7	80

End point values	Placebo Control-Cycle 1			
Subject group type	Subject analysis set			
Number of subjects analysed	35			
Units: Percentage of participants				
number (not applicable)	77.1			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of participants who experienced at least one adverse event (AE) in Cycles 2-6

End point title	Percentage of participants who experienced at least one adverse event (AE) in Cycles 2-6 ^[43]
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End point description:

AE was defined as any untoward medical occurrence in a participant administered a pharmaceutical product and which did not necessarily have to have a causal relationship with this treatment. An AE could therefore be any unfavorable and unintended sign, symptom, or disease temporally associated with the use of a medicinal product/protocol specified procedure, whether or not considered related to the medicinal product/protocol specified procedure. Any worsening of a preexisting condition temporally associated with the use of the product was also an AE.

End point type	Primary
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End point timeframe:

Up to 14 days postdose

Notes:

[43] - 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 statistical analyses for group comparisons were planned for this endpoint.

End point values	Fosaprepitant 5 mg/kg Cycles 2-6	Fosaprepitant 3 mg/kg Cycles 2-6		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	44	80		
Units: Percentage of participants				
number (not applicable)	93.6	75.5		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 14 days after the dose of study drug for each cycle

Adverse event reporting additional description:

AEs were reported for the All Patients as Treated Population that included all randomized participants who received at least one dose of study treatment.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	19.1
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Reporting groups

Reporting group title	Fosaprepitant 0.4 mg/kg-Cycle 1
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Reporting group description:

Participants 12 to 17 years old were administered 20 mg IV Fosaprepitant. Participants 2 to <12 years old were administered a weight-adjusted dose of 0.4 mg/kg (not to exceed 20 mg). Participants were also administered IV ondansetron (0.15 mg/kg x 3 doses for children 6 months to 17 years of age or per local standard of care for children <6 months of age), with or without dexamethasone.

Reporting group title	Fosaprepitant 1.2 mg/kg-Cycle 1
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Reporting group description:

Participants 12 to 17 years old were administered 60 mg IV Fosaprepitant. Participants 2 to <12 years old were administered a weight-adjusted dose of 1.2 mg/kg (not to exceed 60 mg). Participants were also administered IV ondansetron (0.15 mg/kg x 3 doses for children 6 months to 17 years of age or per local standard of care for children <6 months of age), with or without dexamethasone.

Reporting group title	Fosaprepitant 3 mg/kg-Cycle 1
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Reporting group description:

Participants 12 to 17 years old were administered 150 mg IV Fosaprepitant. Participants 2 to <12 years old were administered a weight-adjusted dose of 3 mg/kg (not to exceed 150 mg). Participants were also administered IV ondansetron (0.15 mg/kg x 3 doses for children 6 months to 17 years of age or per local standard of care for children <6 months of age), with or without dexamethasone.

Reporting group title	Fosaprepitant 5 mg/kg-Cycle 1
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Reporting group description:

Participants were administered IV Fosaprepitant at the following weight-adjusted doses: Participants 4 months to <12 years old were administered 5 mg/kg (not to exceed 150 mg), Participants 1 to <4 months old were administered 2.5 mg/kg; Participants 0 to <1 month old were administered 1.25 mg/kg. Participants were also administered IV ondansetron (0.15 mg/kg x 3 doses for children 6 months to 17 years of age or per local standard of care for children <6 months of age), with or without dexamethasone.

Reporting group title	Placebo Control-Cycle 1
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Reporting group description:

Participants were administered IV normal saline at volume to match age and weight specific doses of Fosaprepitant. Participants were also administered IV ondansetron (0.15 mg/kg x 3 doses for children 6 months to 17 years of age or per local standard of care for children <6 months of age), with or without dexamethasone.

Reporting group title	Fosaprepitant 3 mg/kg-Cycles 2-6
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Reporting group description:

For optional Cycles 2-6, participants from Cycle 1 Fosaprepitant arms (3, 1.2, or 0.4 mg/kg) or Cycle 1 Control arm were administered Fosaprepitant 3 mg/kg IV (or age-adjusted equivalent). For Cycle 2, Fosaprepitant was administered IV plus ondansetron with or without dexamethasone. For Cycles 3-6, Fosaprepitant was administered IV plus a 5-HT3 antagonist with or without dexamethasone. Analysis was in the All Patients as Treated Population that included all randomized participants who received at least one dose of study treatment.

Reporting group title	Fosaprepitant 5 mg/kg-Cycles 2-6
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Reporting group description:

For optional Cycles 2-6, participants from the 5 mg/kg Fosaprepitant arm in Cycle 1 were administered Fosaprepitant 5 mg/kg IV (or age-adjusted equivalent). For Cycle 2, Fosaprepitant was administered IV

plus ondansetron with or without dexamethasone. For Cycles 3-6, Fosaprepitant was administered IV plus a 5-hydroxytryptamine 3 (5-HT3) antagonist with or without dexamethasone. Participants 1 year or less were required to receive ondansetron in all cycles as the 5-HT3 antagonist. Analysis was in the All Patients as Treated Population that included all randomized participants who received at least one dose of study treatment.

Serious adverse events	Fosaprepitant 0.4 mg/kg-Cycle 1	Fosaprepitant 1.2 mg/kg-Cycle 1	Fosaprepitant 3 mg/kg-Cycle 1
Total subjects affected by serious adverse events			
subjects affected / exposed	11 / 40 (27.50%)	14 / 43 (32.56%)	12 / 42 (28.57%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
Blood magnesium decreased			
subjects affected / exposed	0 / 40 (0.00%)	1 / 43 (2.33%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood phosphorus decreased			
subjects affected / exposed	0 / 40 (0.00%)	1 / 43 (2.33%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
C-reactive protein increased			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutrophil count decreased			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
White blood cell count decreased			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug level increased			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Vascular disorders			
air embolism			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Hydrocephalus			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile convulsion			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuropathy peripheral			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neurotoxicity			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			

subjects affected / exposed	7 / 40 (17.50%)	10 / 43 (23.26%)	7 / 42 (16.67%)
occurrences causally related to treatment / all	0 / 7	0 / 10	0 / 8
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukopenia			
subjects affected / exposed	0 / 40 (0.00%)	1 / 43 (2.33%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	1 / 40 (2.50%)	1 / 43 (2.33%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			
subjects affected / exposed	1 / 40 (2.50%)	0 / 43 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopaenia			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 40 (0.00%)	1 / 43 (2.33%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mucosal inflammation			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	1 / 40 (2.50%)	0 / 43 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			

Anaphylactic reaction			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 40 (0.00%)	1 / 43 (2.33%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	1 / 40 (2.50%)	0 / 43 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stomatitis			
subjects affected / exposed	0 / 40 (0.00%)	2 / 43 (4.65%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Proctalgia			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Interstitial lung disease			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Renal and urinary disorders			
Cystitis haemorrhagic			
subjects affected / exposed	0 / 40 (0.00%)	1 / 43 (2.33%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal impairment			
subjects affected / exposed	1 / 40 (2.50%)	0 / 43 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Gastroenteritis norovirus			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes virus infection			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenic sepsis			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	2 / 42 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	1 / 40 (2.50%)	0 / 43 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	1 / 40 (2.50%)	0 / 43 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Skin infection			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tooth infection			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacteraemia			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytomegalovirus infection			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile infection			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes simplex			

subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postoperative wound infection			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillitis			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
Device breakage			

subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	1 / 40 (2.50%)	0 / 43 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Fosaprepitant 5 mg/kg-Cycle 1	Placebo Control-Cycle 1	Fosaprepitant 3 mg/kg-Cycles 2-6
Total subjects affected by serious adverse events			
subjects affected / exposed	24 / 74 (32.43%)	12 / 35 (34.29%)	46 / 106 (43.40%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events	0	0	0
Investigations			
Blood magnesium decreased			
subjects affected / exposed	0 / 74 (0.00%)	0 / 35 (0.00%)	0 / 106 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood phosphorus decreased			
subjects affected / exposed	0 / 74 (0.00%)	0 / 35 (0.00%)	0 / 106 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
C-reactive protein increased			
subjects affected / exposed	0 / 74 (0.00%)	0 / 35 (0.00%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Neutrophil count decreased			
subjects affected / exposed	2 / 74 (2.70%)	2 / 35 (5.71%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
White blood cell count decreased			
subjects affected / exposed	0 / 74 (0.00%)	1 / 35 (2.86%)	0 / 106 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug level increased			
subjects affected / exposed	0 / 74 (0.00%)	0 / 35 (0.00%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
air embolism			
subjects affected / exposed	0 / 74 (0.00%)	0 / 35 (0.00%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Hydrocephalus			
subjects affected / exposed	1 / 74 (1.35%)	0 / 35 (0.00%)	0 / 106 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	2 / 74 (2.70%)	0 / 35 (0.00%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile convulsion			
subjects affected / exposed	0 / 74 (0.00%)	0 / 35 (0.00%)	0 / 106 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuropathy peripheral			
subjects affected / exposed	0 / 74 (0.00%)	0 / 35 (0.00%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Neurotoxicity			
subjects affected / exposed	0 / 74 (0.00%)	0 / 35 (0.00%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 74 (0.00%)	1 / 35 (2.86%)	2 / 106 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	13 / 74 (17.57%)	4 / 35 (11.43%)	26 / 106 (24.53%)
occurrences causally related to treatment / all	0 / 13	0 / 4	0 / 47
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukopenia			
subjects affected / exposed	0 / 74 (0.00%)	1 / 35 (2.86%)	4 / 106 (3.77%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 9
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	0 / 74 (0.00%)	1 / 35 (2.86%)	7 / 106 (6.60%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 13
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pancytopenia			
subjects affected / exposed	0 / 74 (0.00%)	0 / 35 (0.00%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 74 (0.00%)	0 / 35 (0.00%)	2 / 106 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 74 (0.00%)	0 / 35 (0.00%)	0 / 106 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Mucosal inflammation			
subjects affected / exposed	2 / 74 (2.70%)	0 / 35 (0.00%)	3 / 106 (2.83%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	1 / 74 (1.35%)	1 / 35 (2.86%)	0 / 106 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	1 / 74 (1.35%)	0 / 35 (0.00%)	0 / 106 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 74 (0.00%)	0 / 35 (0.00%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 74 (0.00%)	0 / 35 (0.00%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stomatitis			
subjects affected / exposed	0 / 74 (0.00%)	1 / 35 (2.86%)	3 / 106 (2.83%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	1 / 74 (1.35%)	0 / 35 (0.00%)	4 / 106 (3.77%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Proctalgia			
subjects affected / exposed	0 / 74 (0.00%)	0 / 35 (0.00%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 74 (1.35%)	0 / 35 (0.00%)	0 / 106 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Interstitial lung disease			
subjects affected / exposed	0 / 74 (0.00%)	0 / 35 (0.00%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Cystitis haemorrhagic			
subjects affected / exposed	0 / 74 (0.00%)	0 / 35 (0.00%)	0 / 106 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal impairment			
subjects affected / exposed	0 / 74 (0.00%)	0 / 35 (0.00%)	0 / 106 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Gastroenteritis norovirus			
subjects affected / exposed	1 / 74 (1.35%)	0 / 35 (0.00%)	0 / 106 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes virus infection			
subjects affected / exposed	0 / 74 (0.00%)	0 / 35 (0.00%)	0 / 106 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			
subjects affected / exposed	0 / 74 (0.00%)	1 / 35 (2.86%)	0 / 106 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenic sepsis			

subjects affected / exposed	0 / 74 (0.00%)	0 / 35 (0.00%)	0 / 106 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 74 (0.00%)	0 / 35 (0.00%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	0 / 74 (0.00%)	0 / 35 (0.00%)	0 / 106 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin infection			
subjects affected / exposed	0 / 74 (0.00%)	1 / 35 (2.86%)	0 / 106 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tooth infection			
subjects affected / exposed	1 / 74 (1.35%)	0 / 35 (0.00%)	0 / 106 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacteraemia			
subjects affected / exposed	0 / 74 (0.00%)	0 / 35 (0.00%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 74 (0.00%)	0 / 35 (0.00%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytomegalovirus infection			
subjects affected / exposed	0 / 74 (0.00%)	0 / 35 (0.00%)	0 / 106 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			

subjects affected / exposed	0 / 74 (0.00%)	0 / 35 (0.00%)	4 / 106 (3.77%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile infection			
subjects affected / exposed	0 / 74 (0.00%)	0 / 35 (0.00%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 74 (0.00%)	0 / 35 (0.00%)	2 / 106 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes simplex			
subjects affected / exposed	0 / 74 (0.00%)	0 / 35 (0.00%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster			
subjects affected / exposed	0 / 74 (0.00%)	0 / 35 (0.00%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postoperative wound infection			
subjects affected / exposed	0 / 74 (0.00%)	0 / 35 (0.00%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			
subjects affected / exposed	0 / 74 (0.00%)	0 / 35 (0.00%)	0 / 106 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	0 / 74 (0.00%)	0 / 35 (0.00%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillitis			

subjects affected / exposed	0 / 74 (0.00%)	0 / 35 (0.00%)	0 / 106 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 74 (0.00%)	0 / 35 (0.00%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection			
subjects affected / exposed	0 / 74 (0.00%)	0 / 35 (0.00%)	0 / 106 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
Device breakage			
subjects affected / exposed	0 / 74 (0.00%)	0 / 35 (0.00%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 74 (2.70%)	0 / 35 (0.00%)	0 / 106 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	0 / 74 (0.00%)	0 / 35 (0.00%)	0 / 106 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	0 / 74 (0.00%)	0 / 35 (0.00%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Fosaprepitant 5 mg/kg-Cycles 2-6		
Total subjects affected by serious adverse events			
subjects affected / exposed	24 / 47 (51.06%)		
number of deaths (all causes)	0		
number of deaths resulting from	0		

adverse events			
Investigations			
Blood magnesium decreased			
subjects affected / exposed	0 / 47 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood phosphorus decreased			
subjects affected / exposed	0 / 47 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
C-reactive protein increased			
subjects affected / exposed	0 / 47 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Neutrophil count decreased			
subjects affected / exposed	0 / 47 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
White blood cell count decreased			
subjects affected / exposed	0 / 47 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Drug level increased			
subjects affected / exposed	0 / 47 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
air embolism			
subjects affected / exposed	0 / 47 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Hydrocephalus			

subjects affected / exposed	1 / 47 (2.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Seizure			
subjects affected / exposed	1 / 47 (2.13%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Febrile convulsion			
subjects affected / exposed	1 / 47 (2.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Neuropathy peripheral			
subjects affected / exposed	0 / 47 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Neurotoxicity			
subjects affected / exposed	0 / 47 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 47 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Febrile neutropenia			
subjects affected / exposed	18 / 47 (38.30%)		
occurrences causally related to treatment / all	0 / 32		
deaths causally related to treatment / all	0 / 0		
Leukopenia			
subjects affected / exposed	1 / 47 (2.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Neutropenia			

subjects affected / exposed	0 / 47 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pancytopenia			
subjects affected / exposed	0 / 47 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Thrombocytopaenia			
subjects affected / exposed	0 / 47 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 47 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Mucosal inflammation			
subjects affected / exposed	0 / 47 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pyrexia			
subjects affected / exposed	2 / 47 (4.26%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 47 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 47 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Diarrhoea			
subjects affected / exposed	0 / 47 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Stomatitis			
subjects affected / exposed	0 / 47 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	0 / 47 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Proctalgia			
subjects affected / exposed	0 / 47 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 47 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Interstitial lung disease			
subjects affected / exposed	0 / 47 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Cystitis haemorrhagic			
subjects affected / exposed	1 / 47 (2.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal impairment			
subjects affected / exposed	0 / 47 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Infections and infestations			
Gastroenteritis norovirus			
subjects affected / exposed	0 / 47 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Herpes virus infection			
subjects affected / exposed	0 / 47 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infection			
subjects affected / exposed	0 / 47 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Neutropenic sepsis			
subjects affected / exposed	0 / 47 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	0 / 47 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Septic shock			
subjects affected / exposed	0 / 47 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin infection			
subjects affected / exposed	0 / 47 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tooth infection			
subjects affected / exposed	0 / 47 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bacteraemia			

subjects affected / exposed	0 / 47 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cellulitis			
subjects affected / exposed	0 / 47 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cytomegalovirus infection			
subjects affected / exposed	1 / 47 (2.13%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Device related infection			
subjects affected / exposed	0 / 47 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Febrile infection			
subjects affected / exposed	0 / 47 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			
subjects affected / exposed	0 / 47 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Herpes simplex			
subjects affected / exposed	0 / 47 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Herpes zoster			
subjects affected / exposed	0 / 47 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Postoperative wound infection			

subjects affected / exposed	0 / 47 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pyelonephritis acute			
subjects affected / exposed	1 / 47 (2.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory tract infection			
subjects affected / exposed	0 / 47 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tonsillitis			
subjects affected / exposed	1 / 47 (2.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	0 / 47 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Viral infection			
subjects affected / exposed	2 / 47 (4.26%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Product issues			
Device breakage			
subjects affected / exposed	0 / 47 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 47 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypokalaemia			

subjects affected / exposed	0 / 47 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dehydration			
subjects affected / exposed	0 / 47 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Fosaprepitant 0.4 mg/kg-Cycle 1	Fosaprepitant 1.2 mg/kg-Cycle 1	Fosaprepitant 3 mg/kg-Cycle 1
Total subjects affected by non-serious adverse events			
subjects affected / exposed	27 / 40 (67.50%)	33 / 43 (76.74%)	32 / 42 (76.19%)
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	4 / 40 (10.00%)	2 / 43 (4.65%)	1 / 42 (2.38%)
occurrences (all)	4	2	2
Aspartate aminotransferase increased			
subjects affected / exposed	3 / 40 (7.50%)	2 / 43 (4.65%)	2 / 42 (4.76%)
occurrences (all)	3	2	4
Neutrophil count decreased			
subjects affected / exposed	3 / 40 (7.50%)	5 / 43 (11.63%)	2 / 42 (4.76%)
occurrences (all)	3	5	3
Platelet count decreased			
subjects affected / exposed	3 / 40 (7.50%)	7 / 43 (16.28%)	5 / 42 (11.90%)
occurrences (all)	3	8	5
White blood cell count decreased			
subjects affected / exposed	5 / 40 (12.50%)	3 / 43 (6.98%)	2 / 42 (4.76%)
occurrences (all)	5	5	3
C-reactive protein increased			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	2 / 42 (4.76%)
occurrences (all)	0	0	2
Nervous system disorders			

Headache subjects affected / exposed occurrences (all)	3 / 40 (7.50%) 5	6 / 43 (13.95%) 9	4 / 42 (9.52%) 7
Blood and lymphatic system disorders			
Anaemia subjects affected / exposed occurrences (all)	9 / 40 (22.50%) 10	11 / 43 (25.58%) 12	12 / 42 (28.57%) 12
Leukopenia subjects affected / exposed occurrences (all)	4 / 40 (10.00%) 4	3 / 43 (6.98%) 3	6 / 42 (14.29%) 6
Neutropenia subjects affected / exposed occurrences (all)	7 / 40 (17.50%) 7	10 / 43 (23.26%) 10	9 / 42 (21.43%) 10
Thrombocytopenia subjects affected / exposed occurrences (all)	9 / 40 (22.50%) 9	6 / 43 (13.95%) 7	11 / 42 (26.19%) 11
Febrile neutropenia subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0	0 / 43 (0.00%) 0	0 / 42 (0.00%) 0
General disorders and administration site conditions			
Mucosal inflammation subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0	5 / 43 (11.63%) 5	2 / 42 (4.76%) 2
Pyrexia subjects affected / exposed occurrences (all)	2 / 40 (5.00%) 2	3 / 43 (6.98%) 4	5 / 42 (11.90%) 6
Gastrointestinal disorders			
Abdominal pain subjects affected / exposed occurrences (all)	6 / 40 (15.00%) 11	4 / 43 (9.30%) 6	6 / 42 (14.29%) 6
Constipation subjects affected / exposed occurrences (all)	3 / 40 (7.50%) 3	2 / 43 (4.65%) 2	4 / 42 (9.52%) 4
Diarrhoea subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0	3 / 43 (6.98%) 3	2 / 42 (4.76%) 2

Nausea			
subjects affected / exposed	6 / 40 (15.00%)	3 / 43 (6.98%)	4 / 42 (9.52%)
occurrences (all)	7	3	5
Proctalgia			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	1 / 42 (2.38%)
occurrences (all)	0	0	1
Stomatitis			
subjects affected / exposed	2 / 40 (5.00%)	2 / 43 (4.65%)	2 / 42 (4.76%)
occurrences (all)	2	2	2
Vomiting			
subjects affected / exposed	9 / 40 (22.50%)	5 / 43 (11.63%)	7 / 42 (16.67%)
occurrences (all)	9	5	8
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 40 (2.50%)	2 / 43 (4.65%)	1 / 42 (2.38%)
occurrences (all)	1	2	2
Hiccups			
subjects affected / exposed	2 / 40 (5.00%)	3 / 43 (6.98%)	2 / 42 (4.76%)
occurrences (all)	10	5	2
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	4 / 42 (9.52%)
occurrences (all)	0	0	4
Hypoalbuminaemia			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	3 / 42 (7.14%)
occurrences (all)	0	0	3
Hypokalaemia			
subjects affected / exposed	0 / 40 (0.00%)	3 / 43 (6.98%)	4 / 42 (9.52%)
occurrences (all)	0	3	4
Hypophosphataemia			
subjects affected / exposed	0 / 40 (0.00%)	1 / 43 (2.33%)	3 / 42 (7.14%)
occurrences (all)	0	1	3

Non-serious adverse events	Fosaprepitant 5 mg/kg-Cycle 1	Placebo Control-Cycle 1	Fosaprepitant 3 mg/kg-Cycles 2-6
Total subjects affected by non-serious adverse events			
subjects affected / exposed	60 / 74 (81.08%)	24 / 35 (68.57%)	69 / 106 (65.09%)

Investigations			
Alanine aminotransferase increased subjects affected / exposed occurrences (all)	6 / 74 (8.11%) 6	2 / 35 (5.71%) 3	15 / 106 (14.15%) 22
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	8 / 74 (10.81%) 8	2 / 35 (5.71%) 2	13 / 106 (12.26%) 21
Neutrophil count decreased subjects affected / exposed occurrences (all)	11 / 74 (14.86%) 11	2 / 35 (5.71%) 2	15 / 106 (14.15%) 38
Platelet count decreased subjects affected / exposed occurrences (all)	16 / 74 (21.62%) 16	3 / 35 (8.57%) 3	15 / 106 (14.15%) 37
White blood cell count decreased subjects affected / exposed occurrences (all)	5 / 74 (6.76%) 5	3 / 35 (8.57%) 3	13 / 106 (12.26%) 23
C-reactive protein increased subjects affected / exposed occurrences (all)	2 / 74 (2.70%) 2	1 / 35 (2.86%) 1	5 / 106 (4.72%) 8
Nervous system disorders			
Headache subjects affected / exposed occurrences (all)	2 / 74 (2.70%) 2	2 / 35 (5.71%) 2	11 / 106 (10.38%) 15
Blood and lymphatic system disorders			
Anaemia subjects affected / exposed occurrences (all)	27 / 74 (36.49%) 28	10 / 35 (28.57%) 10	33 / 106 (31.13%) 54
Leukopenia subjects affected / exposed occurrences (all)	5 / 74 (6.76%) 8	4 / 35 (11.43%) 4	10 / 106 (9.43%) 22
Neutropenia subjects affected / exposed occurrences (all)	18 / 74 (24.32%) 19	8 / 35 (22.86%) 8	14 / 106 (13.21%) 19
Thrombocytopenia subjects affected / exposed occurrences (all)	11 / 74 (14.86%) 11	9 / 35 (25.71%) 9	19 / 106 (17.92%) 44

Febrile neutropenia subjects affected / exposed occurrences (all)	2 / 74 (2.70%) 2	0 / 35 (0.00%) 0	2 / 106 (1.89%) 2
General disorders and administration site conditions			
Mucosal inflammation subjects affected / exposed occurrences (all)	2 / 74 (2.70%) 2	0 / 35 (0.00%) 0	6 / 106 (5.66%) 9
Pyrexia subjects affected / exposed occurrences (all)	8 / 74 (10.81%) 8	3 / 35 (8.57%) 4	13 / 106 (12.26%) 19
Gastrointestinal disorders			
Abdominal pain subjects affected / exposed occurrences (all)	5 / 74 (6.76%) 5	4 / 35 (11.43%) 4	19 / 106 (17.92%) 30
Constipation subjects affected / exposed occurrences (all)	9 / 74 (12.16%) 9	4 / 35 (11.43%) 4	9 / 106 (8.49%) 9
Diarrhoea subjects affected / exposed occurrences (all)	6 / 74 (8.11%) 6	1 / 35 (2.86%) 1	10 / 106 (9.43%) 10
Nausea subjects affected / exposed occurrences (all)	8 / 74 (10.81%) 21	2 / 35 (5.71%) 2	23 / 106 (21.70%) 40
Proctalgia subjects affected / exposed occurrences (all)	0 / 74 (0.00%) 0	2 / 35 (5.71%) 2	2 / 106 (1.89%) 4
Stomatitis subjects affected / exposed occurrences (all)	2 / 74 (2.70%) 2	2 / 35 (5.71%) 2	8 / 106 (7.55%) 8
Vomiting subjects affected / exposed occurrences (all)	14 / 74 (18.92%) 20	3 / 35 (8.57%) 3	30 / 106 (28.30%) 69
Respiratory, thoracic and mediastinal disorders			
Cough subjects affected / exposed occurrences (all)	6 / 74 (8.11%) 6	1 / 35 (2.86%) 1	12 / 106 (11.32%) 13

Hiccups subjects affected / exposed occurrences (all)	1 / 74 (1.35%) 1	1 / 35 (2.86%) 1	3 / 106 (2.83%) 3
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	5 / 74 (6.76%) 5	3 / 35 (8.57%) 3	2 / 106 (1.89%) 2
Hypoalbuminaemia subjects affected / exposed occurrences (all)	1 / 74 (1.35%) 1	0 / 35 (0.00%) 0	4 / 106 (3.77%) 6
Hypokalaemia subjects affected / exposed occurrences (all)	2 / 74 (2.70%) 2	2 / 35 (5.71%) 2	15 / 106 (14.15%) 25
Hypophosphataemia subjects affected / exposed occurrences (all)	4 / 74 (5.41%) 4	1 / 35 (2.86%) 1	9 / 106 (8.49%) 18

Non-serious adverse events	Fosaprepitant 5 mg/kg-Cycles 2-6		
Total subjects affected by non-serious adverse events subjects affected / exposed	31 / 47 (65.96%)		
Investigations Alanine aminotransferase increased subjects affected / exposed occurrences (all)	2 / 47 (4.26%) 2		
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	4 / 47 (8.51%) 5		
Neutrophil count decreased subjects affected / exposed occurrences (all)	11 / 47 (23.40%) 17		
Platelet count decreased subjects affected / exposed occurrences (all)	5 / 47 (10.64%) 8		
White blood cell count decreased subjects affected / exposed occurrences (all)	5 / 47 (10.64%) 6		

C-reactive protein increased subjects affected / exposed occurrences (all)	3 / 47 (6.38%) 7		
Nervous system disorders Headache subjects affected / exposed occurrences (all)	2 / 47 (4.26%) 5		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) Leukopenia subjects affected / exposed occurrences (all) Neutropenia subjects affected / exposed occurrences (all) Thrombocytopenia subjects affected / exposed occurrences (all) Febrile neutropenia subjects affected / exposed occurrences (all)	14 / 47 (29.79%) 18 6 / 47 (12.77%) 16 4 / 47 (8.51%) 8 10 / 47 (21.28%) 19 4 / 47 (8.51%) 5		
General disorders and administration site conditions Mucosal inflammation subjects affected / exposed occurrences (all) Pyrexia subjects affected / exposed occurrences (all)	2 / 47 (4.26%) 2 4 / 47 (8.51%) 8		
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all) Constipation	1 / 47 (2.13%) 1		

subjects affected / exposed occurrences (all)	2 / 47 (4.26%) 2		
Diarrhoea subjects affected / exposed occurrences (all)	4 / 47 (8.51%) 5		
Nausea subjects affected / exposed occurrences (all)	6 / 47 (12.77%) 8		
Proctalgia subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1		
Stomatitis subjects affected / exposed occurrences (all)	3 / 47 (6.38%) 4		
Vomiting subjects affected / exposed occurrences (all)	12 / 47 (25.53%) 17		
Respiratory, thoracic and mediastinal disorders			
Cough subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1		
Hiccups subjects affected / exposed occurrences (all)	0 / 47 (0.00%) 0		
Metabolism and nutrition disorders			
Decreased appetite subjects affected / exposed occurrences (all)	2 / 47 (4.26%) 2		
Hypoalbuminaemia subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1		
Hypokalaemia subjects affected / exposed occurrences (all)	2 / 47 (4.26%) 2		
Hypophosphataemia			

subjects affected / exposed	2 / 47 (4.26%)		
occurrences (all)	3		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 August 2012	Amendment 01: Revised the study phase from 4 to IIb and added additional ondansetron administration guidance.
19 December 2014	Amendment 04: Added an open-label, single-treatment arm, added collection of an optional PK sample approximately 48 hours after completion of fosaprepitant administration, opened enrollment in the birth to <2 years old cohort, and implemented Dexamethasone PK Sampling in participants birth to 1 year old.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
19 May 2014	Enrollment put on hold to allow for authoring of and implementation of Amendment 04.	04 February 2015

Notes:

Limitations and caveats

None reported