



Clinical trial results:

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

Subtitle:

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

Summary

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

Results information

| | |
|--------------------------------|------------------|
| Result version number | v2 (current) |
| This version publication date | 04 November 2017 |
| First version publication date | 18 May 2017 |
| Version creation reason | |

Trial information

Trial identification

| | |
|-----------------------|----------|
| Sponsor protocol code | 0517-029 |
|-----------------------|----------|

Additional study identifiers

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

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

| | |
|--|------------------|
| Analysis stage | Final |
| Date of interim/final analysis | 21 November 2016 |
| Is this the analysis of the primary completion data? | No |

| | |
|----------------------------------|------------------|
| Global end of trial reached? | Yes |
| Global end of trial date | 21 November 2016 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

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

Protection of trial subjects:

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

The following additional measure defined for this individual study was in place for the protection of trial subjects: Participants will be permitted to take "rescue medication" for established (not anticipated) nausea and vomiting throughout the study.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 13 December 2012 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|--------------|
| Country: Number of subjects enrolled | Argentina: 3 |
| Country: Number of subjects enrolled | Austria: 16 |
| Country: Number of subjects enrolled | Brazil: 10 |
| Country: Number of subjects enrolled | Canada: 2 |
| Country: Number of subjects enrolled | Chile: 28 |
| Country: Number of subjects enrolled | Estonia: 4 |
| Country: Number of subjects enrolled | Germany: 6 |

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

Notes:

Subjects enrolled per age group

| | |
|---|-----|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 23 |
| Children (2-11 years) | 149 |
| Adolescents (12-17 years) | 68 |
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

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

Pre-assignment

Screening details:

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

Period 1

| | |
|------------------------------|-------------------------|
| Period 1 title | Base Study-Cycle 1 |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator |

Arms

| | |
|------------------------------|-------------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Fosaprepitant 5 mg/kg-Cycle 1 |

Arm description:

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

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

Dosage and administration details:

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

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

Dosage and administration details:

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

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

Dosage and administration details:

Administered IV

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

Dosage and administration details:

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

| | |
|------------------|---------------------------------|
| Arm title | Fosaprepitant 0.4 mg/kg-Cycle 1 |
|------------------|---------------------------------|

Arm description:

Participants 12 to 17 years old were administered 20 mg IV fosaprepitant. Participants 2 to <12 years old were administered a weight-adjusted dose of 0.4 mg/kg (not to exceed 20 mg). Participants were also administered IV ondansetron 0.15 mg/kg x 3 doses with or without dexamethasone.

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

Dosage and administration details:

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

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

Dosage and administration details:

Administered IV

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

Dosage and administration details:

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

| | |
|------------------|-------------------------|
| Arm title | Placebo Control-Cycle 1 |
|------------------|-------------------------|

Arm description:

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

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

Dosage and administration details:

Placebo Fosaprepitant administered IV as a single dose.

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

Dosage and administration details:

Administered IV

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

Dosage and administration details:

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

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

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

Period 2

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

Arms

| | |
|------------------------------|-----|
| Are arms mutually exclusive? | Yes |
|------------------------------|-----|

| | |
|------------------|---------------------------------|
| Arm title | Fosaprepitant 5 mg/kg Cycle 2-6 |
|------------------|---------------------------------|

Arm description:

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

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

Dosage and administration details:

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

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

Dosage and administration details:

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

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

Dosage and administration details:

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

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

Dosage and administration details:

Administered IV

| | |
|------------------|---------------------------------|
| Arm title | Fosaprepitant 3 mg/kg Cycle 2-6 |
|------------------|---------------------------------|

Arm description:

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

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

Dosage and administration details:

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

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

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

| Number of subjects in period 2^[1] | Fosaprepitant 5 mg/kg Cycle 2-6 | Fosaprepitant 3 mg/kg Cycle 2-6 |
|---|--|--|
| Started | 47 | 106 |
| Completed | 12 | 37 |
| Not completed | 35 | 69 |
| Participant moved | - | 2 |
| Physician decision | 7 | 11 |
| Technical problems | - | 1 |
| Excluded medication | 1 | 2 |
| Additional cycle inclusion/exclusion criteria | 4 | 11 |
| Did not respond to chemotherapy regimen | 1 | - |
| Withdrawal by parent/guardian | 1 | 5 |
| Consent withdrawn by subject | - | 2 |
| Completed chemotherapy regimen | 15 | 24 |
| Death | - | 2 |
| Lost to follow-up | - | 1 |
| Non compliance with protocol | 6 | 4 |
| Protocol deviation | - | 4 |

Notes:

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

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

Baseline characteristics

Reporting groups

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

| Reporting group values | Fosaprepitant 5 mg/kg-Cycle 1 | Fosaprepitant 3 mg/kg-Cycle 1 | Fosaprepitant 1.2 mg/kg-Cycle 1 |
|--|-------------------------------|-------------------------------|---------------------------------|
| Number of subjects | 74 | 43 | 44 |
| Age Categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 23 | 0 | 0 |
| Children (2-11 years) | 51 | 26 | 27 |
| Adolescents (12-17 years) | 0 | 17 | 17 |
| Adults (18-64 years) | 0 | 0 | 0 |
| From 65-84 years | 0 | 0 | 0 |
| 85 years and over | 0 | 0 | 0 |
| Age Continuous | | | |
| Units: months | | | |
| arithmetic mean | 60.2 | 123.8 | 119.4 |
| standard deviation | ± 42.3 | ± 51.3 | ± 52.7 |

| | | | |
|--------------------|----|----|----|
| Gender Categorical | | | |
| Units: Subjects | | | |
| Female | 32 | 18 | 23 |
| Male | 42 | 25 | 21 |

| Reporting group values | Fosaprepitant 0.4 mg/kg-Cycle 1 | Placebo Control- Cycle 1 | Total |
|---|------------------------------------|-----------------------------|-------|
| Number of subjects | 41 | 38 | 240 |
| Age Categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 23 |
| Children (2-11 years) | 24 | 21 | 149 |
| Adolescents (12-17 years) | 17 | 17 | 68 |
| Adults (18-64 years) | 0 | 0 | 0 |
| From 65-84 years | 0 | 0 | 0 |
| 85 years and over | 0 | 0 | 0 |
| Age Continuous | | | |
| Units: months | | | |
| arithmetic mean | 119.2 | 122.5 | |
| standard deviation | ± 54.3 | ± 54.0 | - |
| Gender Categorical | | | |
| Units: Subjects | | | |
| Female | 19 | 19 | 111 |
| Male | 22 | 19 | 129 |

End points

End points reporting groups

| | |
|--|---------------------------------|
| Reporting group title | Fosaprepitant 5 mg/kg-Cycle 1 |
| Reporting group description: Participants were administered intravenous (IV) fosaprepitant at the following weight-adjusted doses: Participants 4 months to <12 years old were administered 5 mg/kg (not to exceed 150 mg), Participants 1 to <4 months old were administered 2.5 mg/kg; Participants 0 to <1 month old were administered 1.25 mg/kg. Participants were also administered IV ondansetron (0.15 mg/kg x 3 doses for children 6 months to 17 years of age or per local standard of care for children <6 months of age), with or without dexamethasone. | |
| Reporting group title | Fosaprepitant 3 mg/kg-Cycle 1 |
| Reporting group description: Participants 12 to 17 years old were administered 150 mg IV fosaprepitant. Participants 2 to <12 years old were administered a weight-adjusted dose of 3 mg/kg (not to exceed 150 mg). Participants were also administered IV ondansetron 0.15 mg/kg x 3 doses with or without dexamethasone. | |
| Reporting group title | Fosaprepitant 1.2 mg/kg-Cycle 1 |
| Reporting group description: Participants 12 to 17 years old were administered 60 mg IV fosaprepitant. Participants 2 to <12 years old were administered a weight-adjusted dose of 1.2 mg/kg (not to exceed 60 mg). Participants were also administered IV ondansetron 0.15 mg/kg x 3 doses with or without dexamethasone. | |
| Reporting group title | Fosaprepitant 0.4 mg/kg-Cycle 1 |
| Reporting group description: Participants 12 to 17 years old were administered 20 mg IV fosaprepitant. Participants 2 to <12 years old were administered a weight-adjusted dose of 0.4 mg/kg (not to exceed 20 mg). Participants were also administered IV ondansetron 0.15 mg/kg x 3 doses with or without dexamethasone. | |
| Reporting group title | Placebo Control-Cycle 1 |
| Reporting group description: Participants were administered IV normal saline at volume to match age and weight specific doses of fosaprepitant. Participants were also administered IV ondansetron (0.15 mg/kg x 3 doses for children 6 months to 17 years of age or per local standard of care for children <6 months of age), with or without dexamethasone. | |
| Reporting group title | Fosaprepitant 5 mg/kg Cycle 2-6 |
| Reporting group description: For optional Cycles 2-6, participants from the 5 mg/kg fosaprepitant arm in Cycle 1 were administered fosaprepitant 5 mg/kg IV (or age-adjusted equivalent). For Cycle 2, fosaprepitant was administered IV plus ondansetron with or without dexamethasone. For Cycles 3-6, fosaprepitant was administered IV plus a 5-hydroxytryptamine 3 (5-HT3) antagonist with or without dexamethasone. Participants 1 year or less were required to receive ondansetron in all cycles as the 5-HT3 antagonist. | |
| Reporting group title | Fosaprepitant 3 mg/kg Cycle 2-6 |
| Reporting group description: For optional Cycles 2-6, participants from Cycle 1 fosaprepitant arms (3, 1.2, or 0.4 mg/kg) or Cycle 1 Control arm were administered fosaprepitant 3 mg/kg IV (or age-adjusted equivalent). For Cycle 2, fosaprepitant was administered IV plus ondansetron with or without dexamethasone. For Cycles 3-6, fosaprepitant was administered IV plus a 5-HT3 antagonist with or without dexamethasone. | |
| Subject analysis set title | Fosaprepitant 5 mg/kg-Cycle 1 |
| Subject analysis set type | Per protocol |
| Subject analysis set description: Participants were administered IV fosaprepitant at the following weight-adjusted doses: Participants 4 months to <12 years old were administered 5 mg/kg (not to exceed 150 mg), Participants 1 to <4 months old were administered 2.5 mg/kg; Participants 0 to <1 month old were administered 1.25 mg/kg. Participants were also administered IV ondansetron (0.15 mg/kg x 3 doses for children 6 months to 17 years of age or per local standard of care for children <6 months of age), with or without dexamethasone. Analysis was in the per-protocol (PP) population which includes all participants that received one dose of study therapy and did not have important deviations from the study protocol. | |
| Subject analysis set title | Fosaprepitant 3 mg/kg-Cycle 1 |
| Subject analysis set type | Per protocol |

Subject analysis set description:

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

| | |
|----------------------------|---------------------------------|
| Subject analysis set title | Fosaprepitant 1.2 mg/kg-Cycle 1 |
| Subject analysis set type | Per protocol |

Subject analysis set description:

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

| | |
|----------------------------|---------------------------------|
| Subject analysis set title | Fosaprepitant 0.4 mg/kg-Cycle 1 |
| Subject analysis set type | Per protocol |

Subject analysis set description:

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

| | |
|----------------------------|-------------------------|
| Subject analysis set title | Placebo Control-Cycle 1 |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Participants were administered IV normal saline at volume to match age and weight specific doses of fosaprepitant. Participants were also administered IV ondansetron (0.15 mg/kg x 3 doses for children 6 months to 17 years of age or per local standard of care for children <6 months of age), with or without dexamethasone. Analysis was in the PP population which includes all participants that received one dose of placebo control and did not have important deviations from the study protocol.

| | |
|----------------------------|--|
| Subject analysis set title | Fosaprepitant 5 mg/kg: 0 to <2 Years-Cycle 1 |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Participants were administered IV fosaprepitant at the following weight-adjusted doses: Participants 4 months to <12 years old were administered 5 mg/kg (not to exceed 150 mg), Participants 1 to <4 months old were administered 2.5 mg/kg; Participants 0 to <1 month old were administered 1.25 mg/kg. Participants were also administered IV ondansetron (0.15 mg/kg x 3 doses for children 6 months to 17 years of age or per local standard of care for children <6 months of age), with or without dexamethasone. Analysis was in the PP population which includes all participants 0 to <2 years of age that received one dose of study therapy, did not have important deviations from the study protocol, and had data that contributed to the outcome being measured.

| | |
|----------------------------|--|
| Subject analysis set title | Fosaprepitant 5 mg/kg: 2 to <6 Years-Cycle 1 |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Participants were administered a weight-adjusted dose of 5 mg/kg fosaprepitant IV (not to exceed 150 mg). Participants also were administered IV ondansetron at 0.15 mg/kg x 3 doses with or without dexamethasone. Analysis was in the PP population which includes all participants 2 to <6 years of age that received one dose of study therapy, did not have important deviations from the study protocol, and had data that contributed to the outcome being measured.

| | |
|----------------------------|---|
| Subject analysis set title | Fosaprepitant 5 mg/kg: 6 to <12 Years-Cycle 1 |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Participants were administered a weight-adjusted dose of 5 mg/kg fosaprepitant IV (not to exceed 150 mg). Participants also were administered IV ondansetron at 0.15 mg/kg x 3 doses with or without dexamethasone. Analysis was in the PP population which includes all participants 6 to <12 years of age that received one dose of study therapy, did not have important deviations from the study protocol, and had data that contributed to the outcome being measured.

| | |
|----------------------------|--|
| Subject analysis set title | Fosaprepitant 3 mg/kg: 2 to <6 Years-Cycle 1 |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Participants were administered a weight-adjusted dose of 3 mg/kg fosaprepitant IV (not to exceed 150 mg). Participants were also administered IV ondansetron at 0.15 mg/kg x 3 doses with or without dexamethasone. Analysis was in the PP population which includes all participants 2 to <6 years of age that received one dose of study therapy, did not have important deviations from the study protocol, and had data that contributed to the outcome being measured.

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

Subject analysis set description:

Participants were administered a weight-adjusted dose of 3 mg/kg fosaprepitant IV (not to exceed 150 mg). Participants were also administered IV ondansetron at 0.15 mg/kg x 3 doses with or without dexamethasone. Analysis was in the PP population which includes all participants 6 to <12 years of age that received one dose of study therapy, did not have important deviations from the study protocol, and had data that contributed to the outcome being measured.

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

Subject analysis set description:

Participants were administered 150 mg fosaprepitant IV. Participants were also administered IV ondansetron at 0.15 mg/kg x 3 doses with or without dexamethasone. Analysis was in the PP population which includes all participants 12 to 17 years of age that received one dose of study therapy, did not have important deviations from the study protocol, and had data that contributed to the outcome being measured.

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

Subject analysis set description:

Participants were administered a weight-adjusted dose of 1.2 mg/kg of fosaprepitant IV (not to exceed 60 mg). Participants were also administered IV ondansetron at 0.15 mg/kg x 3 doses with or without dexamethasone. Analysis was in the PP population which includes all participants 2 to <6 years of age that received one dose of study therapy, did not have important deviations from the study protocol, and had data that contributed to the outcome being measured.

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

Subject analysis set description:

Participants were administered a weight-adjusted dose of 1.2 mg/kg of fosaprepitant IV (not to exceed 60 mg). Participants were also administered IV ondansetron at 0.15 mg/kg x 3 doses with or without dexamethasone. Analysis was in the PP population which includes all participants 6 to <12 years of age that received one dose of study therapy, did not have important deviations from the study protocol, and had data that contributed to the outcome being measured.

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

Subject analysis set description:

Participants were administered 60 mg fosaprepitant IV. Participants were also administered IV ondansetron at 0.15 mg/kg x 3 doses with or without dexamethasone. Analysis was in the PP population which includes all participants 12 to 17 years of age that received one dose of study therapy, did not have important deviations from the study protocol, and had data that contributed to the outcome being measured.

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

Subject analysis set description:

Participants were administered a weight-adjusted dose of 0.4 mg/kg fosaprepitant IV (not to exceed 20 mg). Participants were also administered IV ondansetron at 0.15 mg/kg x 3 doses with or without dexamethasone. Analysis was in the PP population which includes all participants 2 to <6 years of age that received one dose of study therapy, did not have important deviations from the study protocol, and had data that contributed to the outcome being measured.

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

Subject analysis set description:

Participants were administered a weight-adjusted dose of 0.4 mg/kg fosaprepitant IV (not to exceed 20 mg). Participants were also administered IV ondansetron at 0.15 mg/kg x 3 doses with or without dexamethasone. Analysis was in the PP population which includes all participants 6 to <12 years of age

that received one dose of study therapy, did not have important deviations from the study protocol, and had data that contributed to the outcome being measured.

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

Subject analysis set description:

Participants were administered 20 mg fosaprepitant IV. Participants were also administered IV ondansetron at 0.15 mg/kg x 3 doses with or without dexamethasone. Analysis was in the PP population which includes all participants 12 to 17 years of age that received one dose of study therapy, did not have important deviations from the study protocol, and had data that contributed to the outcome being measured.

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

Subject analysis set description:

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

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

Subject analysis set description:

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

Primary: Maximum concentration (C_{max}) of aprepitant in participants 0 to <2 years of age

| | |
|-----------------|---|
| End point title | Maximum concentration (C _{max}) of aprepitant in participants 0 to <2 years of age ^[1] |
|-----------------|---|

End point description:

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

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

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

Notes:

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

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

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

Statistical analyses

No statistical analyses for this end point

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

| | |
|-----------------|--|
| End point title | Time to maximum concentration (Tmax) of aprepitant in participants 0 to <2 years of age ^[2] |
|-----------------|--|

End point description:

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

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

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

Notes:

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

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

| | | | | |
|--------------------------------------|--|--|--|--|
| End point values | Fosaprepitant 5 mg/kg: 0 to <2 Years-Cycle 1 | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 22 | | | |
| Units: hours | | | | |
| arithmetic mean (standard deviation) | 2.01 (± 2.10) | | | |

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

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

Notes:

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

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

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

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

Notes:

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

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

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

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

| | |
|----------------------|--|
| End point type | Primary |
| End point timeframe: | Pre-infusion, immediately after infusion, and 2-4, 5-7, 8-10, 23-25, and 46-50 hours post-infusion |

Notes:

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

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

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Fosaprepitant is a pro-drug that is rapidly converted to aprepitant. Because of this rapid conversion to aprepitant, fosaprepitant cannot be assessed directly. The pharmacokinetics for each fosaprepitant dose were determined by analyzing aprepitant in plasma. The C24hr for aprepitant was determined by measuring aprepitant levels in the time frame of 23 to 25 hours post-infusion.

| | |
|----------------------|--|
| End point type | Primary |
| End point timeframe: | Approximately 24 hours (from 23 to 25 hours) post-infusion |

Notes:

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

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

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Fosaprepitant is a pro-drug that is rapidly converted to aprepitant. Because of this rapid conversion to aprepitant, fosaprepitant cannot be assessed directly. The pharmacokinetics for each fosaprepitant dose were determined by analyzing aprepitant in plasma. The C48hr for aprepitant was determined by measuring aprepitant levels in the time frame of 46 to 50 hours post-infusion. The C48hr was only planned to be measured in the 5 mg/mL dose for each age group.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Approximately 48 hours (from 46 to 50 hours) post-infusion

Notes:

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

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

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

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

Notes:

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

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

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

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

Notes:

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

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

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

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

Notes:

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

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

| End point values | Fosaprepitant 5 mg/kg: 2 to <6 Years-Cycle 1 | Fosaprepitant 3 mg/kg: 2 to <6 Years-Cycle 1 | Fosaprepitant 1.2 mg/kg: 2 to <6 Years-Cycle 1 | Fosaprepitant 0.4 mg/kg: 2 to <6 Years-Cycle 1 |
|--------------------------------------|--|--|--|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 25 | 6 | 8 | 6 |
| Units: hours | | | | |
| arithmetic mean (standard deviation) | 1.90 (± 2.16) | 2.29 (± 2.14) | 1.36 (± 0.868) | 1.34 (± 0.771) |

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

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

Notes:

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

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

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

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

Notes:

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

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

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

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

Notes:

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

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

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

| | | | | |
|--------------------------------------|--------------------|--------------------|--------------------|--------------------|
| arithmetic mean (standard deviation) | 9.27 (\pm 4.17) | 6.55 (\pm 3.62) | 7.27 (\pm 3.47) | 6.18 (\pm 3.51) |
|--------------------------------------|--------------------|--------------------|--------------------|--------------------|

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Fosaprepitant is a pro-drug that is rapidly converted to aprepitant. Because of this rapid conversion to aprepitant, fosaprepitant cannot be assessed directly. The pharmacokinetics for each fosaprepitant dose were determined by analyzing aprepitant in plasma. The C24hr for aprepitant was determined by measuring aprepitant levels in the time frame of 23 to 25 hours post-infusion.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Approximately 24 hours (from 23 to 25 hours) post-infusion

Notes:

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

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

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Fosaprepitant is a pro-drug that is rapidly converted to aprepitant. Because of this rapid conversion to aprepitant, fosaprepitant cannot be assessed directly. The pharmacokinetics for each fosaprepitant dose were determined by analyzing aprepitant in plasma. The C48hr for aprepitant was determined by measuring aprepitant levels in the time frame of 46 to 50 hours post-infusion. The C48hr was only planned to be measured in the 5 mg/mL dose for each age group.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Approximately 48 hours (from 46 to 50 hours) post-infusion

Notes:

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

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

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

Notes:

[16] - Endpoint not calculated

[17] - Endpoint not calculated

[18] - Endpoint not calculated

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

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

Notes:

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

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

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

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

Notes:

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

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

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

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

Notes:

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

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

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

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

Notes:

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

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

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

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

Notes:

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

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

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

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

Notes:

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

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

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Fosaprepitant is a pro-drug that is rapidly converted to aprepitant. Because of this rapid conversion to aprepitant, fosaprepitant cannot be assessed directly. The pharmacokinetics for each fosaprepitant dose were determined by analyzing aprepitant in plasma. The C24hr for aprepitant was determined by measuring aprepitant levels in the time frame of 23 to 25 hours post-infusion.

End point type Primary

End point timeframe:

Approximately 24 hours (from 23 to 25 hours) post-infusion

Notes:

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

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

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Fosaprepitant is a pro-drug that is rapidly converted to aprepitant. Because of this rapid conversion to aprepitant, fosaprepitant cannot be assessed directly. The pharmacokinetics for each fosaprepitant dose were determined by analyzing aprepitant in plasma. The C48hr for aprepitant was determined by measuring aprepitant levels in the time frame of 46 to 50 hours post-infusion. The C48hr was only planned to be measured in the 5 mg/mL dose for each age group.

End point type Primary

End point timeframe:

Approximately 48 hours (from 46 to 50 hours) post-infusion

Notes:

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

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

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

Notes:

[27] - Endpoint not calculated

[28] - Endpoint not calculated

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

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

Notes:

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

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

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

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

Notes:

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

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

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

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

Notes:

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

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

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

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

Notes:

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

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

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

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

Notes:

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

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

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

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

Notes:

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

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

| End point values | Fosaprepitant 3 mg/kg: 12 to 17 Years-Cycle 1 | Fosaprepitant 1.2 mg/kg: 12 to 17 Years-Cycle 1 | Fosaprepitant 0.4 mg/kg: 12 to 17 Years-Cycle 1 | |
|--------------------------------------|---|---|---|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 3 | 8 | 9 | |
| Units: hours | | | | |
| arithmetic mean (standard deviation) | 10.5 (± 1.00) | 7.92 (± 1.38) | 8.27 (± 1.20) | |

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Fosaprepitant is a pro-drug that is rapidly converted to aprepitant. Because of this rapid conversion to aprepitant, fosaprepitant cannot be assessed directly. The pharmacokinetics for each fosaprepitant dose were determined by analyzing aprepitant in plasma. The C24hr for aprepitant was determined by measuring aprepitant levels in the time frame of 23 to 25 hours post-infusion.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Approximately 24 hours (from 23 to 25 hours) post-infusion

Notes:

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

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

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Fosaprepitant is a pro-drug that is rapidly converted to aprepitant. Because of this rapid conversion to aprepitant, fosaprepitant cannot be assessed directly. The pharmacokinetics for each fosaprepitant dose were determined by analyzing aprepitant in plasma. The C48hr for aprepitant was determined by measuring aprepitant levels in the time frame of 46 to 50 hours post-infusion. The C48hr was only planned to be measured in the 5 mg/mL dose for each age group.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Approximately 48 hours (from 46 to 50 hours) post-infusion

Notes:

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

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

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

Notes:

[38] - Endpoint not calculated

[39] - Endpoint not calculated

[40] - Endpoint not calculated

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

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

Notes:

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

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

| End point values | Fosaprepitant 3 mg/kg: 12 to 17 Years-Cycle 1 | Fosaprepitant 1.2 mg/kg: 12 to 17 Years-Cycle 1 | Fosaprepitant 0.4 mg/kg: 12 to 17 Years-Cycle 1 | |
|--------------------------------------|---|---|---|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 3 | 8 | 9 | |
| Units: mL/min | | | | |
| arithmetic mean (standard deviation) | 76.2 (± 16.2) | 91.7 (± 32.5) | 105 (± 29.0) | |

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Up to 14 days postdose in Cycle 1

Notes:

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

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

| End point values | Fosaprepitant 5 mg/kg-Cycle 1 | Fosaprepitant 3 mg/kg-Cycle 1 | Fosaprepitant 1.2 mg/kg-Cycle 1 | Fosaprepitant 0.4 mg/kg-Cycle 1 |
|-----------------------------------|-------------------------------|-------------------------------|---------------------------------|---------------------------------|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 74 | 42 | 43 | 40 |
| Units: Percentage of participants | | | | |
| number (not applicable) | 87.8 | 83.3 | 90.7 | 80.0 |

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Up to 14 days postdose for each cycle (Cycles 2-6)

Notes:

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

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

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

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 14 days after the dose of study drug for Cycles 1-6 (approximately up to 84 days total)

Adverse event reporting additional description:

AEs were reported for the All Patients as Treated Population that included all randomized participants who received at least one dose of study treatment. All AEs (serious and non-serious) were reported in Cycle 1. In Cycles 2-6, only serious AEs and non-serious AEs that were either drug-related AEs or led to discontinuation were reported.

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 19.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|---------------------------------|
| Reporting group title | Fosaprepitant 0.4 mg/kg-Cycle 1 |
|-----------------------|---------------------------------|

Reporting group description:

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

| | |
|-----------------------|-------------------------------|
| Reporting group title | Fosaprepitant 3 mg/kg-Cycle 1 |
|-----------------------|-------------------------------|

Reporting group description:

Participants 12 to 17 years old were administered 150 mg IV fosaprepitant. Participants 2 to <12 years old were administered a weight-adjusted dose of 3 mg/kg (not to exceed 150 mg). Participants were also administered IV ondansetron 0.15 mg/kg x 3 doses with or without dexamethasone.

| | |
|-----------------------|---------------------------------|
| Reporting group title | Fosaprepitant 1.2 mg/kg-Cycle 1 |
|-----------------------|---------------------------------|

Reporting group description:

Participants 12 to 17 years old were administered 60 mg IV fosaprepitant. Participants 2 to <12 years old were administered a weight-adjusted dose of 1.2 mg/kg (not to exceed 60 mg). Participants were also administered IV ondansetron 0.15 mg/kg x 3 doses with or without dexamethasone.

| | |
|-----------------------|-------------------------------|
| Reporting group title | Fosaprepitant 5 mg/kg-Cycle 1 |
|-----------------------|-------------------------------|

Reporting group description:

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

| | |
|-----------------------|-------------------------|
| Reporting group title | Placebo Control-Cycle 1 |
|-----------------------|-------------------------|

Reporting group description:

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

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

Reporting group description:

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

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

Reporting group description:

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

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

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

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

Notes:

Limitations and caveats

None reported