



Clinical trial results:

A Multi-center, Open-label, 5-Part Study to Evaluate the Pharmacokinetics, Safety, and Tolerability of Aprepitant and Fosaprepitant Dimeglumine in Pediatric Patients Receiving Emetogenic Chemotherapy

Summary

EudraCT number	2006-005515-10
Trial protocol	ES SE DE FR Outside EU/EEA HU PL
Global end of trial date	20 January 2014

Results information

Result version number	v1 (current)
This version publication date	01 March 2016
First version publication date	19 March 2015

Trial information

Trial identification

Sponsor protocol code	0869-134
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00818259
WHO universal trial number (UTN)	-
Other trial identifiers	MK-0869-134: Merck protocol number

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)	Yes
EMA paediatric investigation plan number(s)	EMA-000406-PIP01-08, EMA-000144-PIP01-07
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	20 January 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	20 January 2014
Global end of trial reached?	Yes
Global end of trial date	20 January 2014
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

This study was to determine the appropriate dosing regimen of aprepitant and fosaprepitant for the prevention of chemotherapy-induced nausea and vomiting in pediatric participants from 0 months to 17 years of age. The purpose of this study was to estimate aprepitant plasma concentration profiles and pharmacokinetic (PK) parameters obtained in participants 0 months to <2 years, 2 to <6 years, 6 to <12 years and 12 to 17 years of age receiving moderately or highly emetogenic chemotherapy.

Fosaprepitant is a prodrug for aprepitant and is rapidly converted to aprepitant after intravenous (IV) administration. The birth to one year cohort was to be initiated in Parts III and IV upon completion of Part II (Steps A and B) in participants <6 months of age.

The study was terminated early prior to completing targeted enrollment of participants <6 months of age due to recruitment challenges.

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:

Administration of "rescue therapy" was allowed during the treatment phases for nausea and vomiting. Recommended rescue medication were: 5-HT3 antagonists, phenothiazines, butyrophenones, benzamides, corticosteroids, benzodiazepines and domperidone. Participants/parents/guardians recorded the drug, dosage, date and time that the participant took rescue medication in the patient diary.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 February 2009
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	Brazil: 28
Country: Number of subjects enrolled	Canada: 3
Country: Number of subjects enrolled	Israel: 3
Country: Number of subjects enrolled	Peru: 10
Country: Number of subjects enrolled	United States: 7
Country: Number of subjects enrolled	Norway: 3
Country: Number of subjects enrolled	Spain: 21

Country: Number of subjects enrolled	Sweden: 6
Country: Number of subjects enrolled	France: 3
Country: Number of subjects enrolled	Germany: 4
Country: Number of subjects enrolled	Australia: 1
Country: Number of subjects enrolled	Switzerland: 3
Worldwide total number of subjects	92
EEA total number of subjects	37

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)	19
Children (2-11 years)	50
Adolescents (12-17 years)	23
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study recruited participants who were from birth to 17 years of age and were scheduled to receive moderately to highly nausea-inducing chemotherapy or receive a repeat chemotherapy regimen that was not previously tolerated.

Pre-assignment

Screening details:

Of the 92 unique participants who were enrolled and randomized in Parts I (n=23), II (n=39), III (n=19), IV (n=5) and V (n=6), 91 took part in the study. One participant randomized in Part IIB was discontinued prior to treatment.

Period 1

Period 1 title	Randomization Period
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	No
Arm title	Part IA-fosaprepitant 115 mg/aprepitant

Arm description:

Day 1, fosaprepitant intravenously (IV) at a dose of 115 mg and Days 2 and 3, aprepitant 80 mg orally (PO), prior to chemotherapy for participants from 12 to 17 years of age. Participants also receive ondansetron IV as per local standard of care, with or without dexamethasone IV.

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

Dosage and administration details:

Day 1, fosaprepitant IV at a dose of 115 mg.

Investigational medicinal product name	Aprepitant
Investigational medicinal product code	
Other name	MK-0869
Pharmaceutical forms	Oral powder in sachet
Routes of administration	Oral use

Dosage and administration details:

Days 2 and 3, aprepitant 80 mg orally (PO).

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

Dosage and administration details:

Ondansetron solution for infusion, IV, administered per local standard of care.

Arm title	Part IB-fosaprepitant 150 mg
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Arm description:

Day 1, fosaprepitant, IV at a dose of 150 mg, prior to chemotherapy for participants 12 to 17 years of age. Participants also receive ondansetron IV as per local standard of care, with or without dexamethasone IV.

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

Dosage and administration details:

Day 1, fosaprepitant IV at a dose of 150 mg prior to chemotherapy.

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

Dosage and administration details:

Ondansetron solution for infusion, IV, administered per local standard of care.

Arm title	Part IIA-aprepitant 80 mg equiv.
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Arm description:

Day 1, aprepitant PO prior to chemotherapy at the dosing regimens listed for the following age ranges: 6 months to <12 years of age - 47 mg/m²; 4 months to <6 months of age - 2.0 mg/kg; 1 month to <4 months of age - 1.0 mg/kg; birth to <1 month of age - 0.5 mg/kg. Participants also receive ondansetron IV as per local standard of care, with or without dexamethasone IV.

Arm type	Experimental
Investigational medicinal product name	Aprepitant 80 mg equivalent
Investigational medicinal product code	
Other name	MK-0869
Pharmaceutical forms	Oral powder in sachet
Routes of administration	Oral use

Dosage and administration details:

Day 1, aprepitant prior to chemotherapy at the dosing regimens listed for the following age ranges: 6 months to <12 years of age - 47 mg/m²; 4 months to <6 months of age - 2.0 mg/kg; 1 month to <4 months of age - 1.0 mg/kg; birth to <1 month of age - 0.5 mg/kg.

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

Dosage and administration details:

Ondansetron solution for infusion, IV, administered per local standard of care.

Arm title	Part IIB-aprepitant 125 mg equiv.
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Arm description:

Day 1, aprepitant PO prior to chemotherapy at the dosing regimens listed for the following age ranges: 2 years to <12 years of age - 74 mg/m²; 6 months to <2 years of age - 1.3 mg/kg; 4 months to <6 months of age - 3.0 mg/kg; 1 month to <4 months of age - 1.5 mg/kg; birth to <1 month of age - 0.75 mg/kg. Participants also receive ondansetron IV as per local standard of care, with or without dexamethasone IV.

Arm type	Experimental
Investigational medicinal product name	Aprepitant 125 mg equivalent
Investigational medicinal product code	
Other name	MK-0869
Pharmaceutical forms	Oral powder in sachet
Routes of administration	Oral use

Dosage and administration details:

Day 1, aprepitant PO prior to chemotherapy at the dosing regimens listed for the following age ranges: 2 years to <12 years of age - 74 mg/m²; 6 months to <2 years or age - 1.3 mg/kg; 4 months to <6

months of age - 3.0 mg/kg; 1 month to <4 months of age - 1.5 mg/kg; birth to <1 month of age - 0.75 mg/kg.

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

Dosage and administration details:

Ondansetron solution for infusion, IV, administered per local standard of care.

Arm title	Part III-ondansetron
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Arm description:

Ondansetron administered IV per local standard of care on Days 1, 2 and 3 prior to chemotherapy for participants from birth to <12 years of age. The use of IV dexamethsone is optional with the exception of the birth to 1 year cohort. No PK parameters were measured for this group; participants received no fosaprepitant or aprepitant.

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

Dosage and administration details:

Ondansetron solution for infusion, IV, administered per local standard of care.

Arm title	Part IV-aprepitant regimen
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Arm description:

Day 1, aprepitant, PO, prior to chemotherapy at the dosing regimens listed for the following age ranges: 4 months to <12 years of age - 3.0 mg/kg; 1 month to <4 months of age - 1.5 mg/kg; birth to <1 month of age - 0.75 mg/kg; Days 2 and 3, aprepitant, PO, prior to chemotherapy at the dosing regimens listed for the following age ranges: 4 months to <12 years of age - 2.0 mg/kg; 1 month to <4 months of age - 1.0 mg/kg; birth to <1 month of age - 0.5 mg/kg. Participants also receive ondansetron IV as per local standard of care. The use of dexamethasone IV is optional with the exception of the birth to 1 year old cohort.

Arm type	Experimental
Investigational medicinal product name	Aprepitant regimen
Investigational medicinal product code	
Other name	MK-0869
Pharmaceutical forms	Oral powder in sachet
Routes of administration	Oral use

Dosage and administration details:

Day 1, aprepitant, PO, prior to chemotherapy at the dosing regimens listed for the following age ranges: 4 months to <12 years of age - 3.0 mg/kg; 1 month to <4 months of age - 1.5 mg/kg; birth to <1 month of age - 0.75 mg/kg; Days 2 and 3, aprepitant, PO, prior to chemotherapy at the dosing regimens listed for the following age ranges: 4 months to <12 years of age - 2.0 mg/kg; 1 month to <4 months of age - 1.0 mg/kg; birth to <1 month of age - 0.5 mg/kg.

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

Dosage and administration details:

Ondansetron solution for infusion, IV, administered per local standard of care.

Arm title	Part V-fosaprepitant regimen
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Arm description:

Day 1, fosaprepitant, IV at a dose of 3 mg/kg prior to chemotherapy for participants 6 months to <12 years of age. Participants also receive ondansetron IV as per local standard of care, with or without

dexamethasone IV.

Arm type	Experimental
Investigational medicinal product name	Fosaprepitant regimen
Investigational medicinal product code	
Other name	MK-0517
Pharmaceutical forms	Powder for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Day 1, fosaprepitant, IV at a dose of 3 mg/kg prior to chemotherapy for participants 6 months to <12 years of age.

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

Dosage and administration details:

Ondansetron solution for infusion, IV, administered per local standard of care.

Number of subjects in period 1	Part IA- fosaprepitant 115 mg/aprepitant	Part IB-fosaprepitant 150 mg	Part IIA-aprepitant 80 mg equiv.
Started	12	11	19
Completed	12	11	19

Number of subjects in period 1	Part IIB-aprepitant 125 mg equiv.	Part III-ondansetron	Part IV-aprepitant regimen
Started	20	19	5
Completed	20	19	5

Number of subjects in period 1	Part V-fosaprepitant regimen
Started	6
Completed	6

Period 2

Period 2 title	Part I
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	Part IA-fosaprepitant 115 mg/aprepitant
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Arm description:

Day 1, fosaprepitant, IV at a dose of 115 mg and Days 2 and 3, aprepitant 80 mg orally (PO), prior to chemotherapy for participants from 12 to 17 years of age. Participants also receive ondansetron IV as per local standard of care, with or without dexamethasone IV.

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

Dosage and administration details:

Day 1, fosaprepitant IV at a dose of 115 mg.

Investigational medicinal product name	Aprepitant
Investigational medicinal product code	
Other name	MK-0869
Pharmaceutical forms	Oral powder in sachet
Routes of administration	Oral use

Dosage and administration details:

Days 2 and 3, aprepitant 80 mg orally (PO).

Arm title	Part IB-fosaprepitant 150 mg
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Arm description:

Day 1, fosaprepitant, IV at a dose of 150 mg, prior to chemotherapy for participants 12 to 17 years of age. Participants also receive ondansetron IV as per local standard of care, with or without dexamethasone IV.

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

Dosage and administration details:

Day 1, fosaprepitant IV at a dose of 150 mg prior to chemotherapy.

Number of subjects in period 2	Part IA-fosaprepitant 115 mg/aprepitant	Part IB-fosaprepitant 150 mg
Started	12	11
Completed	11	11
Not completed	1	0
Consent withdrawn by subject	1	-

Period 3

Period 3 title	Part II
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	No
Arm title	Part IIA-aprepitant 80 mg equiv.

Arm description:

Day 1, aprepitant PO prior to chemotherapy at the dosing regimens listed for the following age ranges: 6 months to <12 years of age - 47 mg/m²; 4 months to <6 months of age - 2.0 mg/kg; 1 month to <4 months of age - 1.0 mg/kg; birth to <1 month of age - 0.5 mg/kg. Participants also receive ondansetron IV as per local standard of care, with or without dexamethasone IV.

Arm type	Experimental
Investigational medicinal product name	Aprepitant 80 mg equivalent
Investigational medicinal product code	
Other name	MK-0869
Pharmaceutical forms	Oral powder in sachet
Routes of administration	Oral use

Dosage and administration details:

Day 1, aprepitant prior to chemotherapy at the dosing regimens listed for the following age ranges: 6 months to <12 years of age - 47 mg/m²; 4 months to <6 months of age - 2.0 mg/kg; 1 month to <4 months of age - 1.0 mg/kg; birth to <1 month of age - 0.5 mg/kg.

Arm title	Part IIB-aprepitant 125 mg equiv.
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Arm description:

Day 1, aprepitant PO prior to chemotherapy at the dosing regimens listed for the following age ranges: 2 years to <12 years of age - 74 mg/m²; 6 months to <2 years of age - 1.3 mg/kg; 4 months to <6 months of age - 3.0 mg/kg; 1 month to <4 months of age - 1.5 mg/kg; birth to <1 month of age - 0.75 mg/kg. Participants also receive ondansetron IV as per local standard of care, with or without dexamethasone IV.

Arm type	Experimental
Investigational medicinal product name	Aprepitant 125 mg equivalent
Investigational medicinal product code	
Other name	MK-0869
Pharmaceutical forms	Oral powder in sachet
Routes of administration	Oral use

Dosage and administration details:

Day 1, aprepitant PO prior to chemotherapy at the dosing regimens listed for the following age ranges: 2 years to <12 years of age - 74 mg/m²; 6 months to <2 years of age - 1.3 mg/kg; 4 months to <6 months of age - 3.0 mg/kg; 1 month to <4 months of age - 1.5 mg/kg; birth to <1 month of age - 0.75 mg/kg.

Number of subjects in period 3	Part IIA-aprepitant 80 mg equiv.	Part IIB-aprepitant 125 mg equiv.
Started	19	20
Treated	19	19
Completed	18	18
Not completed	1	2
Physician decision	1	-
Lack of efficacy	-	1

Not treated	-	1
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Period 4

Period 4 title	Part III
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Part III-ondansetron
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Arm description:

Ondansetron administered IV per local standard of care on Days 1, 2 and 3 prior to chemotherapy for participants from birth to <12 years of age. The use of IV dexamethsone is optional with the exception of the birth to 1 year cohort. No PK parameters were measured for this group; participants received no fosaprepitant or aprepitant.

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

Dosage and administration details:

Ondansetron solution for infusion, IV, administered per local standard of care.

Number of subjects in period 4	Part III-ondansetron
Started	19
Completed	19

Period 5

Period 5 title	Part IV
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Part IV-aprepitant regimen
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Arm description:

Day 1, aprepitant, PO, prior to chemotherapy at the dosing regimens listed for the following age ranges: 4 months to <12 years of age - 3.0 mg/kg; 1 month to <4 months of age - 1.5 mg/kg; birth to <1 month of age - 0.75 mg/kg; Days 2 and 3, aprepitant, PO, prior to chemotherapy at the dosing regimens listed for the following age ranges: 4 months to <12 years of age - 2.0 mg/kg; 1 month to <4 months of age - 1.0 mg/kg; birth to <1 month of age - 0.5 mg/kg. Participants also receive ondansetron IV as per local standard of care. The use of dexamethasone IV is optional with the exception of the birth to 1 year old cohort. In addition to newly enrolled participants, participants who complete Part III may participate in Part IV.

Arm type	Experimental
Investigational medicinal product name	Aprepitant regimen
Investigational medicinal product code	
Other name	MK-0869
Pharmaceutical forms	Oral powder in sachet
Routes of administration	Oral use

Dosage and administration details:

Day 1, aprepitant, PO, prior to chemotherapy at the dosing regimens listed for the following age ranges: 4 months to <12 years of age - 3.0 mg/kg; 1 month to <4 months of age - 1.5 mg/kg; birth to <1 month of age - 0.75 mg/kg; Days 2 and 3, aprepitant, PO, prior to chemotherapy at the dosing regimens listed for the following age ranges: 4 months to <12 years of age - 2.0 mg/kg; 1 month to <4 months of age - 1.0 mg/kg; birth to <1 month of age - 0.5 mg/kg.

Number of subjects in period 5 ^[1]	Part IV-aprepitant regimen
Started	15
Completed	19
Not completed	1
Physician decision	1
Joined	5
Newly enrolled participants	5

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 who completed Part III had the option to continue into Part IV, but were not required to continue into Part IV. 15 participants from Part III continued into Part IV.

Period 6

Period 6 title	Part V
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Part V-fosaprepitant regimen
Arm description: Day 1, fosaprepitant, IV at a dose of 3 mg/kg prior to chemotherapy for participants 6 months to <12 years of age. Participants also receive ondansetron IV as per local standard of care, with or without dexamethasone IV. In addition to newly enrolled participants, participants who complete Part IV may participate in Part V.	
Arm type	Experimental
Investigational medicinal product name	Fosaprepitant regimen
Investigational medicinal product code	
Other name	MK-0517
Pharmaceutical forms	Powder for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Day 1, fosaprepitant, IV at a dose of 3 mg/kg prior to chemotherapy for participants 6 months to <12 years of age.

Number of subjects in period 6^[2]	Part V-fosaprepitant regimen
Started	17
Completed	22
Not completed	1
Adverse event, non-fatal	1
Joined	6
Newly enrolled participants	6

Notes:

[2] - 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 who completed Part IV had the option to continue into Part V, but were not required to continue into Part V. 17 participants from Part IV continued into Part V.

Baseline characteristics

Reporting groups

Reporting group title	Part IA-fosaprepitant 115 mg/aprepitant
Reporting group description:	
Day 1, fosaprepitant intravenously (IV) at a dose of 115 mg and Days 2 and 3, aprepitant 80 mg orally (PO), prior to chemotherapy for participants from 12 to 17 years of age. Participants also receive ondansetron IV as per local standard of care, with or without dexamethasone IV.	
Reporting group title	Part IB-fosaprepitant 150 mg
Reporting group description:	
Day 1, fosaprepitant, IV at a dose of 150 mg, prior to chemotherapy for participants 12 to 17 years of age. Participants also receive ondansetron IV as per local standard of care, with or without dexamethasone IV.	
Reporting group title	Part IIA-aprepitant 80 mg equiv.
Reporting group description:	
Day 1, aprepitant PO prior to chemotherapy at the dosing regimens listed for the following age ranges: 6 months to <12 years of age - 47 mg/m ² ; 4 months to <6 months of age - 2.0 mg/kg; 1 month to <4 months of age - 1.0 mg/kg; birth to <1 month of age - 0.5 mg/kg. Participants also receive ondansetron IV as per local standard of care, with or without dexamethasone IV.	
Reporting group title	Part IIB-aprepitant 125 mg equiv.
Reporting group description:	
Day 1, aprepitant PO prior to chemotherapy at the dosing regimens listed for the following age ranges: 2 years to <12 years of age - 74 mg/m ² ; 6 months to <2 years of age - 1.3 mg/kg; 4 months to <6 months of age - 3.0 mg/kg; 1 month to <4 months of age - 1.5 mg/kg; birth to <1 month of age - 0.75 mg/kg. Participants also receive ondansetron IV as per local standard of care, with or without dexamethasone IV.	
Reporting group title	Part III-ondansetron
Reporting group description:	
Ondansetron administered IV per local standard of care on Days 1, 2 and 3 prior to chemotherapy for participants from birth to <12 years of age. The use of IV dexamethasone is optional with the exception of the birth to 1 year cohort. No PK parameters were measured for this group; participants received no fosaprepitant or aprepitant.	
Reporting group title	Part IV-aprepitant regimen
Reporting group description:	
Day 1, aprepitant, PO, prior to chemotherapy at the dosing regimens listed for the following age ranges: 4 months to <12 years of age - 3.0 mg/kg; 1 month to <4 months of age - 1.5 mg/kg; birth to <1 month of age - 0.75 mg/kg; Days 2 and 3, aprepitant, PO, prior to chemotherapy at the dosing regimens listed for the following age ranges: 4 months to <12 years of age - 2.0 mg/kg; 1 month to <4 months of age - 1.0 mg/kg; birth to <1 month of age - 0.5 mg/kg. Participants also receive ondansetron IV as per local standard of care. The use of dexamethasone IV is optional with the exception of the birth to 1 year old cohort.	
Reporting group title	Part V-fosaprepitant regimen
Reporting group description:	
Day 1, fosaprepitant, IV at a dose of 3 mg/kg prior to chemotherapy for participants 6 months to <12 years of age. Participants also receive ondansetron IV as per local standard of care, with or without dexamethasone IV.	

Reporting group values	Part IA-fosaprepitant 115 mg/aprepitant	Part IB-fosaprepitant 150 mg	Part IIA-aprepitant 80 mg equiv.
Number of subjects	12	11	19
Age categorical			
Units: Subjects			
Infants and toddlers (28 days to <2 years)	0	0	5
Children (2 years to <6 years)	0	0	8
Children (6 years to <12 years)	0	0	6

Adolescents (12 years to 17 years)	12	11	0
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Gender categorical Units: Subjects			
Female	7	7	12
Male	5	4	7

Reporting group values	Part IIB-aprepitant 125 mg equiv.	Part III-ondansetron	Part IV-aprepitant regimen
Number of subjects	20	19	5
Age categorical Units: Subjects			
Infants and toddlers (28 days to <2 years)	6	6	1
Children (2 years to <6 years)	8	6	0
Children (6 years to <12 years)	6	7	4
Adolescents (12 years to 17 years)	0	0	0
Gender categorical Units: Subjects			
Female	14	13	3
Male	6	6	2

Reporting group values	Part V-fosaprepitant regimen	Total	
Number of subjects	6	92	
Age categorical Units: Subjects			
Infants and toddlers (28 days to <2 years)	1	19	
Children (2 years to <6 years)	3	25	
Children (6 years to <12 years)	2	25	
Adolescents (12 years to 17 years)	0	23	
Gender categorical Units: Subjects			
Female	6	62	
Male	0	30	

End points

End points reporting groups

Reporting group title	Part IA-fosaprepitant 115 mg/aprepitant
Reporting group description: Day 1, fosaprepitant intravenously (IV) at a dose of 115 mg and Days 2 and 3, aprepitant 80 mg orally (PO), prior to chemotherapy for participants from 12 to 17 years of age. Participants also receive ondansetron IV as per local standard of care, with or without dexamethasone IV.	
Reporting group title	Part IB-fosaprepitant 150 mg
Reporting group description: Day 1, fosaprepitant, IV at a dose of 150 mg, prior to chemotherapy for participants 12 to 17 years of age. Participants also receive ondansetron IV as per local standard of care, with or without dexamethasone IV.	
Reporting group title	Part IIA-aprepitant 80 mg equiv.
Reporting group description: Day 1, aprepitant PO prior to chemotherapy at the dosing regimens listed for the following age ranges: 6 months to <12 years of age - 47 mg/m ² ; 4 months to <6 months of age - 2.0 mg/kg; 1 month to <4 months of age - 1.0 mg/kg; birth to <1 month of age - 0.5 mg/kg. Participants also receive ondansetron IV as per local standard of care, with or without dexamethasone IV.	
Reporting group title	Part IIB-aprepitant 125 mg equiv.
Reporting group description: Day 1, aprepitant PO prior to chemotherapy at the dosing regimens listed for the following age ranges: 2 years to <12 years of age - 74 mg/m ² ; 6 months to <2 years of age - 1.3 mg/kg; 4 months to <6 months of age - 3.0 mg/kg; 1 month to <4 months of age - 1.5 mg/kg; birth to <1 month of age - 0.75 mg/kg. Participants also receive ondansetron IV as per local standard of care, with or without dexamethasone IV.	
Reporting group title	Part III-ondansetron
Reporting group description: Ondansetron administered IV per local standard of care on Days 1, 2 and 3 prior to chemotherapy for participants from birth to <12 years of age. The use of IV dexamethasone is optional with the exception of the birth to 1 year cohort. No PK parameters were measured for this group; participants received no fosaprepitant or aprepitant.	
Reporting group title	Part IV-aprepitant regimen
Reporting group description: Day 1, aprepitant, PO, prior to chemotherapy at the dosing regimens listed for the following age ranges: 4 months to <12 years of age - 3.0 mg/kg; 1 month to <4 months of age - 1.5 mg/kg; birth to <1 month of age - 0.75 mg/kg; Days 2 and 3, aprepitant, PO, prior to chemotherapy at the dosing regimens listed for the following age ranges: 4 months to <12 years of age - 2.0 mg/kg; 1 month to <4 months of age - 1.0 mg/kg; birth to <1 month of age - 0.5 mg/kg. Participants also receive ondansetron IV as per local standard of care. The use of dexamethasone IV is optional with the exception of the birth to 1 year old cohort.	
Reporting group title	Part V-fosaprepitant regimen
Reporting group description: Day 1, fosaprepitant, IV at a dose of 3 mg/kg prior to chemotherapy for participants 6 months to <12 years of age. Participants also receive ondansetron IV as per local standard of care, with or without dexamethasone IV.	
Reporting group title	Part IA-fosaprepitant 115 mg/aprepitant
Reporting group description: Day 1, fosaprepitant, IV at a dose of 115 mg and Days 2 and 3, aprepitant 80 mg orally (PO), prior to chemotherapy for participants from 12 to 17 years of age. Participants also receive ondansetron IV as per local standard of care, with or without dexamethasone IV.	
Reporting group title	Part IB-fosaprepitant 150 mg
Reporting group description: Day 1, fosaprepitant, IV at a dose of 150 mg, prior to chemotherapy for participants 12 to 17 years of age. Participants also receive ondansetron IV as per local standard of care, with or without dexamethasone IV.	
Reporting group title	Part IIA-aprepitant 80 mg equiv.

Reporting group description:

Day 1, aprepitant PO prior to chemotherapy at the dosing regimens listed for the following age ranges: 6 months to <12 years of age - 47 mg/m²; 4 months to <6 months of age - 2.0 mg/kg; 1 month to <4 months of age - 1.0 mg/kg; birth to <1 month of age - 0.5 mg/kg. Participants also receive ondansetron IV as per local standard of care, with or without dexamethasone IV.

Reporting group title	Part IIB-aprepitant 125 mg equiv.
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Reporting group description:

Day 1, aprepitant PO prior to chemotherapy at the dosing regimens listed for the following age ranges: 2 years to <12 years of age - 74 mg/m²; 6 months to <2 years of age - 1.3 mg/kg; 4 months to <6 months of age - 3.0 mg/kg; 1 month to <4 months of age - 1.5 mg/kg; birth to <1 month of age - 0.75 mg/kg. Participants also receive ondansetron IV as per local standard of care, with or without dexamethasone IV.

Reporting group title	Part III-ondansetron
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Reporting group description:

Ondansetron administered IV per local standard of care on Days 1, 2 and 3 prior to chemotherapy for participants from birth to <12 years of age. The use of IV dexamethasone is optional with the exception of the birth to 1 year cohort. No PK parameters were measured for this group; participants received no fosaprepitant or aprepitant.

Reporting group title	Part IV-aprepitant regimen
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Reporting group description:

Day 1, aprepitant, PO, prior to chemotherapy at the dosing regimens listed for the following age ranges: 4 months to <12 years of age - 3.0 mg/kg; 1 month to <4 months of age - 1.5 mg/kg; birth to <1 month of age - 0.75 mg/kg; Days 2 and 3, aprepitant, PO, prior to chemotherapy at the dosing regimens listed for the following age ranges: 4 months to <12 years of age - 2.0 mg/kg; 1 month to <4 months of age - 1.0 mg/kg; birth to <1 month of age - 0.5 mg/kg. Participants also receive ondansetron IV as per local standard of care. The use of dexamethasone IV is optional with the exception of the birth to 1 year old cohort. In addition to newly enrolled participants, participants who complete Part III may participate in Part IV.

Reporting group title	Part V-fosaprepitant regimen
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Reporting group description:

Day 1, fosaprepitant, IV at a dose of 3 mg/kg prior to chemotherapy for participants 6 months to <12 years of age. Participants also receive ondansetron IV as per local standard of care, with or without dexamethasone IV. In addition to newly enrolled participants, participants who complete Part IV may participate in Part V.

Primary: Area Under the Time-Concentration Curve from 0 to 24 hours (AUC_{0-24hr}) for Aprepitant - Parts IA and IB

End point title	Area Under the Time-Concentration Curve from 0 to 24 hours (AUC _{0-24hr}) for Aprepitant - Parts IA and IB ^[1]
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End point description:

AUC is a measure of the amount of aprepitant in the plasma. Fosaprepitant is a prodrug for aprepitant and is rapidly converted to aprepitant after intravenous (IV) administration. Blood samples for pharmacokinetic (PK) assessment were collected at the following time points: Part IA - Pre-dose and 0.25, 0.5, 0.75, 1, 1.5, 3, 4, 6, 8 and 24 hours (hr) post fosaprepitant dose; Part IB - Pre-dose and -0.75, -0.5, 0, 0.5, 1.5, 3, 4, 6, 8 and 24 hr post start of chemotherapy.

End point type	Primary
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End point timeframe:

Up to 24 hours post fosaprepitant/aprepitant dose

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: The design and sample size of this study were not designed to test hypotheses; therefore no statistical analyses were planned for this PK end point.

End point values	Part IA- fosaprepitant 115 mg/aprepitant	Part IB- fosaprepitant 150 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8 ^[2]	11 ^[3]		
Units: hr*ng/mL				
arithmetic mean (standard deviation)	19500 (± 8010)	30800 (± 7020)		

Notes:

[2] - Participants who received ≥1 dose fosaprepitant and/or aprepitant and were evaluable for end point.

[3] - Participants who received ≥1 dose fosaprepitant and were evaluable for end point.

Statistical analyses

No statistical analyses for this end point

Primary: Maximum Plasma Concentration (Cmax) for Aprepitant - Parts IA and IB

End point title	Maximum Plasma Concentration (Cmax) for Aprepitant - Parts IA and IB ^[4]
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End point description:

Cmax is a measure of the maximum amount of aprepitant in the plasma. Fosaprepitant is a prodrug for aprepitant and is rapidly converted to aprepitant after IV administration. Blood samples for PK assessment were collected at the following time points: Part IA - Pre-dose and 0.25, 0.5, 0.75, 1, 1.5, 3, 4, 6, 8 and 24 hr post fosaprepitant dose; Part IB - Pre-dose and -0.75, -0.5, 0, 0.5, 1.5, 3, 4, 6, 8, 24, 48 and 72 hr post start of chemotherapy.

End point type	Primary
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End point timeframe:

Up to 72 hours post fosaprepitant/aprepitant dose

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: The design and sample size of this study were not designed to test hypotheses; therefore no statistical analyses were planned for this PK end point.

End point values	Part IA- fosaprepitant 115 mg/aprepitant	Part IB- fosaprepitant 150 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12 ^[5]	11 ^[6]		
Units: ng/mL				
arithmetic mean (standard deviation)	3240 (± 1280)	5870 (± 2770)		

Notes:

[5] - Participants who received ≥1 dose fosaprepitant and/or aprepitant and were evaluable for end point.

[6] - Participants who received ≥1 dose fosaprepitant and were evaluable for end point.

Statistical analyses

No statistical analyses for this end point

Primary: Time to Cmax (Tmax) for Aprepitant - Parts IA and IB

End point title	Time to Cmax (Tmax) for Aprepitant - Parts IA and IB ^[7]
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End point description:

Tmax is a measure of the amount of time after dosing to when the maximum concentration of aprepitant was achieved. Fosaprepitant is a prodrug for aprepitant and is rapidly converted to aprepitant

after IV administration. Blood samples for PK assessment were collected at the following time points: Part IA - Pre-dose and 0.25, 0.5, 0.75, 1, 1.5, 3, 4, 6, 8 and 24 hr post fosaprepitant dose; Part IB - Pre-dose and -0.75, -0.5, 0, 0.5, 1.5, 3, 4, 6, 8, 24, 48 and 72 hr post start of chemotherapy.

End point type	Primary
End point timeframe:	
Up to 72 hours post fosaprepitant/aprepitant dose	

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: The design and sample size of this study were not designed to test hypotheses; therefore no statistical analyses were planned for this PK end point.

End point values	Part IA- fosaprepitant 115 mg/aprepitant	Part IB- fosaprepitant 150 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12 ^[8]	11 ^[9]		
Units: hr				
arithmetic mean (standard deviation)	0.41 (± 0.27)	0.64 (± 0.3)		

Notes:

[8] - Participants who received ≥1 dose fosaprepitant and/or aprepitant and were evaluable for end point.

[9] - Participants who received ≥1 dose fosaprepitant and were evaluable for end point.

Statistical analyses

No statistical analyses for this end point

Primary: Apparent Terminal Half-life (t_{1/2}) for Aprepitant - Parts IA and IB

End point title	Apparent Terminal Half-life (t _{1/2}) for Aprepitant - Parts IA and IB ^[10]
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End point description:

t_{1/2} is the amount of time from dosing until half of the aprepitant was metabolized from the body. Fosaprepitant is a prodrug for aprepitant and is rapidly converted to aprepitant after IV administration. Blood samples for PK assessment were collected at the following time points: Part IA - Pre-dose and 0.25, 0.5, 0.75, 1, 1.5, 3, 4, 6, 8 and 24 hr post fosaprepitant dose; Part IB - Predose and -0.75, -0.5, 0, 0.5, 1.5, 3, 4, 6, 8, 24, 48 and 72 hr post start of chemotherapy.

End point type	Primary
End point timeframe:	
Up to 72 hours post fosaprepitant/aprepitant dose	

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: The design and sample size of this study were not designed to test hypotheses; therefore no statistical analyses were planned for this PK end point.

End point values	Part IA- fosaprepitant 115 mg/aprepitant	Part IB- fosaprepitant 150 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6 ^[11]	11 ^[12]		
Units: hr				
arithmetic mean (standard deviation)	11 (± 4.42)	22.2 (± 19.8)		

Notes:

[11] - Participants who received ≥ 1 dose fosaprepitant and/or aprepitant and were evaluable for end point.

[12] - Participants who received ≥ 1 dose fosaprepitant and were evaluable for end point.

Statistical analyses

No statistical analyses for this end point

Primary: Cmax for Fosaprepitant - Parts IA and IB

End point title	Cmax for Fosaprepitant - Parts IA and IB ^[13]
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End point description:

Cmax is a measure of the maximum amount of fosaprepitant in the plasma. Blood samples for PK assessment were collected at the following time points: Part IA - Pre-dose and 0.25, 0.5, 0.75, 1, 1.5, 3, 4, 6, 8 and 24 hr post fosaprepitant dose, Part IB - Pre-dose and 0.5, 1.5, 3, 4, 6, 8, 24, 48 and 72 hr post fosaprepitant dose. No PK analyses were performed on the Part IA group because blood samples were not handled correctly.

End point type	Primary
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End point timeframe:

Up to 72 hours post fosaprepitant dose

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: The design and sample size of this study were not designed to test hypotheses; therefore no statistical analyses were planned for this PK end point.

End point values	Part IA- fosaprepitant 115 mg/aprepitant	Part IB- fosaprepitant 150 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[14]	11 ^[15]		
Units: ng/mL				
arithmetic mean (standard deviation)	()	1310 (\pm 964)		

Notes:

[14] - No PK analyses were performed on the Part IA group because blood samples were not handled correctly.

[15] - Participants who received ≥ 1 dose fosaprepitant and were evaluable for end point.

Statistical analyses

No statistical analyses for this end point

Primary: Tmax for Fosaprepitant - Parts IA and IB

End point title	Tmax for Fosaprepitant - Parts IA and IB ^[16]
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End point description:

Tmax is a measure of the amount of time after dosing to when the maximum concentration of fosaprepitant was achieved. Blood samples for PK assessment were collected at the following time points: Part IA - Pre-dose and 0.25, 0.5, 0.75, 1, 1.5, 3, 4, 6, 8 and 24 hr post fosaprepitant dose; Part IB - Pre-dose and 0.5, 1.5, 3, 4, 6, 8, 24, 48 and 72 hr post fosaprepitant dose. No PK analyses were performed on the Part IA group because blood samples were not handled correctly.

End point type	Primary
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End point timeframe:

Up to 72 hours post fosaprepitant dose

Notes:

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

Justification: The design and sample size of this study were not designed to test hypotheses; therefore no statistical analyses were planned for this PK end point.

End point values	Part IA- fosaprepitant 115 mg/aprepitant	Part IB- fosaprepitant 150 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[17]	11 ^[18]		
Units: hr				
arithmetic mean (standard deviation)	()	0.614 (± 0.251)		

Notes:

[17] - No PK analyses were performed on the Part IA group because blood samples were not handled correctly.

[18] - Participants who received ≥ 1 dose fosaprepitant and were evaluable for end point.

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants Experiencing at Least One Adverse Event (AE)

End point title	Number of Participants Experiencing at Least One Adverse Event (AE) ^[19]
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End point description:

An AE is defined as any unfavorable and unintended change in the structure, function, or chemistry of the body temporally associated with the use of the study drug, whether or not considered related to the use of the product. Participants were monitored for the occurrence AEs for up to 14 days after last dose of study drug.

End point type	Primary
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End point timeframe:

Up to 14 days after last dose of study drug (Up to 17 days)

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 were planned for this safety end point.

End point values	Part IA- fosaprepitant 115 mg/aprepitant	Part IB- fosaprepitant 150 mg	Part IIA- aprepitant 80 mg equiv.	Part IIB- aprepitant 125 mg equiv.
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12 ^[20]	11 ^[21]	19 ^[22]	19 ^[23]
Units: Participants	11	6	18	16

Notes:

[20] - Participants who received ≥ 1 dose of study drug.

[21] - Participants who received ≥ 1 dose of study drug.

[22] - Participants who received ≥ 1 dose of study drug.

[23] - Participants who received ≥ 1 dose of study drug.

End point values	Part III- ondansetron	Part IV- aprepitant regimen	Part V- fosaprepitant regimen	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	19 ^[24]	20 ^[25]	23 ^[26]	

Units: Participants	15	13	17	
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Notes:

[24] - Participants who received ≥ 1 dose of study drug.

[25] - Participants who received ≥ 1 dose of study drug.

[26] - Participants who received ≥ 1 dose of study drug.

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants Discontinuing Study Drug Due to an AE

End point title	Number of Participants Discontinuing Study Drug Due to an
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End point description:

An AE is defined as any unfavorable and unintended change in the structure, function, or chemistry of the body temporally associated with the use of the study drug, whether or not considered related to the use of the product. The numbers of participants who discontinued study drug due to an AE are summarized.

End point type	Primary
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End point timeframe:

Day 1 up to Day 3

Notes:

[27] - 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 were planned for this safety end point.

End point values	Part IA- fosaprepitant 115 mg/aprepitant	Part IB- fosaprepitant 150 mg	Part IIA- aprepitant 80 mg equiv.	Part IIB- aprepitant 125 mg equiv.
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12 ^[28]	11 ^[29]	19 ^[30]	19 ^[31]
Units: Participants	0	0	0	0

Notes:

[28] - Participants who received ≥ 1 dose of study drug.

[29] - Participants who received ≥ 1 dose of study drug.

[30] - Participants who received ≥ 1 dose of study drug.

[31] - Participants who received ≥ 1 dose of study drug.

End point values	Part III- ondansetron	Part IV- aprepitant regimen	Part V- fosaprepitant regimen	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	19 ^[32]	20 ^[33]	23 ^[34]	
Units: Participants	0	0	1	

Notes:

[32] - Participants who received ≥ 1 dose of study drug.

[33] - Participants who received ≥ 1 dose of study drug.

[34] - Participants who received ≥ 1 dose of study drug.

Statistical analyses

No statistical analyses for this end point

Primary: AUC0-24hr for Aprepitant - Parts IIA and IIB

End point title	AUC0-24hr for Aprepitant - Parts IIA and IIB ^[35]
End point description:	
AUC is a measure of the amount of aprepitant in the plasma. Blood samples for PK assessment were collected at the following time points: Parts IIA and IIB - Pre-dose and 1.5, 3, 4, 6, 8 and 24 hr post aprepitant dose.	
End point type	Primary
End point timeframe:	
Up to 24 hours post aprepitant dose	

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: The design and sample size of this study were not designed to test hypotheses; therefore no statistical analyses were planned for this PK end point.

End point values	Part IIA- aprepitant 80 mg equiv.	Part IIB- aprepitant 125 mg equiv.		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19 ^[36]	18 ^[37]		
Units: hr*ng/mL				
arithmetic mean (standard deviation)				
6 months to <2 years (n=5, 5)	20000 (± 7890)	6310 (± 2040)		
2 years to <6 years (n=8, 7)	16400 (± 8080)	23000 (± 8390)		
6 years to <12 years (n=6, 6)	16000 (± 4810)	22000 (± 9440)		

Notes:

[36] - Participants who received ≥1 dose aprepitant and were evaluable for end point.

[37] - Participants who received ≥1 dose aprepitant and were evaluable for end point.

Statistical analyses

No statistical analyses for this end point

Primary: AUC0-24hr for Aprepitant – Part IV

End point title	AUC0-24hr for Aprepitant – Part IV ^[38]
End point description:	
AUC is a measure of the amount of aprepitant in the plasma. Blood samples for PK assessment were collected at the following time points: Part IV - Pre-dose and 1.5, 3, 4, 6, 8 and 24 hr post aprepitant dose.	
End point type	Primary
End point timeframe:	
Up to 24 hours post aprepitant dose	

Notes:

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

Justification: The design and sample size of this study were not designed to test hypotheses; therefore no statistical analyses were planned for this PK end point.

End point values	Part IV- aprepitant regimen			
Subject group type	Reporting group			
Number of subjects analysed	18 ^[39]			
Units: hr*ng/mL				
arithmetic mean (standard deviation)				

6 months to <2 years (n=6)	21100 (± 11800)			
2 years to <6 years (n=6)	17300 (± 5060)			
6 years to <12 years (n=6)	24400 (± 15800)			

Notes:

[39] - Participants who received ≥ 1 dose aprepitant and were evaluable for end point.

Statistical analyses

No statistical analyses for this end point

Primary: AUC0-24hr for Aprepitant – Part V

End point title	AUC0-24hr for Aprepitant – Part V ^[40]
End point description:	
AUC is a measure of the amount of aprepitant in the plasma. Blood samples for PK assessment were collected at the following time points: Part V - Pre-dose and -0.75, -0.5, 0, 1.5, 3, 4, 6, 8 and 24 hr post start of chemotherapy.	
End point type	Primary
End point timeframe:	
Up to 24 hours post aprepitant dose	

Notes:

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

Justification: The design and sample size of this study were not designed to test hypotheses; therefore no statistical analyses were planned for this PK end point.

End point values	Part V- fosaprepitant regimen			
Subject group type	Reporting group			
Number of subjects analysed	21 ^[41]			
Units: hr*ng/mL				
arithmetic mean (standard deviation)				
6 months to <2 years (n=6)	11700 (± 6980)			
2 years to <6 years (n=7)	18300 (± 11100)			
6 years to <12 years (n=8)	19500 (± 6720)			

Notes:

[41] - Participants who received ≥ 1 dose fosaprepitant and were evaluable for end point.

Statistical analyses

No statistical analyses for this end point

Primary: Cmax for Aprepitant - Parts IIA and IIB

End point title	Cmax for Aprepitant - Parts IIA and IIB ^[42]
End point description:	
Cmax is a measure of the maximum amount of aprepitant in the plasma. Blood samples for PK assessment were collected at the following time points: Parts IIA and IIB - Pre-dose and 1.5, 3, 4, 6, 8, 24, 48 and 72 hr post aprepitant dose.	
End point type	Primary

End point timeframe:

Up to 72 hours post aprepitant dose

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: The design and sample size of this study were not designed to test hypotheses; therefore no statistical analyses were planned for this PK end point.

End point values	Part IIA- aprepitant 80 mg equiv.	Part IIB- aprepitant 125 mg equiv.		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19 ^[43]	18 ^[44]		
Units: ng/mL				
arithmetic mean (standard deviation)				
6 months to <2 years (n=5, 5)	1930 (± 1000)	659 (± 107)		
2 years to <6 years (n=8, 7)	1300 (± 609)	2100 (± 1170)		
6 years to <12 years (n=6, 6)	1300 (± 275)	1930 (± 873)		

Notes:

[43] - Participants who received ≥1 dose aprepitant and were evaluable for end point.

[44] - Participants who received ≥1 dose aprepitant and were evaluable for end point.

Statistical analyses

No statistical analyses for this end point

Primary: Cmax for Aprepitant - Part IV

End point title	Cmax for Aprepitant - Part IV ^[45]
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End point description:

Cmax is a measure of the maximum amount of aprepitant in the plasma. Blood samples for PK assessment were collected at the following time points: Part IV - Pre-dose and 1.5, 3, 4, 6, 8, 24, 48 and 72 hr post aprepitant dose.

End point type	Primary
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End point timeframe:

Up to 72 hours post aprepitant dose

Notes:

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

Justification: The design and sample size of this study were not designed to test hypotheses; therefore no statistical analyses were planned for this PK end point.

End point values	Part IV- aprepitant regimen			
Subject group type	Reporting group			
Number of subjects analysed	19 ^[46]			
Units: ng/mL				
arithmetic mean (standard deviation)				
6 months to <2 years (n=6)	1810 (± 925)			
2 years to <6 years (n=6)	1840 (± 933)			
6 years to <12 years (n=7)	1800 (± 1610)			

Notes:

[46] - Participants who received ≥1 dose aprepitant and were evaluable for end point.

Statistical analyses

No statistical analyses for this end point

Primary: Cmax for Aprepitant - Part V

End point title	Cmax for Aprepitant - Part V ^[47]
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End point description:

Cmax is a measure of the maximum amount of aprepitant in the plasma. Fosaprepitant is a prodrug for aprepitant and is rapidly converted to aprepitant after IV administration. Blood samples for PK assessment were collected at the following time points: Part V - Pre-dose and -0.75, -0.5, 0, 1.5, 3, 4, 6, 8, 24, 48 and 72 hr post start of chemotherapy.

End point type	Primary
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End point timeframe:

Up to 72 hours post fosaprepitant dose

Notes:

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

Justification: The design and sample size of this study were not designed to test hypotheses; therefore no statistical analyses were planned for this PK end point.

End point values	Part V- fosaprepitant regimen			
Subject group type	Reporting group			
Number of subjects analysed	22 ^[48]			
Units: ng/mL				
arithmetic mean (standard deviation)				
6 months to <2 years (n=7)	1700 (± 636)			
2 years to <6 years (n=7)	2430 (± 1100)			
6 years to <12 years (n=8)	2850 (± 641)			

Notes:

[48] - Participants who received ≥1 dose fosaprepitant and were evaluable for end point.

Statistical analyses

No statistical analyses for this end point

Primary: Tmax for Aprepitant - Parts IIA and IIB

End point title	Tmax for Aprepitant - Parts IIA and IIB ^[49]
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End point description:

Tmax is a measure of the amount of time after dosing to when the maximum concentration of aprepitant was achieved. Blood samples for PK assessment were collected at the following time points: Parts IIA and IIB - Pre-dose and 1.5, 3, 4, 6, 8, 24, 48 and 72 hr post aprepitant dose.

End point type	Primary
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End point timeframe:

Up to 72 hours post aprepitant dose

Notes:

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

Justification: The design and sample size of this study were not designed to test hypotheses; therefore no statistical analyses were planned for this PK end point.

End point values	Part IIA- aprepitant 80 mg equiv.	Part IIB- aprepitant 125 mg equiv.		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19 ^[50]	18 ^[51]		
Units: hr				
arithmetic mean (standard deviation)				
6 months to <2 years (n=5, 5)	2.33 (± 1.16)	3.45 (± 2.89)		
2 years to <6 years (n=8, 7)	3.78 (± 1.92)	5.28 (± 1.97)		
6 years to <12 years (n=6, 6)	5.17 (± 1.83)	3.08 (± 0.95)		

Notes:

[50] - Participants who received ≥1 dose aprepitant and were evaluable for end point.

[51] - Participants who received ≥1 dose aprepitant and were evaluable for end point.

Statistical analyses

No statistical analyses for this end point

Primary: Tmax for Aprepitant - Part V

End point title	Tmax for Aprepitant - Part V ^[52]
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End point description:

Tmax is a measure of the amount of time after dosing to when the maximum concentration of aprepitant was achieved. Fosaprepitant is a prodrug for aprepitant and is rapidly converted to aprepitant after IV administration. Blood samples for PK assessment were collected at the following time points: Part V - Pre-dose and -0.75, -0.5, 0, 1.5, 3, 4, 6, 8, 24, 48 and 72 hr post start of chemotherapy.

End point type	Primary
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End point timeframe:

Up to 72 hours post fosaprepitant dose

Notes:

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

Justification: The design and sample size of this study were not designed to test hypotheses; therefore no statistical analyses were planned for this PK end point.

End point values	Part V- fosaprepitant regimen			
Subject group type	Reporting group			
Number of subjects analysed	22 ^[53]			
Units: hr				
arithmetic mean (standard deviation)				
6 months to <2 years (n=7)	1.13 (± 0.17)			
2 years to <6 years (n=7)	1.41 (± 0.83)			
6 years to <12 years (n=8)	1.07 (± 0.11)			

Notes:

[53] - Participants who received ≥1 dose fosaprepitant and were evaluable for end point.

Statistical analyses

No statistical analyses for this end point

Primary: Tmax for Aprepitant - Part IV

End point title	Tmax for Aprepitant - Part IV ^[54]
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End point description:

Tmax is a measure of the amount of time after dosing to when the maximum concentration of aprepitant was achieved. Blood samples for PK assessment were collected at the following time points: Part IV - Pre-dose and 1.5, 3, 4, 6, 8, 24, 48 and 72 hr post aprepitant dose.

End point type	Primary
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End point timeframe:

Up to 72 hours post aprepitant dose

Notes:

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

Justification: The design and sample size of this study were not designed to test hypotheses; therefore no statistical analyses were planned for this PK end point.

End point values	Part IV- aprepitant regimen			
Subject group type	Reporting group			
Number of subjects analysed	19 ^[55]			
Units: hr				
arithmetic mean (standard deviation)				
6 months to <2 years (n=6)	7.34 (± 8.28)			
2 years to <6 years (n=6)	4.92 (± 2.2)			
6 years to <12 years (n=7)	6.42 (± 7.84)			

Notes:

[55] - Participants who received ≥1 dose aprepitant and were evaluable for end point.

Statistical analyses

No statistical analyses for this end point

Primary: t1/2 for Aprepitant - Parts IIA and IIB

End point title	t1/2 for Aprepitant - Parts IIA and IIB ^[56]
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End point description:

t1/2 is the amount of time from dosing until half of the aprepitant was metabolized from the body. Blood samples for PK assessment were collected at the following time points: Parts IIA and IIB - Pre-dose and 1.5, 3, 4, 6, 8, 24, 48 and 72 hr post aprepitant dose.

End point type	Primary
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End point timeframe:

Up to 72 hours post aprepitant dose

Notes:

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

Justification: The design and sample size of this study were not designed to test hypotheses; therefore no statistical analyses were planned for this PK end point.

End point values	Part IIA- aprepitant 80 mg equiv.	Part IIB- aprepitant 125 mg equiv.		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16 ^[57]	13 ^[58]		
Units: hr				
arithmetic mean (standard deviation)				
6 months to <2 years (n=5, 3)	7.28 (± 1.47)	8.09 (± 2.54)		
2 years to <6 years (n=6, 4)	8.27 (± 2.67)	6.06 (± 3.03)		
6 years to <12 years (n=5, 6)	9.17 (± 4)	6.89 (± 1.35)		

Notes:

[57] - Participants who received ≥ 1 dose aprepitant and were evaluable for end point.

[58] - Participants who received ≥ 1 dose aprepitant and were evaluable for end point.

Statistical analyses

No statistical analyses for this end point

Primary: t1/2 for Aprepitant - Part IV

End point title	t1/2 for Aprepitant - Part IV ^[59]
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End point description:

t1/2 is the amount of time from dosing until half of the aprepitant was metabolized from the body. Blood samples for PK assessment were collected at the following time points: Part IV - Pre-dose and 1.5, 3, 4, 6, 8, 24, 48 and 72 hr post aprepitant dose.

End point type	Primary
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End point timeframe:

Up to 72 hours post aprepitant dose

Notes:

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

Justification: The design and sample size of this study were not designed to test hypotheses; therefore no statistical analyses were planned for this PK end point.

End point values	Part IV- aprepitant regimen			
Subject group type	Reporting group			
Number of subjects analysed	12 ^[60]			
Units: hr				
arithmetic mean (standard deviation)				
6 months to <2 years (n=3)	6.18 (± 4.12)			
2 years to <6 years (n=5)	9.21 (± 5.57)			
6 years to <12 years (n=4)	10.8 (± 4.27)			

Notes:

[60] - Participants who received ≥ 1 dose aprepitant and were evaluable for end point.

Statistical analyses

No statistical analyses for this end point

Primary: t1/2 for Aprepitant - Part V

End point title	t1/2 for Aprepitant - Part V ^[61]
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End point description:

t1/2 is the amount of time from dosing until half of the aprepitant was metabolized from the body. Fosaprepitant is a prodrug for aprepitant and is rapidly converted to aprepitant after IV administration. Blood samples for PK assessment were collected at the following time points: Part V - Pre-dose and - 0.75, -0.5, 0, 1.5, 3, 4, 6, 8, 24, 48 and 72 hr post start of chemotherapy.

End point type	Primary
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End point timeframe:

Up to 72 hours post fosaprepitant dose

Notes:

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

Justification: The design and sample size of this study were not designed to test hypotheses; therefore no statistical analyses were planned for this PK end point.

End point values	Part V- fosaprepitant regimen			
Subject group type	Reporting group			
Number of subjects analysed	21 ^[62]			
Units: hr				
arithmetic mean (standard deviation)				
6 months to <2 years (n=6)	7.71 (± 3.1)			
2 years to <6 years (n=7)	6.44 (± 2.35)			
6 years to <12 years (n=8)	8.76 (± 3.34)			

Notes:

[62] - Participants who received ≥1 dose fosaprepitant and were evaluable for end point.

Statistical analyses

No statistical analyses for this end point

Primary: Cmax for Fosaprepitant - Part V

End point title	Cmax for Fosaprepitant - Part V ^[63]
End point description:	
Cmax is a measure of the maximum amount of fosaprepitant in the plasma. Blood samples for PK assessment were collected at the following time points: Part V - Pre-dose and -0.75, -0.5, 0, 0.5, 1.5, 3, 4, 6, 8, 24, 48 and 72 hr post start of chemotherapy.	
End point type	Primary
End point timeframe:	
Up to 72 hours post fosaprepitant dose	

Notes:

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

Justification: The design and sample size of this study were not designed to test hypotheses; therefore no statistical analyses were planned for this PK end point.

End point values	Part V- fosaprepitant regimen			
Subject group type	Reporting group			
Number of subjects analysed	23 ^[64]			
Units: ng/mL				
arithmetic mean (standard deviation)				
6 months to <2 years (n=7)	2756 (± 3364)			
2 years to <6 years (n=8)	3034 (± 1718)			
6 years to <12 years (n=8)	1654 (± 1995)			

Notes:

[64] - Participants who received ≥1 dose fosaprepitant and were evaluable for end point.

Statistical analyses

No statistical analyses for this end point

Primary: Tmax for Fosaprepitant - Part V

End point title	Tmax for Fosaprepitant - Part V ^[65]
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End point description:

Tmax is a measure of the amount of time after dosing to when the maximum concentration of fosaprepitant was achieved. Blood samples for PK assessment were collected at the following time points: Part V - Pre-dose and -0.75, -0.5, 0, 0.5, 1.5, 3, 4, 6, 8, 24, 48 and 72 hr post start of chemotherapy.

End point type	Primary
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End point timeframe:

Up to 72 hours post fosaprepitant dose

Notes:

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

Justification: The design and sample size of this study were not designed to test hypotheses; therefore no statistical analyses were planned for this PK end point.

End point values	Part V- fosaprepitant regimen			
Subject group type	Reporting group			
Number of subjects analysed	22 ^[66]			
Units: hr				
arithmetic mean (standard deviation)				
6 months to <2 years (n=7)	1.13 (± 0.175)			
2 years to <6 years (n=7)	1.05 (± 0.089)			
6 years to <12 years (n=8)	1.04 (± 0.088)			

Notes:

[66] - Participants who received ≥1 dose fosaprepitant and were evaluable for end point.

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentration and PK Parameters of Dexamethasone in Participants from Birth to 1 Year of Age

End point title	Plasma Concentration and PK Parameters of Dexamethasone in Participants from Birth to 1 Year of Age
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End point description:

Blood samples for PK assessment were to be collected at the following time points: Parts II and V - Pre-dose and 1.5, 3, 4, 6, 8 and 24 hr post start of chemotherapy; Parts III and IV - Immediately after infusion of dexamethasone and 0.5, 1.5, 3, 8 and 24 hr post start of chemotherapy. No analyses were conducted; enrollment in the birth to 1 year cohort was not opened as enrollment in birth to <6 month olds in Part II was unsuccessful.

End point type	Secondary
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End point timeframe:

Up to 24 hours post dexamethasone dose

End point values	Part IA- fosaprepitant 115 mg/aprepitant	Part IB- fosaprepitant 150 mg	Part IIA- aprepitant 80 mg equiv.	Part IIB- aprepitant 125 mg equiv.
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0 ^[67]	0 ^[68]	0 ^[69]	0 ^[70]
Units: ng/mL				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[67] - Analysis not conducted; enrollment in birth to 1 year cohort not opened.

[68] - Analysis not conducted; enrollment in birth to 1 year cohort not opened.

[69] - Analysis not conducted; enrollment in birth to 1 year cohort not opened.

[70] - Analysis not conducted; enrollment in birth to 1 year cohort not opened.

End point values	Part III- ondansetron	Part IV- aprepitant regimen	Part V- fosaprepitant regimen	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0 ^[71]	0 ^[72]	0 ^[73]	
Units: ng/mL				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[71] - Analysis not conducted; enrollment in birth to 1 year cohort not opened.

[72] - Analysis not conducted; enrollment in birth to 1 year cohort not opened.

[73] - Analysis not conducted; enrollment in birth to 1 year cohort not opened.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 14 days after last dose of study drug (Up to 17 days)

Adverse event reporting additional description:

The population consisted of all randomized participants who received ≥ 1 dose of study drug. Participants who completed Part III could enter Part IV and participants who completed Part IV could enter Part V. Participants are counted once for each study part in which they participated. AEs are reported based on the study drug taken at the time of AE.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	16.1
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Reporting groups

Reporting group title	Part IA-fosaprepitant 115 mg/aprepitant
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Reporting group description:

Day 1, fosaprepitant, IV at a dose of 115 mg and Days 2 and 3, aprepitant 80 mg PO, prior to chemotherapy for participants from 12 to 17 years of age. Participants also receive ondansetron IV as per local standard of care, with or without dexamethasone IV.

Reporting group title	Part IB-fosaprepitant 150 mg
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Reporting group description:

Day 1, fosaprepitant, IV at a dose of 150 mg, prior to chemotherapy for participants 12 to 17 years of age. Participants also receive ondansetron IV as per local standard of care, with or without dexamethasone IV.

Reporting group title	Part IIA-aprepitant 80 mg equiv.
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Reporting group description:

Day 1, aprepitant, PO prior to chemotherapy at the dosing regimens listed for the following age ranges: 6 months to <12 years of age - 47 mg/m²; 4 months to <6 months of age - 2.0 mg/kg; 1 month to <4 months of age - 1.0 mg/kg; birth to <1 month of age - 0.5 mg/kg. Participants also receive ondansetron IV as per local standard of care, with or without dexamethasone IV.

Reporting group title	Part IIB-aprepitant 125 mg equiv.
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Reporting group description:

Day 1, aprepitant, PO prior to chemotherapy at the dosing regimens listed for the following age ranges: 2 years to <12 years of age - 74 mg/m²; 6 months to <2 years of age - 1.3 mg/kg; 4 months to <6 months of age - 3.0 mg/kg; 1 month to <4 months of age - 1.5 mg/kg; birth to <1 month of age - 0.75 mg/kg. Participants also receive ondansetron IV as per local standard of care, with or without dexamethasone IV.

Reporting group title	Part III-ondansetron
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Reporting group description:

Ondansetron administered IV per local standard of care on Days 1, 2 and 3 prior to chemotherapy for participants from birth to <12 years of age. The use of IV dexamethasone is optional with the exception of the birth to 1 year cohort. No PK parameters were measured for this group; participants received no fosaprepitant or aprepitant.

Reporting group title	Part IV-aprepitant regimen
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Reporting group description:

Day 1, aprepitant, PO prior to chemotherapy at the dosing regimens listed for the following age ranges: 4 months to <12 years of age - 3.0 mg/kg; 1 month to <4 months of age - 1.5 mg/kg; birth to <1 month of age - 0.75 mg/kg; Days 2 and 3, aprepitant, PO, prior to chemotherapy at the dosing regimens listed for the following age ranges: 4 months to <12 years of age - 2.0 mg/kg; 1 month to <4 months of age - 1.0 mg/kg; birth to <1 month of age - 0.5 mg/kg. Participants also receive ondansetron IV as per local standard of care. The use of dexamethasone IV is optional with the exception of the birth to 1 year old cohort.

Reporting group title	Part V-fosaprepitant regimen
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Reporting group description:

Day 1, fosaprepitant, IV at a dose of 3 mg/kg prior to chemotherapy for participants 6 months to <12 years of age. Participants also receive ondansetron IV as per local standard of care, with or without

Serious adverse events	Part IA- fosaprepitant 115 mg/aprepitant	Part IB-fosaprepitant 150 mg	Part IIA-aprepitant 80 mg equiv.
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 12 (33.33%)	1 / 11 (9.09%)	7 / 19 (36.84%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
Neutrophil count decreased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	0 / 19 (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
Injury, poisoning and procedural complications			
Wound dehiscence			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	0 / 19 (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			
Febrile neutropenia			
subjects affected / exposed	2 / 12 (16.67%)	0 / 11 (0.00%)	4 / 19 (21.05%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphopenia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	0 / 19 (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
Neutropenia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 11 (0.00%)	2 / 19 (10.53%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			

subjects affected / exposed	1 / 12 (8.33%)	0 / 11 (0.00%)	0 / 19 (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
General disorders and administration site conditions			
Device dislocation			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mucosal inflammation			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	0 / 19 (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			
Diarrhoea			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enteritis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	0 / 19 (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
Nausea			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	2 / 19 (10.53%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Catheter site cellulitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	0 / 19 (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

Enterobacter bacteraemia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 11 (9.09%)	0 / 19 (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
Septic shock			
subjects affected / exposed	1 / 12 (8.33%)	0 / 11 (0.00%)	0 / 19 (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
Vulval abscess			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
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			
Dehydration			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	0 / 19 (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	0 / 12 (0.00%)	0 / 11 (0.00%)	0 / 19 (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
Hyponatraemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	0 / 19 (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	Part IIB-aprepitant 125 mg equiv.	Part III-ondansetron	Part IV-aprepitant regimen
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 19 (21.05%)	5 / 19 (26.32%)	2 / 20 (10.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
Neutrophil count decreased			

subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	0 / 20 (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
Injury, poisoning and procedural complications			
Wound dehiscence			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 20 (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			
Febrile neutropenia			
subjects affected / exposed	2 / 19 (10.53%)	4 / 19 (21.05%)	2 / 20 (10.00%)
occurrences causally related to treatment / all	0 / 2	0 / 4	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphopenia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	0 / 20 (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
Neutropenia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	0 / 20 (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
Thrombocytopenia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	0 / 20 (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
General disorders and administration site conditions			
Device dislocation			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 20 (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	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 20 (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			
Diarrhoea			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 20 (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
Enteritis			
subjects affected / exposed	0 / 19 (0.00%)	1 / 19 (5.26%)	0 / 20 (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
Nausea			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 20 (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
Vomiting			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 20 (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			
Catheter site cellulitis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	0 / 20 (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
Enterobacter bacteraemia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 20 (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
Septic shock			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 20 (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
Vulval abscess			

subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 20 (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			
Dehydration			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 20 (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 / 19 (5.26%)	0 / 19 (0.00%)	0 / 20 (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
Hyponatraemia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 20 (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	Part V-fosaprepitant regimen		
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 23 (39.13%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Investigations			
Neutrophil count decreased			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Wound dehiscence			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Febrile neutropenia			

subjects affected / exposed	4 / 23 (17.39%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Lymphopenia			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Neutropenia			
subjects affected / exposed	2 / 23 (8.70%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Thrombocytopenia			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Device dislocation			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Mucosal inflammation			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Enteritis			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Nausea			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Catheter site cellulitis			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Enterobacter bacteraemia			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Septic shock			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vulval abscess			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypokalaemia			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Hyponatraemia			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Part IA- fosaprepitant 115 mg/aprepitant	Part IB-fosaprepitant 150 mg	Part IIA-aprepitant 80 mg equiv.
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 12 (91.67%)	5 / 11 (45.45%)	18 / 19 (94.74%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps) Oncologic complication			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 12 (0.00%)	1 / 11 (9.09%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 12 (8.33%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Chills			
subjects affected / exposed	1 / 12 (8.33%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Fatigue			
subjects affected / exposed	1 / 12 (8.33%)	1 / 11 (9.09%)	0 / 19 (0.00%)
occurrences (all)	1	1	0
Hyperthermia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Implant site reaction			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Irritability			

subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Mucosal inflammation			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	2 / 19 (10.53%)
occurrences (all)	0	0	2
Product taste abnormal			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Secretion discharge			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Perineal erythema			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Vaginal haemorrhage			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Asthmatic crisis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Dyspnoea			
subjects affected / exposed	1 / 12 (8.33%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Epistaxis			

subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Oropharyngeal pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Blood bicarbonate decreased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Blood glucose increased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Blood phosphorus decreased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Blood potassium decreased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Blood sodium decreased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Blood uric acid increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Body temperature increased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Drug clearance decreased			

subjects affected / exposed	0 / 12 (0.00%)	1 / 11 (9.09%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Glucose urine present			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Haemoglobin decreased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Lymphocyte count decreased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Neutrophil count decreased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Platelet count decreased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Red blood cell count decreased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Staphylococcus test positive			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
White blood cell count decreased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Accidental overdose			

subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 11 (0.00%) 0	0 / 19 (0.00%) 0
Excoriation subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 11 (0.00%) 0	1 / 19 (5.26%) 1
Traumatic haematoma subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 11 (0.00%) 0	1 / 19 (5.26%) 1
Congenital, familial and genetic disorders Aplasia subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 11 (0.00%) 0	1 / 19 (5.26%) 1
Cardiac disorders Sinus tachycardia subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 11 (9.09%) 1	0 / 19 (0.00%) 0
Tachycardia subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 11 (0.00%) 0	1 / 19 (5.26%) 1
Nervous system disorders Dizziness subjects affected / exposed occurrences (all)	3 / 12 (25.00%) 3	0 / 11 (0.00%) 0	0 / 19 (0.00%) 0
Dysgeusia subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 11 (0.00%) 0	0 / 19 (0.00%) 0
Formication subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 11 (0.00%) 0	0 / 19 (0.00%) 0
Headache subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 11 (0.00%) 0	2 / 19 (10.53%) 4
Parosmia subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 11 (0.00%) 0	0 / 19 (0.00%) 0
Sensory disturbance			

subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 11 (9.09%) 1	0 / 19 (0.00%) 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 12 (25.00%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	3	0	0
Bone marrow failure			
subjects affected / exposed	1 / 12 (8.33%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Coagulopathy			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Febrile neutropenia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Leukocytosis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Leukopenia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 11 (9.09%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Lymphopenia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Neutropenia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 11 (0.00%)	2 / 19 (10.53%)
occurrences (all)	1	0	2
Thrombocytopenia			
subjects affected / exposed	2 / 12 (16.67%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	2	0	0
Eye disorders			
Conjunctivitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Eye irritation			

subjects affected / exposed	0 / 12 (0.00%)	1 / 11 (9.09%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Eye pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Eye pruritus			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Vision blurred			
subjects affected / exposed	1 / 12 (8.33%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 12 (8.33%)	0 / 11 (0.00%)	2 / 19 (10.53%)
occurrences (all)	2	0	2
Diarrhoea			
subjects affected / exposed	0 / 12 (0.00%)	1 / 11 (9.09%)	1 / 19 (5.26%)
occurrences (all)	0	1	1
Constipation			
subjects affected / exposed	0 / 12 (0.00%)	1 / 11 (9.09%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Flatulence			
subjects affected / exposed	1 / 12 (8.33%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Haematemesis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Gingival bleeding			
subjects affected / exposed	1 / 12 (8.33%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Lip blister			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	3 / 12 (25.00%)	0 / 11 (0.00%)	2 / 19 (10.53%)
occurrences (all)	4	0	3

Odynophagia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 11 (0.00%)	2 / 19 (10.53%)
occurrences (all)	1	0	2
Perianal erythema			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Retching			
subjects affected / exposed	1 / 12 (8.33%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	2
Salivary hypersecretion			
subjects affected / exposed	1 / 12 (8.33%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Stomatitis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 11 (9.09%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Tongue ulceration			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Toothache			
subjects affected / exposed	1 / 12 (8.33%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Vomiting			
subjects affected / exposed	5 / 12 (41.67%)	0 / 11 (0.00%)	9 / 19 (47.37%)
occurrences (all)	7	0	23
Hepatobiliary disorders			
Liver disorder			
subjects affected / exposed	0 / 12 (0.00%)	1 / 11 (9.09%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 11 (9.09%)	0 / 19 (0.00%)
occurrences (all)	0	2	0
Night sweats			
subjects affected / exposed	1 / 12 (8.33%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Pruritus			

subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 11 (0.00%) 0	0 / 19 (0.00%) 0
Rash subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 11 (0.00%) 0	2 / 19 (10.53%) 3
Skin fissures subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 11 (0.00%) 0	0 / 19 (0.00%) 0
Renal and urinary disorders Haematuria subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 11 (9.09%) 1	0 / 19 (0.00%) 0
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 11 (9.09%) 1	0 / 19 (0.00%) 0
Myalgia subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 11 (0.00%) 0	0 / 19 (0.00%) 0
Pain in extremity subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 11 (0.00%) 0	1 / 19 (5.26%) 1
Infections and infestations Cystitis subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 11 (0.00%) 0	0 / 19 (0.00%) 0
Influenza subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 11 (0.00%) 0	0 / 19 (0.00%) 0
Nasopharyngitis subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 11 (0.00%) 0	0 / 19 (0.00%) 0
Oral bacterial infection subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 11 (0.00%) 0	1 / 19 (5.26%) 1
Upper respiratory tract infection			

subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 11 (0.00%) 0	1 / 19 (5.26%) 1
Oral candidiasis subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 11 (0.00%) 0	0 / 19 (0.00%) 0
Urinary tract infection subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 11 (0.00%) 0	1 / 19 (5.26%) 1
Metabolism and nutrition disorders			
Decreased appetite subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 11 (0.00%) 0	0 / 19 (0.00%) 0
Dehydration subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 11 (0.00%) 0	0 / 19 (0.00%) 0
Hyperglycaemia subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 11 (0.00%) 0	0 / 19 (0.00%) 0
Hypoalbuminaemia subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 11 (0.00%) 0	0 / 19 (0.00%) 0
Hypocalcaemia subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 11 (0.00%) 0	0 / 19 (0.00%) 0
Hypokalaemia subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 11 (0.00%) 0	0 / 19 (0.00%) 0
Hypomagnesaemia subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 11 (0.00%) 0	1 / 19 (5.26%) 1
Hypophosphataemia subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 11 (0.00%) 0	0 / 19 (0.00%) 0

Non-serious adverse events	Part IIB-aprepitant 125 mg equiv.	Part III-ondansetron	Part IV-aprepitant regimen
Total subjects affected by non-serious adverse events			

subjects affected / exposed	15 / 19 (78.95%)	15 / 19 (78.95%)	13 / 20 (65.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Oncologic complication			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Chills			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	0 / 19 (0.00%)	1 / 19 (5.26%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Hyperthermia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Implant site reaction			
subjects affected / exposed	0 / 19 (0.00%)	1 / 19 (5.26%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Irritability			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
Mucosal inflammation			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Pyrexia			

subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	1 / 19 (5.26%) 1	1 / 20 (5.00%) 1
Product taste abnormal subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 19 (0.00%) 0	0 / 20 (0.00%) 0
Secretion discharge subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 19 (0.00%) 0	0 / 20 (0.00%) 0
Reproductive system and breast disorders Perineal erythema subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0	1 / 19 (5.26%) 1	0 / 20 (0.00%) 0
Vaginal haemorrhage subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0	1 / 19 (5.26%) 1	0 / 20 (0.00%) 0
Respiratory, thoracic and mediastinal disorders Asthmatic crisis subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0	1 / 19 (5.26%) 1	0 / 20 (0.00%) 0
Cough subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0	1 / 19 (5.26%) 1	1 / 20 (5.00%) 1
Dyspnoea subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0	0 / 19 (0.00%) 0	0 / 20 (0.00%) 0
Epistaxis subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0	0 / 19 (0.00%) 0	0 / 20 (0.00%) 0
Oropharyngeal pain subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	1 / 19 (5.26%) 1	0 / 20 (0.00%) 0
Investigations Alanine aminotransferase increased subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0	0 / 19 (0.00%) 0	1 / 20 (5.00%) 1
Aspartate aminotransferase			

increased			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Blood bicarbonate decreased			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Blood glucose increased			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Blood phosphorus decreased			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Blood potassium decreased			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Blood sodium decreased			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Blood uric acid increased			
subjects affected / exposed	0 / 19 (0.00%)	1 / 19 (5.26%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Body temperature increased			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Drug clearance decreased			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 19 (0.00%)	1 / 19 (5.26%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Glucose urine present			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Haemoglobin decreased			
subjects affected / exposed	1 / 19 (5.26%)	1 / 19 (5.26%)	0 / 20 (0.00%)
occurrences (all)	1	1	0

Lymphocyte count decreased subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0	3 / 19 (15.79%) 3	0 / 20 (0.00%) 0
Neutrophil count decreased subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	3 / 19 (15.79%) 3	0 / 20 (0.00%) 0
Platelet count decreased subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	3 / 19 (15.79%) 3	1 / 20 (5.00%) 1
Red blood cell count decreased subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0	1 / 19 (5.26%) 1	0 / 20 (0.00%) 0
Staphylococcus test positive subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0	1 / 19 (5.26%) 1	0 / 20 (0.00%) 0
Weight decreased subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0	2 / 19 (10.53%) 2	0 / 20 (0.00%) 0
White blood cell count decreased subjects affected / exposed occurrences (all)	2 / 19 (10.53%) 2	3 / 19 (15.79%) 3	0 / 20 (0.00%) 0
Injury, poisoning and procedural complications			
Accidental overdose subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 19 (0.00%) 0	0 / 20 (0.00%) 0
Excoriation subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0	0 / 19 (0.00%) 0	0 / 20 (0.00%) 0
Traumatic haematoma subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0	0 / 19 (0.00%) 0	0 / 20 (0.00%) 0
Congenital, familial and genetic disorders			
Aplasia subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0	0 / 19 (0.00%) 0	0 / 20 (0.00%) 0
Cardiac disorders			

Sinus tachycardia subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0	0 / 19 (0.00%) 0	0 / 20 (0.00%) 0
Tachycardia subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0	0 / 19 (0.00%) 0	0 / 20 (0.00%) 0
Nervous system disorders			
Dizziness subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0	0 / 19 (0.00%) 0	1 / 20 (5.00%) 1
Dysgeusia subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0	1 / 19 (5.26%) 1	0 / 20 (0.00%) 0
Formication subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0	0 / 19 (0.00%) 0	0 / 20 (0.00%) 0
Headache subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	3 / 19 (15.79%) 3	1 / 20 (5.00%) 1
Parosmia subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0	1 / 19 (5.26%) 1	0 / 20 (0.00%) 0
Sensory disturbance subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0	0 / 19 (0.00%) 0	0 / 20 (0.00%) 0
Blood and lymphatic system disorders			
Anaemia subjects affected / exposed occurrences (all)	5 / 19 (26.32%) 5	5 / 19 (26.32%) 5	3 / 20 (15.00%) 3
Bone marrow failure subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0	0 / 19 (0.00%) 0	0 / 20 (0.00%) 0
Coagulopathy subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0	1 / 19 (5.26%) 1	0 / 20 (0.00%) 0
Febrile neutropenia			

subjects affected / exposed	0 / 19 (0.00%)	2 / 19 (10.53%)	1 / 20 (5.00%)
occurrences (all)	0	2	1
Leukocytosis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Leukopenia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Lymphopenia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Neutropenia			
subjects affected / exposed	4 / 19 (21.05%)	3 / 19 (15.79%)	3 / 20 (15.00%)
occurrences (all)	4	3	3
Thrombocytopenia			
subjects affected / exposed	3 / 19 (15.79%)	4 / 19 (21.05%)	5 / 20 (25.00%)
occurrences (all)	3	5	5
Eye disorders			
Conjunctivitis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Eye irritation			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Eye pain			
subjects affected / exposed	0 / 19 (0.00%)	1 / 19 (5.26%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Eye pruritus			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Vision blurred			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal pain			

subjects affected / exposed	4 / 19 (21.05%)	1 / 19 (5.26%)	1 / 20 (5.00%)
occurrences (all)	4	1	1
Diarrhoea			
subjects affected / exposed	1 / 19 (5.26%)	3 / 19 (15.79%)	1 / 20 (5.00%)
occurrences (all)	1	3	1
Constipation			
subjects affected / exposed	0 / 19 (0.00%)	3 / 19 (15.79%)	1 / 20 (5.00%)
occurrences (all)	0	3	1
Flatulence			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Haematemesis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Gingival bleeding			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Lip blister			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Nausea			
subjects affected / exposed	6 / 19 (31.58%)	0 / 19 (0.00%)	1 / 20 (5.00%)
occurrences (all)	6	0	2
Odynophagia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Perianal erythema			
subjects affected / exposed	0 / 19 (0.00%)	1 / 19 (5.26%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Retching			
subjects affected / exposed	1 / 19 (5.26%)	1 / 19 (5.26%)	0 / 20 (0.00%)
occurrences (all)	1	1	0
Salivary hypersecretion			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Stomatitis			

subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0	3 / 19 (15.79%) 3	0 / 20 (0.00%) 0
Tongue ulceration subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0	0 / 19 (0.00%) 0	0 / 20 (0.00%) 0
Toothache subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0	0 / 19 (0.00%) 0	0 / 20 (0.00%) 0
Vomiting subjects affected / exposed occurrences (all)	8 / 19 (42.11%) 21	2 / 19 (10.53%) 2	1 / 20 (5.00%) 1
Hepatobiliary disorders Liver disorder subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0	0 / 19 (0.00%) 0	0 / 20 (0.00%) 0
Skin and subcutaneous tissue disorders Dermatitis subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 19 (0.00%) 0	0 / 20 (0.00%) 0
Night sweats subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0	0 / 19 (0.00%) 0	0 / 20 (0.00%) 0
Pruritus subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0	1 / 19 (5.26%) 1	0 / 20 (0.00%) 0
Rash subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0	1 / 19 (5.26%) 1	1 / 20 (5.00%) 1
Skin fissures subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0	0 / 19 (0.00%) 0	0 / 20 (0.00%) 0
Renal and urinary disorders Haematuria subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0	0 / 19 (0.00%) 0	0 / 20 (0.00%) 0
Musculoskeletal and connective tissue disorders			

Back pain			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Pain in extremity			
subjects affected / exposed	0 / 19 (0.00%)	1 / 19 (5.26%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Cystitis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 19 (0.00%)	1 / 19 (5.26%)	2 / 20 (10.00%)
occurrences (all)	0	1	2
Oral bacterial infection			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Oral candidiasis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Urinary tract infection			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 19 (0.00%)	1 / 19 (5.26%)	2 / 20 (10.00%)
occurrences (all)	0	1	2
Dehydration			

subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	2 / 20 (10.00%)
occurrences (all)	0	0	2
Hyperglycaemia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0
Hypoalbuminaemia			
subjects affected / exposed	2 / 19 (10.53%)	0 / 19 (0.00%)	2 / 20 (10.00%)
occurrences (all)	2	0	2
Hypocalcaemia			
subjects affected / exposed	2 / 19 (10.53%)	0 / 19 (0.00%)	1 / 20 (5.00%)
occurrences (all)	2	0	1
Hypokalaemia			
subjects affected / exposed	0 / 19 (0.00%)	2 / 19 (10.53%)	0 / 20 (0.00%)
occurrences (all)	0	2	0
Hypomagnesaemia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
Hypophosphataemia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1

Non-serious adverse events	Part V-fosaprepitant regimen		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 23 (69.57%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Oncologic complication			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Vascular disorders			
Hypotension			
subjects affected / exposed	2 / 23 (8.70%)		
occurrences (all)	2		
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		

Chills			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Fatigue			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Hyperthermia			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Implant site reaction			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Irritability			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Mucosal inflammation			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Pain			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Pyrexia			
subjects affected / exposed	7 / 23 (30.43%)		
occurrences (all)	8		
Product taste abnormal			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Secretion discharge			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Reproductive system and breast disorders			
Perineal erythema			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Vaginal haemorrhage			

subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Asthmatic crisis			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Cough			
subjects affected / exposed	2 / 23 (8.70%)		
occurrences (all)	2		
Dyspnoea			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Epistaxis			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Oropharyngeal pain			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Blood bicarbonate decreased			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Blood glucose increased			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Blood phosphorus decreased			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Blood potassium decreased			

subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Blood sodium decreased			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Blood uric acid increased			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Body temperature increased			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Drug clearance decreased			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Glucose urine present			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Haemoglobin decreased			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Lymphocyte count decreased			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Neutrophil count decreased			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Platelet count decreased			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Red blood cell count decreased			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Staphylococcus test positive			

subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Weight decreased			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
White blood cell count decreased			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Excoriation			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Traumatic haematoma			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Congenital, familial and genetic disorders			
Aplasia			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Sinus tachycardia			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Tachycardia			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Dysgeusia			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		

Formication			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Headache			
subjects affected / exposed	2 / 23 (8.70%)		
occurrences (all)	2		
Parosmia			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Sensory disturbance			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 23 (13.04%)		
occurrences (all)	3		
Bone marrow failure			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Coagulopathy			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Febrile neutropenia			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Leukocytosis			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Leukopenia			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Lymphopenia			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Neutropenia			

subjects affected / exposed	5 / 23 (21.74%)		
occurrences (all)	5		
Thrombocytopenia			
subjects affected / exposed	4 / 23 (17.39%)		
occurrences (all)	5		
Eye disorders			
Conjunctivitis			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Eye irritation			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Eye pain			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Eye pruritus			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Vision blurred			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	3 / 23 (13.04%)		
occurrences (all)	4		
Diarrhoea			
subjects affected / exposed	2 / 23 (8.70%)		
occurrences (all)	2		
Constipation			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Flatulence			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Haematemesis			

subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Gingival bleeding			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Lip blister			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Nausea			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Odynophagia			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Perianal erythema			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Retching			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Salivary hypersecretion			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Stomatitis			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Tongue ulceration			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Toothache			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Vomiting			
subjects affected / exposed	5 / 23 (21.74%)		
occurrences (all)	7		
Hepatobiliary disorders			

Liver disorder subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0		
Skin and subcutaneous tissue disorders Dermatitis subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0		
Night sweats subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0		
Pruritus subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0		
Rash subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0		
Skin fissures subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0		
Renal and urinary disorders Haematuria subjects affected / exposed occurrences (all)	1 / 23 (4.35%) 1		
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	1 / 23 (4.35%) 2		
Myalgia subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0		
Pain in extremity subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0		
Infections and infestations Cystitis			

subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Influenza			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Nasopharyngitis			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Oral bacterial infection			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Upper respiratory tract infection			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Oral candidiasis			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Urinary tract infection			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Dehydration			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Hyperglycaemia			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Hypoalbuminaemia			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Hypocalcaemia			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		

Hypokalaemia			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Hypomagnesaemia			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Hypophosphataemia			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 January 2010	Amendment 01: Per request of the United States Food and Drug Administration (US FDA), participants in Parts I and V of the study (ages 12-17 years) were to have additional blood pressure monitoring prior to, during and following the fosaprepitant infusion, as well as serum electrolytes including sodium, potassium, magnesium, chloride, bicarbonate, total calcium, ionized calcium, and albumin collected prior to the initiation of chemotherapy; Parts III, IV, and V would not be started until data from an additional non-clinical study in juvenile animals were available, in addition to waiting until data from Part I were available. Another main change was the sample size for Part I was increased by 5 participants to increase the exposure database in participants 12-17 years of age.
09 November 2011	Amendment 02: Per request of the US FDA, the age range of participants in Parts II, III, and IV was expanded to include participants from birth to 6 months old; also, the PK of IV dexamethasone was to be evaluated as part of an antiemetic regimen both with and without concomitant administration of aprepitant in participants birth to 17 years of age, as well as part of an antiemetic regimen with concomitant administration of single IV dose of fosaprepitant in participants >6 months of age. Other main changes were: a change in dosing recommendation in participants <12 years of age was implemented from body surface area (BSA)-based dosing to weight-based dosing; Part V was changed from evaluating the safety/exploratory efficacy and PK of an IV fosaprepitant/oral aprepitant regimen to a single IV dose of fosaprepitant equivalent to 150 mg in participants 6 months to <12 years of age.
11 June 2012	Amendment 03: Per request of the US FDA, due to changes in the ondansetron label, expanded safety monitoring was implemented to include additional vital sign and electrolyte monitoring in all participants receiving ondansetron and post dose electrocardiogram (ECG) for those participants with baseline electrolyte abnormalities. Other main changes include: change in the oral aprepitant dosing regimen in participants birth to <4 months of age; and remove the requirement to obtain dexamethasone PK in participants >1 year old.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
20 January 2014	Study terminated early prior to completing targeted enrollment of participants <6 months of age due to recruitment challenges.	-

Notes:

Limitations and caveats

None reported