# 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 | v1 |
| This version publication date | 08 April 2017 |
| First version publication date | 08 April 2017 |

## 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 is to evaluate the pharmacokinetics (PK), safety, and tolerability of aprepitant for the prevention of post-operative nausea and vomiting (PONV) in pediatric participants.

Postoperative aprepitant plasma concentrations will be evaluated with a non-compartmental analysis (NCA) at each dose and for each age cohort. Full PK profiles analyzed using population PK modeling and simulation will be reported 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 |

### 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 | 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.

| | |
|---|---|
| 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.

| | |
|---|---|
| **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 | ± 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 | | |
| standard deviation | ± 65 | - | |
| 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:

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. Postoperative 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) | | | |

### 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:

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. Postoperative 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:

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. Postoperative 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:

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. Postoperative 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:

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. Postoperative 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) | | | |

## 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:

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. Postoperative 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:

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. Postoperative 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:

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. Postoperative 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:

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. Postoperative 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:

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. Postoperative 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:

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. Postoperative 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:

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. Postoperative 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:

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. Postoperative 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:

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. Postoperative 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:

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. Postoperative 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:

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. Postoperative 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:

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. Postoperative 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:

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. Postoperative 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:

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. Postoperative 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:

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. Postoperative 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:

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. Postoperative 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) | | | |

## 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:

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. Postoperative 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 | 7 | | | |
| 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:

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. Postoperative 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:

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. Postoperative 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) | | | |

## 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:

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. Postoperative 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) | 1390 (± 77) | | | |

## 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:

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. Postoperative 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) | 289 (± 128.4) | | | |

## 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:

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. Postoperative 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) | 3.75 (± 57.9) | | | |

## Statistical analyses

No statistical analyses for this end point

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

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. Postoperative 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) | 1580 (± 45.2) | | | |

### 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:

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. Postoperative 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) | 300 (± 49.9) | | | |

### 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:

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. Postoperative 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) | 3.36 (± 45.8) | | | |

## Statistical analyses

No statistical analyses for this end point

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

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. Postoperative 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:

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. Postoperative 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:

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. Postoperative 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:

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. Postoperative 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:

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. Postoperative 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) | | | |

## 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:

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. Postoperative 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 125 mg dose equivalent

| | |
|---|---|
| End point title | Area under the concentration-time curve of aprepitant from time 0 to infinity (AUC0-inf) following administration of 125 mg dose equivalent[37] |

End point description:

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 125 mg dose equivalent

| End point title | Apparent total clearance (CL/F) of aprepitant from plasma following administration of 125 mg dose equivalent[42] |
|---|---|

End point description:

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 125 mg dose equivalent

| End point title | Apparent terminal half-life (t ½) of aprepitant following administration of 125 mg dose equivalent[47] |
|---|---|

End point description:

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 |
| 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 |
| 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 |
| 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 |

## 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<br>subjects affected / exposed | 16 / 52 (30.77%) | | |
| Injury, poisoning and procedural complications<br>Accidental overdose<br>subjects affected / exposed<br>occurrences (all)<br><br>Procedural pain<br>subjects affected / exposed<br>occurrences (all) | <br><br>3 / 52 (5.77%)<br>3<br><br><br>5 / 52 (9.62%)<br>6 | | |
| General disorders and administration site conditions<br>Pyrexia<br>subjects affected / exposed<br>occurrences (all) | <br><br>0 / 52 (0.00%)<br>0 | | |
| Gastrointestinal disorders<br>Abdominal pain<br>subjects affected / exposed<br>occurrences (all)<br><br>Vomiting<br>subjects affected / exposed<br>occurrences (all) | <br><br>4 / 52 (7.69%)<br>6<br><br><br>4 / 52 (7.69%)<br>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