Clinical trial results:
A Phase IIb, Partially-Blinded, Randomized, Active Comparator-Controlled Study to Evaluate the Pharmacokinetics/Pharmacodynamics, Safety, and Tolerability of Aprepitant in Pediatric Patients for the Prevention of Post-Operative Nausea and Vomiting

Summary

EudraCT number	2011-006006-27
Trial protocol	HU ES CZ IT Outside EU/EEA
Global end of trial date	26 September 2016

Results information

Result version number	v2 (current)
This version publication date	02 December 2017
First version publication date	08 April 2017
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	0869-219

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01732458
WHO universal trial number (UTN)	-

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	26 September 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 September 2016
Global end of trial reached?	Yes
Global end of trial date	26 September 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study was to evaluate the pharmacokinetics (PK), safety, and tolerability of aprepitant for the prevention of post-operative nausea and vomiting (PONV) in pediatric participants.

Post-operative aprepitant plasma concentrations were evaluated with a non-compartmental analysis (NCA) at each dose and for each age cohort. Because the opportunity to collect specimens for PK analyses in children is limited, a flexible sparse sampling scheme using ranges of collection times was to be utilized which would limit the burden to participants. Full PK profiles analyzed using population PK modeling and simulation were described in a separate report.

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.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 February 2013
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: 7
Country: Number of subjects enrolled	Canada: 1
Country: Number of subjects enrolled	Chile: 35
Country: Number of subjects enrolled	Czech Republic: 20
Country: Number of subjects enrolled	Guatemala: 19
Country: Number of subjects enrolled	Hungary: 52
Country: Number of subjects enrolled	Italy: 6
Country: Number of subjects enrolled	Mexico: 3
Country: Number of subjects enrolled	Russian Federation: 4
Country: Number of subjects enrolled	South Africa: 22
Country: Number of subjects enrolled	Spain: 12
Country: Number of subjects enrolled	Turkey: 31
Country: Number of subjects enrolled	Ukraine: 3
Country: Number of subjects enrolled	United States: 13
Worldwide total number of subjects	228
EEA total number of subjects	90

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)	53
Children (2-11 years)	116
Adolescents (12-17 years)	59
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Of 262 screened for inclusion, 229 were randomized to treatment. 1 participant was inadvertently randomized to a 2.5 mg aprepitant dose arm that was not evaluated in this study; therefore the participant was not included in any analyses (data reported separately in a narrative). Of remaining 228 randomized participants, 8 did not receive treatment.

Period 1

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

Blinding implementation details:

This study conducted as a partially blinded study. PK samples were not collected from participants in the control group. To maintain a partial blind, ~3 participants randomly selected from each age group in each of the aprepitant treatment arms did not have PK sampling.

Arms

Are arms mutually exclusive?	Yes
Arm title	Aprepitant Dose 1: Equivalent to 125 mg in Adults

Arm description:

Pediatric participants received a single dose of apprepitant that was equivalent to 125 mg in adults on Day 1 between 1 and 3 hours prior to expected induction of anesthesia, plus placebo for odansetron administered intravenously (IV) immediately prior to anesthesia.

Arm type	Experimental
Investigational medicinal product name	Aprepitant
Investigational medicinal product code	
Other name	Emend, MK-0869
Pharmaceutical forms	Powder for oral suspension
Routes of administration	Oral use

Dosage and administration details:

Administered as a single oral dose on Day 1 between 1 and 3 hours prior to expected induction of anesthesia. Aprepitant was supplied in a sachet containing a powder for suspension (PFS) that was reconstituted up to total volume of 5 mL using potable water.

Investigational medicinal product name	Placebo to Ondansetron
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Participants in the aprepitant regimen received normal saline IV (provided by the site) as the placebo for ondansetron on Day 1, immediately prior to induction of anesthesia.

Arm title	Aprepitant Dose 2: Equivalent to 40 mg in Adults

Arm description:

Pediatric participants received a single dose of apprepitant that was equivalent to 40 mg in adults on Day 1 between 1 and 3 hours prior to expected induction of anesthesia, plus placebo for odansetron administered IV immediately prior to anesthesia.

Arm type	Experimental

Investigational medicinal product name	Aprepitant
Investigational medicinal product code	
Other name	Emend, MK-0869
Pharmaceutical forms	Powder for oral suspension
Routes of administration	Oral use

Dosage and administration details:

Administered as a single oral dose on Day 1 between 1 and 3 hours prior to expected induction of anesthesia. Aprepitant was supplied in a sachet containing a powder for suspension (PFS) that was reconstituted up to total volume of 5 mL using potable water.

Investigational medicinal product name	Placebo to Ondansetron
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Participants in the aprepitant regimen received normal saline IV (provided by the site) as the placebo for ondansetron on Day 1, immediately prior to induction of anesthesia.

Arm title	Aprepitant Dose 3: Equivalent to 10 mg in Adults

Arm description:

Pediatric participants received a single dose of apprepitant that was equivalent to 10 mg in adults on Day 1 between 1 and 3 hours prior to expected induction of anesthesia, plus placebo for odansetron administered IV immediately prior to anesthesia.

Arm type	Experimental
Investigational medicinal product name	Aprepitant
Investigational medicinal product code	
Other name	Emend, MK-0869
Pharmaceutical forms	Powder for oral suspension
Routes of administration	Oral use

Dosage and administration details:

Administered as a single oral dose on Day 1 between 1 and 3 hours prior to expected induction of anesthesia. Aprepitant was supplied in a sachet containing a powder for suspension (PFS) that was reconstituted up to total volume of 5 mL using potable water.

Investigational medicinal product name	Placebo to Ondansetron
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Participants in the aprepitant regimen received normal saline IV (provided by the site) as the placebo for ondansetron on Day 1, immediately prior to induction of anesthesia.

Arm title	Ondansetron

Arm description:

Pediatric participants in the control regimen were administered ondansetron IV on Day 1 immediately prior to induction of anesthesia plus a matching placebo dose to aprepitant as a single oral dose on Day 1 between 1 and 3 hours prior to expected induction of anesthesia.

Arm type	Active comparator
Investigational medicinal product name	Placebo to Aprepitant
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for oral suspension
Routes of administration	Oral use

Dosage and administration details:

Matching placebo to aprepritant was administered as a single oral dose on Day 1 between 1 and 3 hours prior to expected induction of anesthesia.

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

Dosage and administration details:

Administered IV at a dose of 4 mg for participants >40 kg in weight and 0.1 mg/kg for participants ≤40 kg in weight. In participants <1 month of age, the dose of ondansetron was administered per the product label or based on local standard of care. Ondansetron was supplied by the Sponsor as vials or ampules, depending on the country.

Number of subjects in period 1	Aprepitant Dose 1: Equivalent to 125 mg in Adults	Aprepitant Dose 2: Equivalent to 40 mg in Adults	Aprepitant Dose 3: Equivalent to 10 mg in Adults
Started	60	58	58
Treated	57	55	56
Completed	57	53	55
Not completed	3	5	3
Physician decision	1	2	2
Screen Failure	-	1	-
Non-Compliance With Study Drug	-	-	1
Lost to follow-up	-	2	-
Protocol deviation	2	-	-

Number of subjects in period 1	Ondansetron
Started	52
Treated	52
Completed	50
Not completed	2
Physician decision	-
Screen Failure	-
Non-Compliance With Study Drug	-
Lost to follow-up	-
Protocol deviation	2

Baseline characteristics

Reporting groups	
Reporting group title	Aprepitant Dose 1: Equivalent to 125 mg in Adults
Reporting group description:	
Pediatric participants received a single dose of apprepitant that was equivalent to 125 mg in adults on Day 1 between 1 and 3 hours prior to expected induction of anesthesia, plus placebo for odansetron administered intravenously (IV) immediately prior to anesthesia.	
Reporting group title	Aprepitant Dose 2: Equivalent to 40 mg in Adults
Reporting group description:	
Pediatric participants received a single dose of apprepitant that was equivalent to 40 mg in adults on Day 1 between 1 and 3 hours prior to expected induction of anesthesia, plus placebo for odansetron administered IV immediately prior to anesthesia.	
Reporting group title	Aprepitant Dose 3: Equivalent to 10 mg in Adults
Reporting group description:	
Pediatric participants received a single dose of apprepitant that was equivalent to 10 mg in adults on Day 1 between 1 and 3 hours prior to expected induction of anesthesia, plus placebo for odansetron administered IV immediately prior to anesthesia.	
Reporting group title	Ondansetron
Reporting group description:	
Pediatric participants in the control regimen were administered ondansetron IV on Day 1 immediately prior to induction of anesthesia plus a matching placebo dose to aprepitant as a single oral dose on Day 1 between 1 and 3 hours prior to expected induction of anesthesia.	

Reporting group values	Aprepitant Dose 1: Equivalent to 125 mg in Adults	Aprepitant Dose 2: Equivalent to 40 mg in Adults	Aprepitant Dose 3: Equivalent to 10 mg in Adults
Number of subjects	60	58	58
Age Categorical			
All Participants as Treated (N=220)			
Units: Subjects			
Birth to <2 years	14	12	13
2 years to <6 years	14	14	15
6 years to <12 years	13	15	14
12 years to 17 years	16	14	14
Not Reported	3	3	2
Age Continuous			
All Randomized Participants (N=228)			
Units: months			
arithmetic mean	90.7	86.1	84.4
standard deviation	± 64.6	± 64.0	± 59.7
Gender Categorical			
All Randomized Participants (N=228)			
Units: Subjects			
Female	24	20	29
Male	36	38	29

Reporting group values	Ondansetron	Total	
Number of subjects	52	228	
Age Categorical			
All Participants as Treated (N=220)			
Units: Subjects			

Birth to <2 years	11	50	
2 years to <6 years	14	57	
6 years to <12 years	13	55	
12 years to 17 years	14	58	
Not Reported	0	8	
Age Continuous			
All Randomized Participants (N=228)			
Units: months			
arithmetic mean	86.0		
standard deviation	± 65.0	-	
Gender Categorical			
All Randomized Participants (N=228)			
Units: Subjects			
Female	16	89	
Male	36	139	

End points

End points reporting groups

Reporting group title	Aprepitant Dose 1: Equivalent to 125 mg in Adults
Reporting group description:	
Pediatric participants received a single dose of apprepitant that was equivalent to 125 mg in adults on Day 1 between 1 and 3 hours prior to expected induction of anesthesia, plus placebo for odansetron administered intravenously (IV) immediately prior to anesthesia.	
Reporting group title	Aprepitant Dose 2: Equivalent to 40 mg in Adults
Reporting group description:	
Pediatric participants received a single dose of apprepitant that was equivalent to 40 mg in adults on Day 1 between 1 and 3 hours prior to expected induction of anesthesia, plus placebo for odansetron administered IV immediately prior to anesthesia.	
Reporting group title	Aprepitant Dose 3: Equivalent to 10 mg in Adults
Reporting group description:	
Pediatric participants received a single dose of apprepitant that was equivalent to 10 mg in adults on Day 1 between 1 and 3 hours prior to expected induction of anesthesia, plus placebo for odansetron administered IV immediately prior to anesthesia.	
Reporting group title	Ondansetron
Reporting group description:	
Pediatric participants in the control regimen were administered ondansetron IV on Day 1 immediately prior to induction of anesthesia plus a matching placebo dose to aprepitant as a single oral dose on Day 1 between 1 and 3 hours prior to expected induction of anesthesia.	
Subject analysis set title	Aprepitant 125 mg (Dose 1): 12 to 17 Year Age Group
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Pediatric participants aged 12 to 17 years old received a single dose of apprepitant that was equivalent to 125 mg in adults on Day 1 between 1 and 3 hours prior to expected induction of anesthesia.	
Subject analysis set title	Aprepitant 125 mg (Dose 1): 6 to <12 Year Age Group
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Pediatric participants aged 6 to <12 years old received a single dose of apprepitant that was equivalent to 125 mg in adults on Day 1 between 1 and 3 hours prior to expected induction of anesthesia.	
Subject analysis set title	Aprepitant 125 mg (Dose 1): 2 to <6 Year Age Group
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Pediatric participants aged 2 to <6 years old received a single dose of apprepitant that was equivalent to 125 mg in adults on Day 1 between 1 and 3 hours prior to expected induction of anesthesia.	
Subject analysis set title	Aprepitant 125 mg (Dose 1): Birth to <2 Year Age Group
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Pediatric participants aged birth to <2 years old received a single dose of apprepitant that was equivalent to 125 mg in adults on Day 1 between 1 and 3 hours prior to expected induction of anesthesia.	
Subject analysis set title	Aprepitant 40 mg (Dose 2): 12 to 17 Year Age Group
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Pediatric participants aged 12 to 17 years old received a single dose of apprepitant that was equivalent to 40 mg in adults on Day 1 between 1 and 3 hours prior to expected induction of anesthesia.	
Subject analysis set title	Aprepitant 40 mg (Dose 2): 6 to <12 Year Age Group
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Pediatric participants aged 6 to <12 years old received a single dose of apprepitant that was equivalent to 40 mg in adults on Day 1 between 1 and 3 hours prior to expected induction of anesthesia.	
Subject analysis set title	Aprepitant 40 mg (Dose 2): 2 to <6 Year Age Group

Subject analysis set type	Sub-group analysis

Subject analysis set description:

Pediatric participants aged 2 to <6 years old received a single dose of apprepitant that was equivalent to 40 mg in adults on Day 1 between 1 and 3 hours prior to expected induction of anesthesia.

Subject analysis set title	Aprepitant 40 mg (Dose 2): Birth to <2 Year Age Group
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Pediatric participants aged birth to <2 years old received a single dose of apprepitant that was equivalent to 40 mg in adults on Day 1 between 1 and 3 hours prior to expected induction of anesthesia.

Subject analysis set title	Aprepitant 10 mg (Dose 3): 12 to 17 Year Age Group
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Pediatric participants aged 12 to 17 years old received a single dose of apprepitant that was equivalent to 10 mg in adults on Day 1 between 1 and 3 hours prior to expected induction of anesthesia.

Subject analysis set title	Aprepitant 10 mg (Dose 3): 6 to <12 Year Age Group
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Pediatric participants aged 6 to <12 years old received a single dose of apprepitant that was equivalent to 10 mg in adults on Day 1 between 1 and 3 hours prior to expected induction of anesthesia.

Subject analysis set title	Aprepitant 10 mg (Dose 3): 2 to <6 Year Age Group
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Pediatric participants aged 2 to <6 years old received a single dose of apprepitant that was equivalent to 10 mg in adults on Day 1 between 1 and 3 hours prior to expected induction of anesthesia.

Subject analysis set title	Aprepitant 10 mg (Dose 3): Birth to <2 Year Age Group
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Pediatric participants aged birth to <2 years old received a single dose of apprepitant that was equivalent to 10 mg in adults on Day 1 between 1 and 3 hours prior to expected induction of anesthesia.

Primary: Area under the concentration-time curve of aprepitant from time 0 to the last measurable concentration (AUC0-last) following administration of 125 mg dose equivalent in 12 to 17 year age group

End point title	Area under the concentration-time curve of aprepitant from time 0 to the last measurable concentration (AUC0-last) following administration of 125 mg dose equivalent in 12 to 17 year age group[1]

End point description:

AUC0-last was analyzed independently for participants in the 125 mg dose equivalent arm aged 12 to 17 years old due to age- and dose-dependent differences in aprepitant absorption and clearance. Because the opportunity to collect specimens for PK analyses in children is limited, a flexible sparse sampling scheme using ranges of collection times was to be utilized which would limit the burden to participants. Plasma for aprepitant PK assessment was obtained at 30-60 minutes prior to aprepitant administration, 2-4 hours post aprepitant administration, 5-7 hours post aprepitant administration, and 8-10 hours post aprepitant administration. Post-operative aprepitant plasma AUC0-last was evaluated with a non-compartmental analysis (NCA). The limit of quantitation (LOQ) value for this analysis was 10 ng/mL. Participants aged 12 to 17 years who received a single dose of 125 mg aprepitant prior to surgery with evaluable plasma samples were analyzed.

End point type	Primary

End point timeframe:

30-60 minutes pre-administration, 2-4 hours post administration, 5-7 hours post administration, 8-10 hours post administration

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: Descriptive statistics only were presented for this NCA PK endpoint, and there were no between-group statistical comparisons performed.

End point values	Aprepitant 125 mg (Dose 1): 12 to 17 Year Age Group			
Subject group type	Subject analysis set			
Number of subjects analysed	10			
Units: hr*ng/mL				
geometric mean (geometric coefficient of variation)	7120 (± 33.0)			

Statistical analyses

No statistical analyses for this end point

Primary: Maximum concentration (Cmax) of aprepitant following administration of 125 mg dose equivalent in 12 to 17 year age group

End point title	Maximum concentration (Cmax) of aprepitant following administration of 125 mg dose equivalent in 12 to 17 year age group[2]

End point description:

Cmax was analyzed independently for participants in the 125 mg dose equivalent arm aged 12 to 17 years old due to age- and dose-dependent differences in aprepitant absorption and clearance. Because the
opportunity to collect specimens for PK analyses in children is limited, a flexible sparse sampling scheme using ranges of collection times was to be utilized which would limit the burden to participants. Plasma for aprepitant PK assessment was obtained at 30-60 minutes prior to aprepitant administration, 2-4 hours post aprepitant administration, 5-7 hours post aprepitant administration, and 8-10 hours post aprepitant administration. Post-operative aprepitant plasma Cmax was evaluated with a NCA. The LOQ value for this analysis was 10 ng/mL. Participants aged 12 to 17 years who received a single dose of 125 mg aprepitant prior to surgery with evaluable plasma samples were analyzed.

End point type	Primary

End point timeframe:

30-60 minutes pre-administration, 2-4 hours post administration, 5-7 hours post administration, 8-10 hours post administration

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics only were presented for this NCA PK endpoint, and there were no between-group statistical comparisons performed.

End point values	Aprepitant 125 mg (Dose 1): 12 to 17 Year Age Group			
Subject group type	Subject analysis set			
Number of subjects analysed	10			
Units: ng/mL				
geometric mean (geometric coefficient of variation)	1340 (± 43.9)			

Statistical analyses

No statistical analyses for this end point

Primary: Time to maximum concentration (Tmax) of aprepitant following administration of 125 mg dose equivalent in 12 to 17 year age group

End point title	Time to maximum concentration (Tmax) of aprepitant following administration of 125 mg dose equivalent in 12 to 17 year age group[3]

End point description:

Tmax was analyzed independently for participants in the 125 mg dose equivalent arm aged 12 to 17 years old due to age- and dose-dependent differences in aprepitant absorption and clearance. Because the
opportunity to collect specimens for PK analyses in children is limited, a flexible sparse sampling scheme using ranges of collection times was to be utilized which would limit the burden to participants. Plasma for aprepitant PK assessment was obtained at 30-60 minutes prior to aprepitant administration, 2-4 hours post aprepitant administration, 5-7 hours post aprepitant administration, and 8-10 hours post aprepitant administration. Post-operative aprepitant plasma Tmax was evaluated with a NCA. The LOQ value for this analysis was 10 ng/mL. Participants aged 12 to 17 years who received a single dose of 125 mg aprepitant prior to surgery with evaluable plasma samples were analyzed.

End point type	Primary

End point timeframe:

30-60 minutes pre-administration, 2-4 hours post administration, 5-7 hours post administration, 8-10 hours post administration

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics only were presented for this NCA PK endpoint, and there were no between-group statistical comparisons performed.

End point values	Aprepitant 125 mg (Dose 1): 12 to 17 Year Age Group			
Subject group type	Subject analysis set			
Number of subjects analysed	10			
Units: hr				
geometric mean (geometric coefficient of variation)	4.86 (± 56.5)			

Statistical analyses

No statistical analyses for this end point

Primary: AUC0-last of aprepitant following administration of 125 mg dose equivalent in 6 to <12 year age group

End point title	AUC0-last of aprepitant following administration of 125 mg dose equivalent in 6 to <12 year age group[4]

End point description:

AUC0-last was analyzed independently for participants in the 125 mg dose equivalent arm aged 6 to <12 years old due to age- and dose-dependent differences in aprepitant absorption and clearance. Because the opportunity to collect specimens for PK analyses in children is limited, a flexible sparse sampling scheme using ranges of collection times was to be utilized which would limit the burden to participants. Plasma for aprepitant PK assessment was obtained at 30-60 minutes prior to aprepitant administration, 2-4 hours post aprepitant administration, 5-7 hours post aprepitant administration, and 8-10 hours post aprepitant administration. Post-operative aprepitant plasma AUC0-last was evaluated with a NCA. The LOQ value for this analysis was 10 ng/mL. Participants aged 6 to <12 years who received a single dose of 125 mg aprepitant prior to surgery with evaluable plasma samples were analyzed.

End point type	Primary

End point timeframe:

30-60 minutes pre-administration, 2-4 hours post administration, 5-7 hours post administration, 8-10 hours post administration

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: Descriptive statistics only were presented for this NCA PK endpoint, and there were no between-group statistical comparisons performed.

End point values	Aprepitant 125 mg (Dose 1): 6 to <12 Year Age Group			
Subject group type	Subject analysis set			
Number of subjects analysed	11			
Units: hr*ng/mL				
geometric mean (geometric coefficient of variation)	10300 (± 39.5)			

Statistical analyses

No statistical analyses for this end point

Primary: Cmax of aprepitant following administration of 125 mg dose equivalent in 6 to <12 year age group

End point title	Cmax of aprepitant following administration of 125 mg dose equivalent in 6 to <12 year age group[5]

End point description:

Cmax was analyzed independently for participants in the 125 mg dose equivalent arm aged 6 to <12 years old due to age- and dose-dependent differences in aprepitant absorption and clearance. Because the opportunity to collect specimens for PK analyses in children is limited, a flexible sparse sampling scheme using ranges of collection times was to be utilized which would limit the burden to participants. Plasma for aprepitant PK assessment was obtained at 30-60 minutes prior to aprepitant administration, 2-4 hours post aprepitant administration, 5-7 hours post aprepitant administration, and 8-10 hours post aprepitant administration. Post-operative aprepitant plasma Cmax was evaluated with a NCA. The LOQ value for this analysis was 10 ng/mL. Participants aged 6 to <12 years who received a single dose of 125 mg aprepitant prior to surgery with evaluable plasma samples were analyzed.

End point type	Primary

End point timeframe:

30-60 minutes pre-administration, 2-4 hours post administration, 5-7 hours post administration, 8-10 hours post administration

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics only were presented for this NCA PK endpoint, and there were no between-group statistical comparisons performed.

End point values	Aprepitant 125 mg (Dose 1): 6 to <12 Year Age Group			
Subject group type	Subject analysis set			
Number of subjects analysed	11			
Units: ng/mL				
geometric mean (geometric coefficient of variation)	1870 (± 53.0)			

Statistical analyses

No statistical analyses for this end point

Primary: Tmax of aprepitant following administration of 125 mg dose equivalent in 6 to <12 year age group

End point title	Tmax of aprepitant following administration of 125 mg dose equivalent in 6 to <12 year age group[6]

End point description:

Tmax was analyzed independently for participants in the 125 mg dose equivalent arm aged 6 to <12 years old due to age- and dose-dependent differences in aprepitant absorption and clearance. Because the
opportunity to collect specimens for PK analyses in children is limited, a flexible sparse sampling scheme using ranges of collection times was to be utilized which would limit the burden to participants. Plasma for aprepitant PK assessment was obtained at 30-60 minutes prior to aprepitant administration, 2-4 hours post aprepitant administration, 5-7 hours post aprepitant administration, and 8-10 hours post aprepitant administration. Post-operative aprepitant plasma Tmax was evaluated with a NCA. The LOQ value for this analysis was 10 ng/mL. Participants aged 6 to <12 years who received a single dose of 125 mg aprepitant prior to surgery with evaluable plasma samples were analyzed.

End point type	Primary

End point timeframe:

30-60 minutes pre-administration, 2-4 hours post administration, 5-7 hours post administration, 8-10 hours post administration

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics only were presented for this NCA PK endpoint, and there were no between-group statistical comparisons performed.

End point values	Aprepitant 125 mg (Dose 1): 6 to <12 Year Age Group			
Subject group type	Subject analysis set			
Number of subjects analysed	11			
Units: hr				
geometric mean (geometric coefficient of variation)	6.82 (± 26.8)			

Statistical analyses

No statistical analyses for this end point

Primary: AUC0-last of aprepitant following administration of 125 mg dose equivalent in 2 to <6 year age group

End point title	AUC0-last of aprepitant following administration of 125 mg dose equivalent in 2 to <6 year age group[7]

End point description:

AUC0-last was analyzed independently for participants in the 125 mg dose equivalent arm aged 2 to <6 years old due to age- and dose-dependent differences in aprepitant absorption and clearance. Because the opportunity to collect specimens for PK analyses in children is limited, a flexible sparse sampling scheme using ranges of collection times was to be utilized which would limit the burden to participants. Plasma for aprepitant PK assessment was obtained at 30-60 minutes prior to aprepitant administration, 2-4 hours post aprepitant administration, 5-7 hours post aprepitant administration, and 8-10 hours post aprepitant administration. Post-operative aprepitant plasma AUC0-last was evaluated with a NCA. The LOQ value for this analysis was 10 ng/mL. Participants aged 2 to <6 years who received a single dose of 125 mg aprepitant prior to surgery with evaluable plasma samples were analyzed.

End point type	Primary

End point timeframe:

30-60 minutes pre-administration, 2-4 hours post administration, 5-7 hours post administration, 8-10 hours post administration

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: Descriptive statistics only were presented for this NCA PK endpoint, and there were no between-group statistical comparisons performed.

End point values	Aprepitant 125 mg (Dose 1): 2 to <6 Year Age Group			
Subject group type	Subject analysis set			
Number of subjects analysed	10			
Units: hr*ng/mL				
geometric mean (geometric coefficient of variation)	12000 (± 39.7)			

Statistical analyses

No statistical analyses for this end point

Primary: Cmax of aprepitant following administration of 125 mg dose equivalent in 2 to <6 year age group

End point title	Cmax of aprepitant following administration of 125 mg dose equivalent in 2 to <6 year age group[8]

End point description:

Cmax was analyzed independently for participants in the 125 mg dose equivalent arm aged 2 to <6 years old due to age- and dose-dependent differences in aprepitant absorption and clearance. Because the opportunity to collect specimens for PK analyses in children is limited, a flexible sparse sampling scheme using ranges of collection times was to be utilized which would limit the burden to participants. Plasma for aprepitant PK assessment was obtained at 30-60 minutes prior to aprepitant administration, 2-4 hours post aprepitant administration, 5-7 hours post aprepitant administration, and 8-10 hours post aprepitant administration. Post-operative aprepitant plasma Cmax was evaluated with a NCA. The LOQ value for this analysis was 10 ng/mL. Participants aged 2 to <6 years who received a single dose of 125 mg aprepitant prior to surgery with evaluable plasma samples were analyzed.

End point type	Primary

End point timeframe:

30-60 minutes pre-administration, 2-4 hours post administration, 5-7 hours post administration, 8-10 hours post administration

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics only were presented for this NCA PK endpoint, and there were no between-group statistical comparisons performed.

End point values	Aprepitant 125 mg (Dose 1): 2 to <6 Year Age Group			
Subject group type	Subject analysis set			
Number of subjects analysed	10			
Units: ng/mL				
geometric mean (geometric coefficient of variation)	2260 (± 35.7)			

Statistical analyses

No statistical analyses for this end point

Primary: Tmax of aprepitant following administration of 125 mg dose equivalent in 2 to <6 year age group

End point title	Tmax of aprepitant following administration of 125 mg dose equivalent in 2 to <6 year age group[9]

End point description:

Tmax was analyzed independently for participants in the 125 mg dose equivalent arm aged 2 to <6 years old due to age- and dose-dependent differences in aprepitant absorption and clearance. Because the
opportunity to collect specimens for PK analyses in children is limited, a flexible sparse sampling scheme using ranges of collection times was to be utilized which would limit the burden to participants. Plasma for aprepitant PK assessment was obtained at 30-60 minutes prior to aprepitant administration, 2-4 hours post aprepitant administration, 5-7 hours post aprepitant administration, and 8-10 hours post aprepitant administration. Post-operative aprepitant plasma Tmax was evaluated with a NCA. The LOQ value for this analysis was 10 ng/mL. Participants aged 2 to <6 years who received a single dose of 125 mg aprepitant prior to surgery with evaluable plasma samples were analyzed.

End point type	Primary

End point timeframe:

30-60 minutes pre-administration, 2-4 hours post administration, 5-7 hours post administration, 8-10 hours post administration

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics only were presented for this NCA PK endpoint, and there were no between-group statistical comparisons performed.

End point values	Aprepitant 125 mg (Dose 1): 2 to <6 Year Age Group			
Subject group type	Subject analysis set			
Number of subjects analysed	10			
Units: hr				
geometric mean (geometric coefficient of variation)	4.91 (± 51.9)			

Statistical analyses

No statistical analyses for this end point

Primary: AUC0-last of aprepitant following administration of 125 mg dose equivalent in birth to <2 year age group

End point title	AUC0-last of aprepitant following administration of 125 mg dose equivalent in birth to <2 year age group[10]

End point description:

AUC0-last was analyzed independently for participants in the 125 mg dose equivalent arm aged birth to <2 years old due to age- and dose-dependent differences in aprepitant absorption and clearance. Because the opportunity to collect specimens for PK analyses in children is limited, a flexible sparse sampling scheme using ranges of collection times was to be utilized which would limit the burden to participants. Plasma for aprepitant PK assessment was obtained at 30-60 minutes prior to aprepitant administration, 2-4 hours post aprepitant administration, 5-7 hours post aprepitant administration, and 8-10 hours post aprepitant administration. Post-operative aprepitant plasma AUC0-last was evaluated with a NCA. The LOQ value for this analysis was 10 ng/mL. Participants aged birth to <2 years who received a single dose of 125 mg aprepitant prior to surgery with evaluable plasma samples were analyzed.

End point type	Primary

End point timeframe:

30-60 minutes pre-administration, 2-4 hours post administration, 5-7 hours post administration, 8-10 hours post administration

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: Descriptive statistics only were presented for this NCA PK endpoint, and there were no between-group statistical comparisons performed.

End point values	Aprepitant 125 mg (Dose 1): Birth to <2 Year Age Group			
Subject group type	Subject analysis set			
Number of subjects analysed	8			
Units: hr*ng/mL				
geometric mean (geometric coefficient of variation)	6410 (± 67.8)			

Statistical analyses

No statistical analyses for this end point

Primary: Cmax of aprepitant following administration of 125 mg dose equivalent in birth to <2 year age group

End point title	Cmax of aprepitant following administration of 125 mg dose equivalent in birth to <2 year age group[11]

End point description:

Cmax was analyzed independently for participants in the 125 mg dose equivalent arm aged birth to <2 years old due to age- and dose-dependent differences in aprepitant absorption and clearance. Because the opportunity to collect specimens for PK analyses in children is limited, a flexible sparse sampling scheme using ranges of collection times was to be utilized which would limit the burden to participants. Plasma for aprepitant PK assessment was obtained at 30-60 minutes prior to aprepitant administration, 2-4 hours post aprepitant administration, 5-7 hours post aprepitant administration, and 8-10 hours post aprepitant administration. Post-operative aprepitant plasma Cmax was evaluated with a NCA. The LOQ value for this analysis was 10 ng/mL. Participants aged birth to <2 years who received a single dose of 125 mg aprepitant prior to surgery with evaluable plasma samples were analyzed.

End point type	Primary

End point timeframe:

30-60 minutes pre-administration, 2-4 hours post administration, 5-7 hours post administration, 8-10

hours post administration

Notes:

[11] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics only were presented for this NCA PK endpoint, and there were no between-group statistical comparisons performed.

End point values	Aprepitant 125 mg (Dose 1): Birth to <2 Year Age Group			
Subject group type	Subject analysis set			
Number of subjects analysed	9			
Units: ng/mL				
geometric mean (geometric coefficient of variation)	1280 (± 78.5)			

Statistical analyses

No statistical analyses for this end point

Primary: Tmax of aprepitant following administration of 125 mg dose equivalent in birth to <2 year age group

End point title	Tmax of aprepitant following administration of 125 mg dose equivalent in birth to <2 year age group[12]

End point description:

Tmax was analyzed independently for participants in the 125 mg dose equivalent arm aged birth to <2 years old due to age- and dose-dependent differences in aprepitant absorption and clearance. Because the opportunity to collect specimens for PK analyses in children is limited, a flexible sparse sampling scheme using ranges of collection times was to be utilized which would limit the burden to participants. Plasma for aprepitant PK assessment was obtained at 30-60 minutes prior to aprepitant administration, 2-4 hours post aprepitant administration, 5-7 hours post aprepitant administration, and 8-10 hours post aprepitant administration. Post-operative aprepitant plasma Tmax was evaluated with a NCA. The LOQ value for this analysis was 10 ng/mL. Participants aged birth to <2 years who received a single dose of 125 mg aprepitant prior to surgery with evaluable plasma samples were analyzed.

End point type	Primary

End point timeframe:

30-60 minutes pre-administration, 2-4 hours post administration, 5-7 hours post administration, 8-10 hours post administration

Notes:

[12] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics only were presented for this NCA PK endpoint, and there were no between-group statistical comparisons performed.

End point values	Aprepitant 125 mg (Dose 1): Birth to <2 Year Age Group			
Subject group type	Subject analysis set			
Number of subjects analysed	10			
Units: hr				
geometric mean (geometric coefficient of variation)	4.71 (± 51.3)			

Statistical analyses

No statistical analyses for this end point

Primary: AUC0-last following administration of 40 mg dose equivalent in 12 to 17 year age group

End point title	AUC0-last following administration of 40 mg dose equivalent in 12 to 17 year age group[13]

End point description:

AUC0-last was analyzed independently for participants in the 40 mg dose equivalent arm aged 12 to 17 years old due to age- and dose-dependent differences in aprepitant absorption and clearance. Because the opportunity to collect specimens for PK analyses in children is limited, a flexible sparse sampling scheme using ranges of collection times was to be utilized which would limit the burden to participants. Plasma for aprepitant PK assessment was obtained at 30-60 minutes prior to aprepitant administration, 2-4 hours post aprepitant administration, 5-7 hours post aprepitant administration, and 8-10 hours post aprepitant administration. Post-operative aprepitant plasma AUC0-last was evaluated with a NCA. The LOQ value for this analysis was 10 ng/mL. Participants aged 12 to 17 years who received a single dose of 40 mg aprepitant prior to surgery with evaluable plasma samples were analyzed.

End point type	Primary

End point timeframe:

30-60 minutes pre-administration, 2-4 hours post administration, 5-7 hours post administration, 8-10 hours post administration

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: Descriptive statistics only were presented for this NCA PK endpoint, and there were no between-group statistical comparisons performed.

End point values	Aprepitant 40 mg (Dose 2): 12 to 17 Year Age Group			
Subject group type	Subject analysis set			
Number of subjects analysed	11			
Units: hr*ng/mL				
geometric mean (geometric coefficient of variation)	2570 (± 41.5)			

Statistical analyses

No statistical analyses for this end point

Primary: Cmax of aprepitant following administration of 40 mg dose equivalent in 12 to 17 year age group

End point title	Cmax of aprepitant following administration of 40 mg dose equivalent in 12 to 17 year age group[14]

End point description:

Cmax was analyzed independently for participants in the 40 mg dose equivalent arm aged 12 to 17

years old due to age- and dose-dependent differences in aprepitant absorption and clearance. Because the
opportunity to collect specimens for PK analyses in children is limited, a flexible sparse sampling scheme using ranges of collection times was to be utilized which would limit the burden to participants. Plasma for aprepitant PK assessment was obtained at 30-60 minutes prior to aprepitant administration, 2-4 hours post aprepitant administration, 5-7 hours post aprepitant administration, and 8-10 hours post aprepitant administration. Post-operative aprepitant plasma Cmax was evaluated with a NCA. The LOQ value for this analysis was 10 ng/mL. Participants aged 12 to 17 years who received a single dose of 40 mg aprepitant prior to surgery with evaluable plasma samples were analyzed.

End point type	Primary

End point timeframe:

30-60 minutes pre-administration, 2-4 hours post administration, 5-7 hours post administration, 8-10 hours post administration

Notes:

[14] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics only were presented for this NCA PK endpoint, and there were no between-group statistical comparisons performed.

End point values	Aprepitant 40 mg (Dose 2): 12 to 17 Year Age Group			
Subject group type	Subject analysis set			
Number of subjects analysed	11			
Units: ng/mL				
geometric mean (geometric coefficient of variation)	513 (± 41.6)			

Statistical analyses

No statistical analyses for this end point

Primary: Tmax of aprepitant following administration of 40 mg dose equivalent in 12 to 17 year age group

End point title	Tmax of aprepitant following administration of 40 mg dose equivalent in 12 to 17 year age group[15]

End point description:

Tmax was analyzed independently for participants in the 40 mg dose equivalent arm aged 12 to 17 years old due to age- and dose-dependent differences in aprepitant absorption and clearance. Because the
opportunity to collect specimens for PK analyses in children is limited, a flexible sparse sampling scheme using ranges of collection times was to be utilized which would limit the burden to participants. Plasma for aprepitant PK assessment was obtained at 30-60 minutes prior to aprepitant administration, 2-4 hours post aprepitant administration, 5-7 hours post aprepitant administration, and 8-10 hours post aprepitant administration. Post-operative aprepitant plasma Tmax was evaluated with a NCA. The LOQ value for this analysis was 10 ng/mL. Participants aged 12 to 17 years who received a single dose of 40 mg aprepitant prior to surgery with evaluable plasma samples were analyzed.

End point type	Primary

End point timeframe:

30-60 minutes pre-administration, 2-4 hours post administration, 5-7 hours post administration, 8-10 hours post administration

Notes:

[15] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics only were presented for this NCA PK endpoint, and there were no between-group statistical comparisons performed.

End point values	Aprepitant 40 mg (Dose 2): 12 to 17 Year Age Group			
Subject group type	Subject analysis set			
Number of subjects analysed	11			
Units: hr				
geometric mean (geometric coefficient of variation)	4.17 (± 69.4)			

Statistical analyses

No statistical analyses for this end point

Primary: AUC0-last of aprepitant following administration of 40 mg dose equivalent in 6 to <12 year age group

End point title	AUC0-last of aprepitant following administration of 40 mg dose equivalent in 6 to <12 year age group[16]

End point description:

AUC0-last was analyzed independently for participants in the 40 mg dose equivalent arm aged 6 to <12 years old due to age- and dose-dependent differences in aprepitant absorption and clearance. Because the opportunity to collect specimens for PK analyses in children is limited, a flexible sparse sampling scheme using ranges of collection times was to be utilized which would limit the burden to participants. Plasma for aprepitant PK assessment was obtained at 30-60 minutes prior to aprepitant administration, 2-4 hours post aprepitant administration, 5-7 hours post aprepitant administration, and 8-10 hours post aprepitant administration. Post-operative aprepitant plasma AUC0-last was evaluated with a NCA. The LOQ value for this analysis was 10 ng/mL. Participants aged 6 to <12 years who received a single dose of 40 mg aprepitant prior to surgery with evaluable plasma samples were analyzed.

End point type	Primary

End point timeframe:

30-60 minutes pre-administration, 2-4 hours post administration, 5-7 hours post administration, 8-10 hours post administration

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: Descriptive statistics only were presented for this NCA PK endpoint, and there were no between-group statistical comparisons performed.

End point values	Aprepitant 40 mg (Dose 2): 6 to <12 Year Age Group			
Subject group type	Subject analysis set			
Number of subjects analysed	11			
Units: hr*ng/mL				
geometric mean (geometric coefficient of variation)	4730 (± 60.7)			

Statistical analyses

No statistical analyses for this end point

Primary: Cmax of aprepitant following administration of 40 mg dose equivalent in 6 to <12 year age group

End point title	Cmax of aprepitant following administration of 40 mg dose equivalent in 6 to <12 year age group[17]

End point description:

Cmax was analyzed independently for participants in the 40 mg dose equivalent arm aged 6 to <12 years old due to age- and dose-dependent differences in aprepitant absorption and clearance. Because the opportunity to collect specimens for PK analyses in children is limited, a flexible sparse sampling scheme using ranges of collection times was to be utilized which would limit the burden to participants. Plasma for aprepitant PK assessment was obtained at 30-60 minutes prior to aprepitant administration, 2-4 hours post aprepitant administration, 5-7 hours post aprepitant administration, and 8-10 hours post aprepitant administration. Post-operative aprepitant plasma Cmax was evaluated with a NCA. The LOQ value for this analysis was 10 ng/mL. Participants aged 6 to <12 years who received a single dose of 40 mg aprepitant prior to surgery with evaluable plasma samples were analyzed.

End point type	Primary

End point timeframe:

30-60 minutes pre-administration, 2-4 hours post administration, 5-7 hours post administration, 8-10 hours post administration

Notes:

[17] - 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: Descriptive statistics only were presented for this NCA PK endpoint, and there were no between-group statistical comparisons performed.

End point values	Aprepitant 40 mg (Dose 2): 6 to <12 Year Age Group			
Subject group type	Subject analysis set			
Number of subjects analysed	11			
Units: ng/mL				
geometric mean (geometric coefficient of variation)	930 (± 66.7)			

Statistical analyses

No statistical analyses for this end point

Primary: Tmax of aprepitant following administration of 40 mg dose equivalent in 6 to <12 year age group

End point title	Tmax of aprepitant following administration of 40 mg dose equivalent in 6 to <12 year age group[18]

End point description:

Tmax was analyzed independently for participants in the 40 mg dose equivalent arm aged 6 to <12 years old due to age- and dose-dependent differences in aprepitant absorption and clearance. Because the
opportunity to collect specimens for PK analyses in children is limited, a flexible sparse sampling scheme using ranges of collection times was to be utilized which would limit the burden to participants. Plasma for aprepitant PK assessment was obtained at 30-60 minutes prior to aprepitant administration, 2-4 hours post aprepitant administration, 5-7 hours post aprepitant administration, and 8-10 hours post aprepitant administration. Post-operative aprepitant plasma Tmax was evaluated with a NCA. The LOQ value for this analysis was 10 ng/mL. Participants aged 6 to <12 years who received a single dose of 40 mg aprepitant prior to surgery with evaluable plasma samples were analyzed.

End point type	Primary

End point timeframe:

30-60 minutes pre-administration, 2-4 hours post administration, 5-7 hours post administration, 8-10 hours post administration

Notes:

[18] - 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: Descriptive statistics only were presented for this NCA PK endpoint, and there were no between-group statistical comparisons performed.

End point values	Aprepitant 40 mg (Dose 2): 6 to <12 Year Age Group			
Subject group type	Subject analysis set			
Number of subjects analysed	11			
Units: hr				
geometric mean (geometric coefficient of variation)	4.22 (± 53.4)			

Statistical analyses

No statistical analyses for this end point

Primary: AUC0-last of aprepitant following administration of 40 mg dose equivalent in 2 to <6 year age group

End point title	AUC0-last of aprepitant following administration of 40 mg dose equivalent in 2 to <6 year age group[19]

End point description:

AUC0-last was analyzed independently for participants in the 40 mg dose equivalent arm aged 2 to <6 years old due to age- and dose-dependent differences in aprepitant absorption and clearance. Because the opportunity to collect specimens for PK analyses in children is limited, a flexible sparse sampling scheme using ranges of collection times was to be utilized which would limit the burden to participants. Plasma for aprepitant PK assessment was obtained at 30-60 minutes prior to aprepitant administration, 2-4 hours post aprepitant administration, 5-7 hours post aprepitant administration, and 8-10 hours post aprepitant administration. Post-operative aprepitant plasma AUC0-last was evaluated with a NCA. The LOQ value for this analysis was 10 ng/mL. Participants aged 2 to <6 years who received a single dose of 40 mg aprepitant prior to surgery with evaluable plasma samples were analyzed.

End point type	Primary

End point timeframe:

30-60 minutes pre-administration, 2-4 hours post administration, 5-7 hours post administration, 8-10 hours post administration

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: Descriptive statistics only were presented for this NCA PK endpoint, and there were no between-group statistical comparisons performed.

End point values	Aprepitant 40 mg (Dose 2): 2 to <6 Year Age Group			
Subject group type	Subject analysis set			
Number of subjects analysed	9			
Units: hr*ng/mL				
geometric mean (geometric coefficient of variation)	6320 (± 78.1)			

Statistical analyses

No statistical analyses for this end point

Primary: Cmax of aprepitant following administration of 40 mg dose equivalent in 2 to <6 year age group

End point title	Cmax of aprepitant following administration of 40 mg dose equivalent in 2 to <6 year age group[20]

End point description:

Cmax was analyzed independently for participants in the 40 mg dose equivalent arm aged 2 to <6 years old due to age- and dose-dependent differences in aprepitant absorption and clearance. Because the opportunity to collect specimens for PK analyses in children is limited, a flexible sparse sampling scheme using ranges of collection times was to be utilized which would limit the burden to participants. Plasma for aprepitant PK assessment was obtained at 30-60 minutes prior to aprepitant administration, 2-4 hours post aprepitant administration, 5-7 hours post aprepitant administration, and 8-10 hours post aprepitant administration. Post-operative aprepitant plasma Cmax was evaluated with a NCA. The LOQ value for this analysis was 10 ng/mL. Participants aged 2 to <6 years who received a single dose of 40 mg aprepitant prior to surgery with evaluable plasma samples were analyzed.

End point type	Primary

End point timeframe:

30-60 minutes pre-administration, 2-4 hours post administration, 5-7 hours post administration, 8-10 hours post administration

Notes:

[20] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics only were presented for this NCA PK endpoint, and there were no between-group statistical comparisons performed.

End point values	Aprepitant 40 mg (Dose 2): 2 to <6 Year Age Group			
Subject group type	Subject analysis set			
Number of subjects analysed	9			
Units: ng/mL				
geometric mean (geometric coefficient of variation)	1290 (± 81.7)			

Statistical analyses

No statistical analyses for this end point

Primary: Tmax of aprepitant following administration of 40 mg dose equivalent in 2 to <6 year age group

End point title	Tmax of aprepitant following administration of 40 mg dose equivalent in 2 to <6 year age group[21]

End point description:

Tmax was analyzed independently for participants in the 40 mg dose equivalent arm aged 2 to <6 years

old due to age- and dose-dependent differences in aprepitant absorption and clearance. Because the opportunity to collect specimens for PK analyses in children is limited, a flexible sparse sampling scheme using ranges of collection times was to be utilized which would limit the burden to participants. Plasma for aprepitant PK assessment was obtained at 30-60 minutes prior to aprepitant administration, 2-4 hours post aprepitant administration, 5-7 hours post aprepitant administration, and 8-10 hours post aprepitant administration. Post-operative aprepitant plasma Tmax was evaluated with a NCA. The LOQ value for this analysis was 10 ng/mL. Participants aged 2 to <6 years who received a single dose of 40 mg aprepitant prior to surgery with evaluable plasma samples were analyzed.

End point type	Primary

End point timeframe:

30-60 minutes pre-administration, 2-4 hours post administration, 5-7 hours post administration, 8-10 hours post administration

Notes:

[21] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics only were presented for this NCA PK endpoint, and there were no between-group statistical comparisons performed.

End point values	Aprepitant 40 mg (Dose 2): 2 to <6 Year Age Group			
Subject group type	Subject analysis set			
Number of subjects analysed	9			
Units: hr				
geometric mean (geometric coefficient of variation)	3.35 (± 43.0)			

Statistical analyses

No statistical analyses for this end point

Primary: AUC0-last of aprepitant following administration of 40 mg dose equivalent in birth to <2 year age group

End point title	AUC0-last of aprepitant following administration of 40 mg dose equivalent in birth to <2 year age group[22]

End point description:

AUC0-last was analyzed independently for participants in the 40 mg dose equivalent arm aged birth to <2 years old due to age- and dose-dependent differences in aprepitant absorption and clearance. Because the opportunity to collect specimens for PK analyses in children is limited, a flexible sparse sampling scheme using ranges of collection times was to be utilized which would limit the burden to participants. Plasma for aprepitant PK assessment was obtained at 30-60 minutes prior to aprepitant administration, 2-4 hours post aprepitant administration, 5-7 hours post aprepitant administration, and 8-10 hours post aprepitant administration. Post-operative aprepitant plasma AUC0-last was evaluated with a NCA. The LOQ value for this analysis was 10 ng/mL. Participants aged birth to <2 years who received a single dose of 40 mg aprepitant prior to surgery with evaluable plasma samples were analyzed.

End point type	Primary

End point timeframe:

30-60 minutes pre-administration, 2-4 hours post administration, 5-7 hours post administration, 8-10 hours post administration

Notes:

[22] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics only were presented for this NCA PK endpoint, and there were no between-group statistical comparisons performed.

End point values	Aprepitant 40 mg (Dose 2): Birth to <2 Year Age Group			
Subject group type	Subject analysis set			
Number of subjects analysed	6			
Units: hr*ng/mL				
geometric mean (geometric coefficient of variation)	7910 (± 153.2)			

Statistical analyses

No statistical analyses for this end point

Primary: Cmax of aprepitant following administration of 40 mg dose equivalent in birth to <2 year age group

End point title	Cmax of aprepitant following administration of 40 mg dose equivalent in birth to <2 year age group[23]

End point description:

Cmax was analyzed independently for participants in the 40 mg dose equivalent arm aged birth to <2 years old due to age- and dose-dependent differences in aprepitant absorption and clearance. Because the opportunity to collect specimens for PK analyses in children is limited, a flexible sparse sampling scheme using ranges of collection times was to be utilized which would limit the burden to participants. Plasma for aprepitant PK assessment was obtained at 30-60 minutes prior to aprepitant administration, 2-4 hours post aprepitant administration, 5-7 hours post aprepitant administration, and 8-10 hours post aprepitant administration. Post-operative aprepitant plasma Cmax was evaluated with a NCA. The LOQ value for this analysis was 10 ng/mL. Participants aged birth to <2 years who received a single dose of 40 mg aprepitant prior to surgery with evaluable plasma samples were analyzed.

End point type	Primary

End point timeframe:

30-60 minutes pre-administration, 2-4 hours post administration, 5-7 hours post administration, 8-10 hours post administration

Notes:

[23] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics only were presented for this NCA PK endpoint, and there were no between-group statistical comparisons performed.

End point values	Aprepitant 40 mg (Dose 2): Birth to <2 Year Age Group			
Subject group type	Subject analysis set			
Number of subjects analysed	6			
Units: ng/mL				
geometric mean (geometric coefficient of variation)	1570 (± 146.3)			

Statistical analyses

No statistical analyses for this end point

Primary: Tmax of aprepitant following administration of 40 mg dose equivalent in birth to <2 year age group

End point title	Tmax of aprepitant following administration of 40 mg dose equivalent in birth to <2 year age group[24]

End point description:

Tmax was analyzed independently for participants in the 40 mg dose equivalent arm aged birth to <2 years old due to age- and dose-dependent differences in aprepitant absorption and clearance. Because the opportunity to collect specimens for PK analyses in children is limited, a flexible sparse sampling scheme using ranges of collection times was to be utilized which would limit the burden to participants. Plasma for aprepitant PK assessment was obtained at 30-60 minutes prior to aprepitant administration, 2-4 hours post aprepitant administration, 5-7 hours post aprepitant administration, and 8-10 hours post aprepitant administration. Post-operative aprepitant plasma Tmax was evaluated with a NCA. The LOQ value for this analysis was 10 ng/mL. Participants aged birth to <2 years who received a single dose of 40 mg aprepitant prior to surgery with evaluable plasma samples were analyzed.

End point type	Primary

End point timeframe:

30-60 minutes pre-administration, 2-4 hours post administration, 5-7 hours post administration, 8-10 hours post administration

Notes:

[24] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics only were presented for this NCA PK endpoint, and there were no between-group statistical comparisons performed.

End point values	Aprepitant 40 mg (Dose 2): Birth to <2 Year Age Group			
Subject group type	Subject analysis set			
Number of subjects analysed	7			
Units: hr				
geometric mean (geometric coefficient of variation)	4.94 (± 38.0)			

Statistical analyses

No statistical analyses for this end point

Primary: AUC0-last following administration of 10 mg dose equivalent in 12 to 17 year age group

End point title	AUC0-last following administration of 10 mg dose equivalent in 12 to 17 year age group[25]

End point description:

AUC0-last was analyzed independently for participants in the 10 mg dose equivalent arm aged 12 to 17 years old due to age- and dose-dependent differences in aprepitant absorption and clearance. Because the opportunity to collect specimens for PK analyses in children is limited, a flexible sparse sampling scheme using ranges of collection times was to be utilized which would limit the burden to participants. Plasma for aprepitant PK assessment was obtained at 30-60 minutes prior to aprepitant administration, 2-4 hours post aprepitant administration, 5-7 hours post aprepitant administration, and 8-10 hours post aprepitant administration. Post-operative aprepitant plasma AUC0-last was evaluated with a NCA. The LOQ value for this analysis was 10 ng/mL. Participants aged 12 to 17 years who received a single dose of 10 mg aprepitant prior to surgery with evaluable plasma samples were analyzed.

End point type	Primary

End point timeframe:

30-60 minutes pre-administration, 2-4 hours post administration, 5-7 hours post administration, 8-10

hours post administration

Notes:

[25] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics only were presented for this NCA PK endpoint, and there were no between-group statistical comparisons performed.

End point values	Aprepitant 10 mg (Dose 3): 12 to 17 Year Age Group			
Subject group type	Subject analysis set			
Number of subjects analysed	10			
Units: hr*ng/mL				
geometric mean (geometric coefficient of variation)	806 (± 51.9)			

Statistical analyses

No statistical analyses for this end point

Primary: Cmax of aprepitant following administration of 10 mg dose equivalent in 12 to 17 year age group

End point title	Cmax of aprepitant following administration of 10 mg dose equivalent in 12 to 17 year age group[26]

End point description:

Cmax was analyzed independently for participants in the 10 mg dose equivalent arm aged 12 to 17 years old due to age- and dose-dependent differences in aprepitant absorption and clearance. Because the opportunity to collect specimens for PK analyses in children is limited, a flexible sparse sampling scheme using ranges of collection times was to be utilized which would limit the burden to participants. Plasma for aprepitant PK assessment was obtained at 30-60 minutes prior to aprepitant administration, 2-4 hours post aprepitant administration, 5-7 hours post aprepitant administration, and 8-10 hours post aprepitant administration. Post-operative aprepitant plasma Cmax was evaluated with a NCA. The LOQ value for this analysis was 10 ng/mL. Participants aged 12 to 17 years who received a single dose of 10 mg aprepitant prior to surgery with evaluable plasma samples were analyzed.

End point type	Primary

End point timeframe:

30-60 minutes pre-administration, 2-4 hours post administration, 5-7 hours post administration, 8-10 hours post administration

Notes:

[26] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics only were presented for this NCA PK endpoint, and there were no between-group statistical comparisons performed.

End point values	Aprepitant 10 mg (Dose 3): 12 to 17 Year Age Group			
Subject group type	Subject analysis set			
Number of subjects analysed	10			
Units: ng/mL				
geometric mean (geometric coefficient of variation)	131 (± 50.8)			

Statistical analyses

No statistical analyses for this end point

Primary: Tmax of aprepitant following administration of 10 mg dose equivalent in 12 to 17 year age group

End point title	Tmax of aprepitant following administration of 10 mg dose equivalent in 12 to 17 year age group[27]

End point description:

Tmax was analyzed independently for participants in the 10 mg dose equivalent arm aged 12 to 17 years old due to age- and dose-dependent differences in aprepitant absorption and clearance. Because the opportunity to collect specimens for PK analyses in children is limited, a flexible sparse sampling scheme using ranges of collection times was to be utilized which would limit the burden to participants. Plasma for aprepitant PK assessment was obtained at 30-60 minutes prior to aprepitant administration, 2-4 hours post aprepitant administration, 5-7 hours post aprepitant administration, and 8-10 hours post aprepitant administration. Post-operative aprepitant plasma Tmax was evaluated with a NCA. The LOQ value for this analysis was 10 ng/mL. Participants aged 12 to 17 years who received a single dose of 10 mg aprepitant prior to surgery with evaluable plasma samples were analyzed.

End point type	Primary

End point timeframe:

30-60 minutes pre-administration, 2-4 hours post administration, 5-7 hours post administration, 8-10 hours post administration

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: Descriptive statistics only were presented for this NCA PK endpoint, and there were no between-group statistical comparisons performed.

End point values	Aprepitant 10 mg (Dose 3): 12 to 17 Year Age Group			
Subject group type	Subject analysis set			
Number of subjects analysed	10			
Units: hr				
geometric mean (geometric coefficient of variation)	3.53 (± 54.1)			

Statistical analyses

No statistical analyses for this end point

Primary: AUC0-last of aprepitant following administration of 10 mg dose equivalent in 6 to <12 year age group

End point title	AUC0-last of aprepitant following administration of 10 mg dose equivalent in 6 to <12 year age group[28]

End point description:

AUC0-last was analyzed independently for participants in the 10 mg dose equivalent arm aged 6 to <12

years old due to age- and dose-dependent differences in aprepitant absorption and clearance. Because the opportunity to collect specimens for PK analyses in children is limited, a flexible sparse sampling scheme using ranges of collection times was to be utilized which would limit the burden to participants. Plasma for aprepitant PK assessment was obtained at 30-60 minutes prior to aprepitant administration, 2-4 hours post aprepitant administration, 5-7 hours post aprepitant administration, and 8-10 hours post aprepitant administration. Post-operative aprepitant plasma AUC0-last was evaluated with a NCA. The LOQ value for this analysis was 10 ng/mL. Participants aged 6 to <12 years who received a single dose of 10 mg aprepitant prior to surgery with evaluable plasma samples were analyzed.

End point type	Primary

End point timeframe:

30-60 minutes pre-administration, 2-4 hours post administration, 5-7 hours post administration, 8-10 hours post administration

Notes:

[28] - 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: Descriptive statistics only were presented for this NCA PK endpoint, and there were no between-group statistical comparisons performed.

End point values	Aprepitant 10 mg (Dose 3): 6 to <12 Year Age Group			
Subject group type	Subject analysis set			
Number of subjects analysed	10			
Units: hr*ng/mL				
geometric mean (geometric coefficient of variation)	1390 (± 77.0)			

Statistical analyses

No statistical analyses for this end point

Primary: Cmax of aprepitant following administration of 10 mg dose equivalent in 6 to <12 year age group

End point title	Cmax of aprepitant following administration of 10 mg dose equivalent in 6 to <12 year age group[29]

End point description:

Cmax was analyzed independently for participants in the 10 mg dose equivalent arm aged 6 to <12 years old due to age- and dose-dependent differences in aprepitant absorption and clearance. Because the opportunity to collect specimens for PK analyses in children is limited, a flexible sparse sampling scheme using ranges of collection times was to be utilized which would limit the burden to participants. Plasma for aprepitant PK assessment was obtained at 30-60 minutes prior to aprepitant administration, 2-4 hours post aprepitant administration, 5-7 hours post aprepitant administration, and 8-10 hours post aprepitant administration. Post-operative aprepitant plasma Cmax was evaluated with a NCA. The LOQ value for this analysis was 10 ng/mL. Participants aged 6 to <12 years who received a single dose of 10 mg aprepitant prior to surgery with evaluable plasma samples were analyzed.

End point type	Primary

End point timeframe:

30-60 minutes pre-administration, 2-4 hours post administration, 5-7 hours post administration, 8-10 hours post administration

Notes:

[29] - 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: Descriptive statistics only were presented for this NCA PK endpoint, and there were no between-group statistical comparisons performed.

End point values	Aprepitant 10 mg (Dose 3): 6 to <12 Year Age Group			
Subject group type	Subject analysis set			
Number of subjects analysed	10			
Units: ng/mL				
geometric mean (geometric coefficient of variation)	289 (± 128.4)			

Statistical analyses

No statistical analyses for this end point

Primary: Tmax of aprepitant following administration of 10 mg dose equivalent in 6 to <12 year age group

End point title	Tmax of aprepitant following administration of 10 mg dose equivalent in 6 to <12 year age group[30]

End point description:

Tmax was analyzed independently for participants in the 10 mg dose equivalent arm aged 6 to <12 years old due to age- and dose-dependent differences in aprepitant absorption and clearance. Because the opportunity to collect specimens for PK analyses in children is limited, a flexible sparse sampling scheme using ranges of collection times was to be utilized which would limit the burden to participants. Plasma for aprepitant PK assessment was obtained at 30-60 minutes prior to aprepitant administration, 2-4 hours post aprepitant administration, 5-7 hours post aprepitant administration, and 8-10 hours post aprepitant administration. Post-operative aprepitant plasma Tmax was evaluated with a NCA. The LOQ value for this analysis was 10 ng/mL. Participants aged 6 to <12 years who received a single dose of 40 mg aprepitant prior to surgery with evaluable plasma samples were analyzed.

End point type	Primary

End point timeframe:

30-60 minutes pre-administration, 2-4 hours post administration, 5-7 hours post administration, 8-10 hours post administration

Notes:

[30] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics only were presented for this NCA PK endpoint, and there were no between-group statistical comparisons performed.

End point values	Aprepitant 10 mg (Dose 3): 6 to <12 Year Age Group			
Subject group type	Subject analysis set			
Number of subjects analysed	10			
Units: hr				
geometric mean (geometric coefficient of variation)	3.75 (± 57.9)			

Statistical analyses

No statistical analyses for this end point

Primary: AUC0-last of aprepitant following administration of 10 mg dose equivalent

in 2 to <6 year age group

End point title	AUC0-last of aprepitant following administration of 10 mg dose equivalent in 2 to <6 year age group[31]

End point description:

AUC0-last was analyzed independently for participants in the 10 mg dose equivalent arm aged 2 to <6 years old due to age- and dose-dependent differences in aprepitant absorption and clearance. Because the opportunity to collect specimens for PK analyses in children is limited, a flexible sparse sampling scheme using ranges of collection times was to be utilized which would limit the burden to participants. Plasma for aprepitant PK assessment was obtained at 30-60 minutes prior to aprepitant administration, 2-4 hours post aprepitant administration, 5-7 hours post aprepitant administration, and 8-10 hours post aprepitant administration. Post-operative aprepitant plasma AUC0-last was evaluated with a NCA. The LOQ value for this analysis was 10 ng/mL. Participants aged 2 to <6 years who received a single dose of 10 mg aprepitant prior to surgery with evaluable plasma samples were analyzed.

End point type	Primary

End point timeframe:

30-60 minutes pre-administration, 2-4 hours post administration, 5-7 hours post administration, 8-10 hours post administration

Notes:

[31] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics only were presented for this NCA PK endpoint, and there were no between-group statistical comparisons performed.

End point values	Aprepitant 10 mg (Dose 3): 2 to <6 Year Age Group			
Subject group type	Subject analysis set			
Number of subjects analysed	10			
Units: hr*ng/mL				
geometric mean (geometric coefficient of variation)	1580 (± 45.2)			

Statistical analyses

No statistical analyses for this end point

Primary: Cmax of aprepitant following administration of 10 mg dose equivalent in 2 to <6 year age group

End point title	Cmax of aprepitant following administration of 10 mg dose equivalent in 2 to <6 year age group[32]

End point description:

Cmax was analyzed independently for participants in the 10 mg dose equivalent arm aged 2 to <6 years old due to age- and dose-dependent differences in aprepitant absorption and clearance. Because the opportunity to collect specimens for PK analyses in children is limited, a flexible sparse sampling scheme using ranges of collection times was to be utilized which would limit the burden to participants. Plasma for aprepitant PK assessment was obtained at 30-60 minutes prior to aprepitant administration, 2-4 hours post aprepitant administration, 5-7 hours post aprepitant administration, and 8-10 hours post aprepitant administration. Post-operative aprepitant plasma Cmax was evaluated with a NCA. The LOQ value for this analysis was 10 ng/mL. Participants aged 2 to <6 years who received a single dose of 10 mg aprepitant prior to surgery with evaluable plasma samples were analyzed.

End point type	Primary

End point timeframe:

30-60 minutes pre-administration, 2-4 hours post administration, 5-7 hours post administration, 8-10 hours post administration

Notes:

[32] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics only were presented for this NCA PK endpoint, and there were no between-group statistical comparisons performed.

End point values	Aprepitant 10 mg (Dose 3): 2 to <6 Year Age Group			
Subject group type	Subject analysis set			
Number of subjects analysed	10			
Units: ng/mL				
geometric mean (geometric coefficient of variation)	300 (± 49.9)			

Statistical analyses

No statistical analyses for this end point

Primary: Tmax of aprepitant following administration of 10 mg dose equivalent in 2 to <6 year age group

End point title	Tmax of aprepitant following administration of 10 mg dose equivalent in 2 to <6 year age group[33]

End point description:

Tmax was analyzed independently for participants in the 10 mg dose equivalent arm aged 2 to <6 years old due to age- and dose-dependent differences in aprepitant absorption and clearance. Because the opportunity to collect specimens for PK analyses in children is limited, a flexible sparse sampling scheme using ranges of collection times was to be utilized which would limit the burden to participants. Plasma for aprepitant PK assessment was obtained at 30-60 minutes prior to aprepitant administration, 2-4 hours post aprepitant administration, 5-7 hours post aprepitant administration, and 8-10 hours post aprepitant administration. Post-operative aprepitant plasma Tmax was evaluated with a NCA. The LOQ value for this analysis was 10 ng/mL. Participants aged 2 to <6 years who received a single dose of 10 mg aprepitant prior to surgery with evaluable plasma samples were analyzed.

End point type	Primary

End point timeframe:

30-60 minutes pre-administration, 2-4 hours post administration, 5-7 hours post administration, 8-10 hours post administration

Notes:

[33] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics only were presented for this NCA PK endpoint, and there were no between-group statistical comparisons performed.

End point values	Aprepitant 10 mg (Dose 3): 2 to <6 Year Age Group			
Subject group type	Subject analysis set			
Number of subjects analysed	10			
Units: hr				
geometric mean (geometric coefficient of variation)	3.36 (± 45.8)			

Statistical analyses

No statistical analyses for this end point

Primary: AUC0-last of aprepitant following administration of 10 mg dose equivalent in birth to <2 year age group

End point title	AUC0-last of aprepitant following administration of 10 mg dose equivalent in birth to <2 year age group[34]

End point description:

AUC0-last was analyzed independently for participants in the 10 mg dose equivalent arm aged from birth to <2 years old due to age- and dose-dependent differences in aprepitant absorption and clearance. Because the opportunity to collect specimens for PK analyses in children is limited, a flexible sparse sampling scheme using ranges of collection times was to be utilized which would limit the burden to participants. Plasma for aprepitant PK assessment was obtained at 30-60 minutes prior to aprepitant administration, 2-4 hours post aprepitant administration, 5-7 hours post aprepitant administration, and 8-10 hours post aprepitant administration. Post-operative aprepitant plasma AUC0-last was evaluated with a NCA. The LOQ value for this analysis was 10 ng/mL. Participants aged birth to <2 years who received a single dose of 10 mg aprepitant prior to surgery with evaluable plasma samples were analyzed.

End point type	Primary

End point timeframe:

30-60 minutes pre-administration, 2-4 hours post administration, 5-7 hours post administration, 8-10 hours post administration

Notes:

[34] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics only were presented for this NCA PK endpoint, and there were no between-group statistical comparisons performed.

End point values	Aprepitant 10 mg (Dose 3): Birth to <2 Year Age Group			
Subject group type	Subject analysis set			
Number of subjects analysed	10			
Units: hr*ng/mL				
geometric mean (geometric coefficient of variation)	1800 (± 107.8)			

Statistical analyses

No statistical analyses for this end point

Primary: Cmax of aprepitant following administration of 10 mg dose equivalent in birth to <2 year age group

End point title	Cmax of aprepitant following administration of 10 mg dose equivalent in birth to <2 year age group[35]

End point description:

Cmax was analyzed independently for participants in the 10 mg dose equivalent arm aged from birth to <2 years old due to age- and dose-dependent differences in aprepitant absorption and clearance. Because the opportunity to collect specimens for PK analyses in children is limited, a flexible sparse sampling scheme using ranges of collection times was to be utilized which would limit the burden to participants. Plasma for aprepitant PK assessment was obtained at 30-60 minutes prior to aprepitant administration, 2-4 hours post aprepitant administration, 5-7 hours post aprepitant administration, and 8-10 hours post aprepitant administration. Post-operative aprepitant plasma Cmax was evaluated with a NCA. The LOQ value for this analysis was 10 ng/mL. Participants aged birth to <2 years who received a single dose of 10 mg aprepitant prior to surgery with evaluable plasma samples were analyzed.

End point type	Primary

End point timeframe:

30-60 minutes pre-administration, 2-4 hours post administration, 5-7 hours post administration, 8-10 hours post administration

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: Descriptive statistics only were presented for this NCA PK endpoint, and there were no between-group statistical comparisons performed.

End point values	Aprepitant 10 mg (Dose 3): Birth to <2 Year Age Group			
Subject group type	Subject analysis set			
Number of subjects analysed	10			
Units: ng/mL				
geometric mean (geometric coefficient of variation)	336 (± 112.0)			

Statistical analyses

No statistical analyses for this end point

Primary: Tmax of aprepitant following administration of 10 mg dose equivalent in birth to <2 year age group

End point title	Tmax of aprepitant following administration of 10 mg dose equivalent in birth to <2 year age group[36]

End point description:

Tmax was analyzed independently for participants in the 10 mg dose equivalent arm aged from birth to <2 years old due to age- and dose-dependent differences in aprepitant absorption and clearance. Because the opportunity to collect specimens for PK analyses in children is limited, a flexible sparse sampling scheme using ranges of collection times was to be utilized which would limit the burden to participants. Plasma for aprepitant PK assessment was obtained at 30-60 minutes prior to aprepitant administration, 2-4 hours post aprepitant administration, 5-7 hours post aprepitant administration, and 8-10 hours post aprepitant administration. Post-operative aprepitant plasma Tmax was evaluated with a NCA. The LOQ value for this analysis was 10 ng/mL. Participants aged birth to <2 years who received a single dose of 10 mg aprepitant prior to surgery with evaluable plasma samples were analyzed.

End point type	Primary

End point timeframe:

30-60 minutes pre-administration, 2-4 hours post administration, 5-7 hours post administration, 8-10 hours post administration

Notes:

[36] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics only were presented for this NCA PK endpoint, and there were no between-group statistical comparisons performed.

End point values	Aprepitant 10 mg (Dose 3): Birth to <2 Year Age Group			
Subject group type	Subject analysis set			
Number of subjects analysed	10			
Units: hr				

geometric mean (geometric coefficient of variation)	4.11 (± 48.2)			

Statistical analyses

No statistical analyses for this end point

Primary: Area under the concentration-time curve of aprepitant from time 0 to infinity (AUC0-inf) following administration of single dose

End point title	Area under the concentration-time curve of aprepitant from time 0 to infinity (AUC0-inf) following administration of single dose[37]

End point description:

Plasma for aprepitant AUC0-inf assessment was obtained at 30-60 minutes prior to aprepitant administration, 2-4 hours post aprepitant administration, 5-7 hours post aprepitant administration, and 8-10 hours post aprepitant administration. Because the opportunity to collect specimens for PK analyses in children is limited, a flexible sparse sampling scheme using ranges of collection times was to be utilized which would limit the burden to participants. AUC0-inf data were to be log transformed and analyzed via a linear mixed-effects model containing fixed effects for age for each dose level tested. Due to the lack of samples beyond 8 hours after dose, the assessment of the terminal elimination phase of the PK profiles was limited and derivation of parameters dependent on lambda (e.g. AUC0-inf) was not possible.

End point type	Primary

End point timeframe:

30-60 minutes pre-administration, 2-4 hours post administration, 5-7 hours post administration, 8-10 hours post administration

Notes:

[37] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Due to a limited PK sampling scheme (up to 8 hours post-dose), NCA analysis was not performed for this endpoint.

End point values	Aprepitant Dose 1: Equivalent to 125 mg in Adults	Aprepitant Dose 2: Equivalent to 40 mg in Adults	Aprepitant Dose 3: Equivalent to 10 mg in Adults	Ondansetron
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[38]	0[39]	0[40]	0[41]
Units: hr*ng/mL				
geometric mean (geometric coefficient of variation)	()	()	()	()

Notes:

[38] - Due to a limited PK sampling scheme (up to 8 hours post-dose), PK parameter not derived using NCA.
[39] - Due to a limited PK sampling scheme (up to 8 hours post-dose), PK parameter not derived using NCA.
[40] - Due to a limited PK sampling scheme (up to 8 hours post-dose), PK parameter not derived using NCA.
[41] - Due to a limited PK sampling scheme (up to 8 hours post-dose), PK parameter not derived using NCA.

Statistical analyses

No statistical analyses for this end point

Primary: Apparent total clearance (CL/F) of aprepitant from plasma following administration of single dose

End point title	Apparent total clearance (CL/F) of aprepitant from plasma following administration of single dose[42]

End point description:

Plasma for aprepitant CL/F assessment was obtained at 30-60 minutes prior to aprepitant administration, 2-4 hours post aprepitant administration, 5-7 hours post aprepitant administration, and 8-10 hours post aprepitant administration. Because the opportunity to collect specimens for PK analyses in children is limited, a flexible sparse sampling scheme using ranges of collection times was to be utilized which would limit the burden to participants. CL/F data were to be log transformed and analyzed via a linear mixed-effects model containing fixed effects for age for each dose level tested. Due to the lack of samples beyond 8 hours after dose, the assessment of the terminal elimination phase of the PK profiles was limited and derivation of parameters dependent on lambda (e.g. CL/F) was not possible.

End point type	Primary

End point timeframe:

30-60 minutes pre-administration, 2-4 hours post administration, 5-7 hours post administration, 8-10 hours post administration

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: Due to a limited PK sampling scheme (up to 8 hours post-dose), NCA analysis was not performed for this endpoint.

End point values	Aprepitant Dose 1: Equivalent to 125 mg in Adults	Aprepitant Dose 2: Equivalent to 40 mg in Adults	Aprepitant Dose 3: Equivalent to 10 mg in Adults	Ondansetron
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[43]	0[44]	0[45]	0[46]
Units: L/h				
geometric mean (geometric coefficient of variation)	()	()	()	()

Notes:

[43] - Due to a limited PK sampling scheme (up to 8 hours post-dose), PK parameter not derived using NCA.
[44] - Due to a limited PK sampling scheme (up to 8 hours post-dose), PK parameter not derived using NCA.
[45] - Due to a limited PK sampling scheme (up to 8 hours post-dose), PK parameter not derived using NCA.
[46] - Due to a limited PK sampling scheme (up to 8 hours post-dose), PK parameter not derived using NCA.

Statistical analyses

No statistical analyses for this end point

Primary: Apparent terminal half-life (t ½) of aprepitant following administration of single dose

End point title	Apparent terminal half-life (t ½) of aprepitant following administration of single dose[47]

End point description:

Plasma for aprepitant t ½ assessment was obtained at 30-60 minutes prior to aprepitant administration, 2-4 hours post aprepitant administration, 5-7 hours post aprepitant administration, and 8-10 hours post aprepitant administration. Because the opportunity to collect specimens for PK analyses in children is limited, a flexible sparse sampling scheme using ranges of collection times was to be utilized which would limit the burden to participants. t ½ data were to be log transformed and analyzed via a linear mixed-effects model containing fixed effects for age for each dose level tested. Due to the lack of samples beyond 8 hours after dose, the assessment of the terminal elimination phase of the PK profiles was limited and derivation of parameters dependent on lambda (e.g. t ½) was not possible.

End point type	Primary

End point timeframe:

30-60 minutes pre-administration, 2-4 hours post administration, 5-7 hours post administration, 8-10 hours post administration

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: Due to a limited PK sampling scheme (up to 8 hours post-dose), NCA analysis was not performed for this endpoint.

End point values	Aprepitant Dose 1: Equivalent to 125 mg in Adults	Aprepitant Dose 2: Equivalent to 40 mg in Adults	Aprepitant Dose 3: Equivalent to 10 mg in Adults	Ondansetron
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[48]	0[49]	0[50]	0[51]
Units: hr				
geometric mean (geometric coefficient of variation)	()	()	()	()

Notes:

[48] - Due to a limited PK sampling scheme (up to 8 hours post-dose), PK parameter not derived using NCA.
[49] - Due to a limited PK sampling scheme (up to 8 hours post-dose), PK parameter not derived using NCA.
[50] - Due to a limited PK sampling scheme (up to 8 hours post-dose), PK parameter not derived using NCA.
[51] - Due to a limited PK sampling scheme (up to 8 hours post-dose), PK parameter not derived using NCA.

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of participants experiencing at least one adverse event (AE)

End point title	Percentage of participants experiencing at least one adverse event (AE)

End point description:

An AE is defined as any unfavorable and unintended change in the structure, function, or chemistry of the body temporally ssociated with the use of the SPONSOR’s product, whether or not considered related to the use of the product. Any worsening of a preexisting condition which is temporally associated with the use of the SPONSOR’s product, is also an AE. Changes resulting from normal growth and development which do not vary significantly in frequency or severity from expected levels are not to be considered adverse events. Events related to the exploratory efficacy endpoint (e.g., vomiting and retching) were not defined as AEs during the period of efficacy data collection (24 hours following the end of surgery) unless they met the definition of an SAE.

The percentage of participants experiencing ≥1 AE was reported by dose group. All randomized participants who received at least one dose of study treatment were analyzed.

End point type	Primary

End point timeframe:

From pre-operative phase up to Follow-up (Day 1 to Day 15)

End point values	Aprepitant Dose 1: Equivalent to 125 mg in Adults	Aprepitant Dose 2: Equivalent to 40 mg in Adults	Aprepitant Dose 3: Equivalent to 10 mg in Adults	Ondansetron
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	57	55	56	52
Units: percentage of participants				
number (not applicable)	31.6	43.6	35.7	48.1

Statistical analyses

Statistical analysis title	125 mg Aprepitant vs Odansetron: % Difference
Statistical analysis description:	
The Miettinen and Nurminen method was used to provide 95% confidence intervals (CIs) for between-treatment differences in the percentage of participants with events.	
Comparison groups	Aprepitant Dose 1: Equivalent to 125 mg in Adults v Ondansetron
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in Percentage vs. Ondansetron
Point estimate	-16.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-34
upper limit	2

Statistical analysis title	40 mg Aprepitant vs Odansetron: % Difference
Statistical analysis description:	
The Miettinen and Nurminen method was used to provide 95% confidence intervals (CIs) for between-treatment differences in the percentage of participants with events.	
Comparison groups	Aprepitant Dose 2: Equivalent to 40 mg in Adults v Ondansetron
Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in Percentage vs. Ondansetron
Point estimate	-4.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-22.9
upper limit	14.3

Statistical analysis title	10 mg Aprepitant vs Odansetron: % Difference

Statistical analysis description:

The Miettinen and Nurminen method was used to provide 95% confidence intervals (CIs) for between-treatment differences in the percentage of participants with events.

Comparison groups	Aprepitant Dose 3: Equivalent to 10 mg in Adults v Ondansetron
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in Percentage vs. Ondansetron
Point estimate	-12.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-30.3
upper limit	6.3

Primary: Percentage of participants discontinuing study due to an AE

End point title	Percentage of participants discontinuing study due to an AE[52]

End point description:

An AE is defined as any unfavorable and unintended change in the structure, function, or chemistry of the body temporally ssociated with the use of the SPONSOR’s product, whether or not considered related to the use of the product. Any worsening of a preexisting condition which is temporally associated with the use of the SPONSOR’s product, is also an AE. Changes resulting from normal growth and development which do not vary significantly in frequency or severity from expected levels are not to be considered adverse events. Events related to the exploratory efficacy endpoint (e.g., vomiting and retching) were not defined as AEs during the period of efficacy data collection (24 hours following the end of surgery) unless they met the definition of an SAE.

The percentage of participants discontinuing study treatment due to an AE was reported by dose group. All randomized participants who received at least one dose of study treatment were analyzed.

End point type	Primary

End point timeframe:

From pre-operative phase up to hospital discharge (Day 1)

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: Descriptive statistics only were presented for this safety endpoint, and there were no between-group statistical comparisons performed.

End point values	Aprepitant Dose 1: Equivalent to 125 mg in Adults	Aprepitant Dose 2: Equivalent to 40 mg in Adults	Aprepitant Dose 3: Equivalent to 10 mg in Adults	Ondansetron
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	57	55	56	52
Units: percentage of participants				
number (not applicable)	0.0	0.0	0.0	0.0

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From pre-operative phase up to Follow-up (Day 1 to Day 15)

Adverse event reporting additional description:

All randomized participants who received at least one dose of study treatment were analyzed. 1 participant was inadvertently randomized to a 2.5 mg aprepitant dose group which was not assessed for overall efficacy and safety, thus participant was not included in this safety analysis (data reported as narrative).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.1

Reporting groups

Reporting group title	Aprepitant Dose 1: Equivalent to 125 mg in Adults

Reporting group description:

Pediatric participants received a single dose of apprepitant that was equivalent to 125 mg in adults on Day 1 between 1 and 3 hours prior to expected induction of anesthesia, plus placebo for odansetron administered IV immediately prior to anesthesia.

Reporting group title	Aprepitant Dose 2: Equivalent to 40 mg in Adults

Reporting group description:

Pediatric participants received a single dose of apprepitant that was equivalent to 40 mg in adults on Day 1 between 1 and 3 hours prior to expected induction of anesthesia, plus placebo for odansetron administered IV immediately prior to anesthesia.

Reporting group title	Aprepitant Dose 3: Equivalent to 10 mg in Adults

Reporting group description:

Pediatric participants received a single dose of apprepitant that was equivalent to 10 mg in adults Day 1 between 1 and 3 hours prior to expected induction of anesthesia, plus placebo for odansetron administered IV immediately prior to anesthesia.

Reporting group title	Ondansetron

Reporting group description:

Pediatric participants in the control regimen were administered ondansetron IV on Day 1 immediately prior to induction of anesthesia plus a matching placebo dose to aprepitant as a single oral dose on Day 1 between 1 and 3 hours prior to expected induction of anesthesia.

Serious adverse events	Aprepitant Dose 1: Equivalent to 125 mg in Adults	Aprepitant Dose 2: Equivalent to 40 mg in Adults	Aprepitant Dose 3: Equivalent to 10 mg in Adults
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 57 (0.00%)	6 / 55 (10.91%)	1 / 56 (1.79%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Post procedural haemorrhage			
subjects affected / exposed	0 / 57 (0.00%)	3 / 55 (5.45%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Procedural complication			
subjects affected / exposed	0 / 57 (0.00%)	0 / 55 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Thrombosis			
subjects affected / exposed	0 / 57 (0.00%)	1 / 55 (1.82%)	0 / 56 (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
Cardiac disorders			
Cardio-respiratory arrest			
subjects affected / exposed	0 / 57 (0.00%)	1 / 55 (1.82%)	0 / 56 (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
Reproductive system and breast disorders			
Male genital tract fistula			
subjects affected / exposed	0 / 57 (0.00%)	0 / 55 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pulmonary oedema			
subjects affected / exposed	0 / 57 (0.00%)	1 / 55 (1.82%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Bladder perforation			
subjects affected / exposed	0 / 57 (0.00%)	1 / 55 (1.82%)	0 / 56 (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
Infections and infestations			
Bronchiolitis			
subjects affected / exposed	0 / 57 (0.00%)	0 / 55 (0.00%)	1 / 56 (1.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Ondansetron		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 52 (3.85%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Post procedural haemorrhage			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Procedural complication			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Thrombosis			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Cardio-respiratory arrest			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Male genital tract fistula			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pulmonary oedema			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			

Bladder perforation			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Bronchiolitis			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Aprepitant Dose 1: Equivalent to 125 mg in Adults	Aprepitant Dose 2: Equivalent to 40 mg in Adults	Aprepitant Dose 3: Equivalent to 10 mg in Adults
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 57 (19.30%)	11 / 55 (20.00%)	12 / 56 (21.43%)
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	0 / 57 (0.00%)	0 / 55 (0.00%)	1 / 56 (1.79%)
occurrences (all)	0	0	1
Procedural pain			
subjects affected / exposed	4 / 57 (7.02%)	4 / 55 (7.27%)	3 / 56 (5.36%)
occurrences (all)	8	4	3
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	3 / 57 (5.26%)	1 / 55 (1.82%)	3 / 56 (5.36%)
occurrences (all)	5	1	5
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	3 / 57 (5.26%)	3 / 55 (5.45%)	4 / 56 (7.14%)
occurrences (all)	6	4	6
Vomiting			
subjects affected / exposed	2 / 57 (3.51%)	3 / 55 (5.45%)	2 / 56 (3.57%)
occurrences (all)	3	3	3

Non-serious adverse events	Ondansetron		

Total subjects affected by non-serious adverse events subjects affected / exposed	16 / 52 (30.77%)		
Injury, poisoning and procedural complications Accidental overdose subjects affected / exposed occurrences (all) Procedural pain subjects affected / exposed occurrences (all)	 3 / 52 (5.77%) 3 5 / 52 (9.62%) 6		
General disorders and administration site conditions Pyrexia subjects affected / exposed occurrences (all)	 0 / 52 (0.00%) 0		
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all)	 4 / 52 (7.69%) 6 4 / 52 (7.69%) 6		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported