



Clinical trial results:

A Phase III, Randomized, Double-Blind, Active Comparator-Controlled Clinical Trial, Conducted Under In-House Blinding Conditions, to Examine the Efficacy and Safety of Aprepitant for the Prevention of Chemotherapy-Induced Nausea and Vomiting (CINV) in Pediatric Patients

Summary

EudraCT number	2011-000651-16
Trial protocol	SE PT LT ES NL DK HU SI GR GB IT Outside EU/EEA
Global end of trial date	16 August 2013

Results information

Result version number	v1 (current)
This version publication date	13 April 2016
First version publication date	25 February 2015

Trial information

Trial identification

Sponsor protocol code	0869-208
-----------------------	----------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01362530
WHO universal trial number (UTN)	-
Other trial identifiers	MK-0869: Aprepitant

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	16 August 2013
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	16 August 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This study will compare the safety and efficacy of a three-day oral aprepitant regimen (aprepitant plus ondansetron) to ondansetron alone in the prevention of chemotherapy-induced nausea and vomiting (CINV) in the 120 hours following the initiation of chemotherapy in pediatric participants. Those who complete this first cycle of treatment and meet certain eligibility criteria will have the option of continuing for 5 additional cycles of open-label aprepitant.

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:

Subjects were permitted to take "rescue medication" for established (not anticipated) nausea and vomiting throughout the study. Recommended rescue medications included: 5-HT3 antagonists, phenothiazines, butyrophenones, benzamides, corticosteroids, benzodiazepines, and domperidone. In all cases, rescue medication was administered consistent with local regulations and standards of practice.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 September 2011
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	Denmark: 6
Country: Number of subjects enrolled	Greece: 17
Country: Number of subjects enrolled	Italy: 16
Country: Number of subjects enrolled	Netherlands: 17
Country: Number of subjects enrolled	Spain: 20
Country: Number of subjects enrolled	Sweden: 8
Country: Number of subjects enrolled	United Kingdom: 13
Country: Number of subjects enrolled	Lithuania: 11
Country: Number of subjects enrolled	Slovenia: 5
Country: Number of subjects enrolled	Poland: 18

Country: Number of subjects enrolled	Hungary: 16
Country: Number of subjects enrolled	Russian Federation: 15
Country: Number of subjects enrolled	Korea, Republic of: 25
Country: Number of subjects enrolled	United States: 8
Country: Number of subjects enrolled	Chile: 18
Country: Number of subjects enrolled	Israel: 19
Country: Number of subjects enrolled	Croatia: 9
Country: Number of subjects enrolled	Ecuador: 13
Country: Number of subjects enrolled	Colombia: 11
Country: Number of subjects enrolled	Dominican Republic: 6
Country: Number of subjects enrolled	Peru: 10
Country: Number of subjects enrolled	Argentina: 3
Country: Number of subjects enrolled	Mexico: 4
Country: Number of subjects enrolled	Turkey: 19
Worldwide total number of subjects	307
EEA total number of subjects	156

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)	35
Children (2-11 years)	177
Adolescents (12-17 years)	95
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The base study consisted of one cycle of treatment (Cycle 1). Participants in either treatment group who met the eligibility criteria were eligible to participate in optional open-label aprepitant treatment for an additional 5 cycles (Cycles 2-6).

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, Carer

Arms

Are arms mutually exclusive?	Yes
Arm title	Aprepitant Regimen

Arm description:

Cycle 1: Participants 12 to 17 years of age, Day 1: aprepitant 125 mg capsule orally (PO) +ondansetron, Days 2 to 3: aprepitant 80 mg capsule PO. Participants 6 months to <12 years of age, Day 1: aprepitant powder for suspension (PFS), 3.0 mg/kg (up to 125 mg) + ondansetron, Days 2 to 3: aprepitant PFS, 2.0 mg/kg (up to 80 mg).

Arm type	Experimental
Investigational medicinal product name	Aprepitant 125 mg
Investigational medicinal product code	A04AD12
Other name	MK-0869, Emend
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

On the morning of Day 1: one 125 mg capsule PO 60 minutes prior to chemotherapy for participants 12 to 17 years of age

Investigational medicinal product name	Aprepitant 80 mg
Investigational medicinal product code	A04AD12
Other name	MK-0869, Emend
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

On the morning of Days 2 and 3: one 80 mg capsule PO for participants 12 to 17 years of age

Investigational medicinal product name	Aprepitant powder for suspension (PFS)
Investigational medicinal product code	A04AD12
Other name	MK-0869, Emend
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

On the morning of Day 1: 3.0 mg/kg (up to 125 mg) PO 60 minutes prior to chemotherapy for participants 6 months to <12 years of age. On the morning of Days 2 and 3: 2.0 mg/kg (up to 80 mg) PO 60 minutes prior to chemotherapy (if applicable) for participants 6 months to <12 years of age

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

Dosage and administration details:

Day 1: Administered according to product label for pediatric usage or local standard of care.

Investigational medicinal product name	Emetogenic chemotherapy
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Any moderately emetic, highly emetic, or very highly emetic chemotherapeutic agent such as cyclophosphamide, doxorubicin, methotrexate, carboplatin, cisplatin, irinotecan, carmustine, ifosfamide, and streptozocin, or chemotherapeutics of a lower emetogenicity that were not previously tolerated. No chemotherapeutic agents were specified by the protocol, and many could potentially have been used.

Arm title	Control Regimen
------------------	-----------------

Arm description:

Cycle 1: Participants 12 to 17 years of age, Day 1: dose-matched placebo for aprepitant 125 mg capsule oral (PO) + ondansetron. Days 2 to 3: matching placebo for aprepitant 80 mg capsule PO. Participants 6 months to <12 years of age, Day 1: dose-matched placebo for PFS (3.0 mg/kg, up to 125 mg) + ondansetron. Days 2 to 3: dose-matched placebo for PFS (2.0 mg/kg, up to 80 mg).

Arm type	Placebo
Investigational medicinal product name	Placebo for Aprepitant 125 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

On the morning of Day 1: one dose-matched (125 mg) capsule PO 60 minutes prior to chemotherapy for participants 12 to 17 years of age

Investigational medicinal product name	Placebo for Aprepitant 80 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

On the morning of Days 2 and 3: one dose-matched (80 mg) capsule PO for participants 12 to 17 years of age

Investigational medicinal product name	Placebo for Aprepitant PFS
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for oral suspension
Routes of administration	Oral use

Dosage and administration details:

On the morning of Day 1: dose-matched suspension (3.0 mg/kg, up to 125 mg) PO 60 minutes prior to chemotherapy for participants 6 months to <12 years of age. On the morning of Days 2 and 3: dose-matched suspension (2.0 mg/kg, up to 80 mg) PO 60 minutes prior to chemotherapy (if applicable) for participants 6 months to <12 years of age.

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

Dosage and administration details:

Day 1: Administered according to product label for pediatric usage or local standard of care.

Investigational medicinal product name	Emetogenic chemotherapy
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Any moderately emetic, highly emetic, or very highly emetic chemotherapeutic agent such as cyclophosphamide, doxorubicin, methotrexate, carboplatin, cisplatin, irinotecan, carmustine, ifosfamide, and streptozocin, or chemotherapeutics of a lower emetogenicity that were not previously tolerated. No chemotherapeutic agents were specified by the protocol, and many could potentially have been used.

Number of subjects in period 1	Aprepitant Regimen	Control Regimen
Started	155	152
Treated (Intent To Treat Population)	152	150
Completed	150	149
Not completed	5	3
Consent withdrawn by subject	1	2
Physician decision	-	1
Adverse event, non-fatal	2	-
Protocol deviation	2	-

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

Arm title	Open Label Aprepitant (Cycles 2-6)
-----------	------------------------------------

Arm description:

Participants completing Cycle 1 from either the aprepitant or the control regimen who met eligibility criteria received open-label aprepitant administered in the same manner as in Cycle 1: Participants 12 to 17 years of age, Day 1: aprepitant 125 mg capsule PO + ondansetron, Days 2 to 3: aprepitant 80 mg capsule PO. Participants 6 months to <12 years of age, Day 1: aprepitant PFS, 3.0 mg/kg (up to 125 mg) + ondansetron, Days 2 to 3: aprepitant PFS, 2.0 mg/kg (up to 80 mg).

Arm type	Experimental
Investigational medicinal product name	Aprepitant 125 mg
Investigational medicinal product code	A04AD12
Other name	MK-0869, Emend
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

On the morning of Day 1: one 125 mg capsule PO 60 minutes prior to chemotherapy for participants 12 to 17 years of age

Investigational medicinal product name	Aprepitant 80 mg
Investigational medicinal product code	A04AD12
Other name	MK-0869, Emend
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

On the morning of Days 2 and 3: one 80 mg capsule PO for participants 12 to 17 years of age

Investigational medicinal product name	Aprepitant powder for suspension (PFS)
Investigational medicinal product code	A04AD12
Other name	MK-0869, Emend
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

On the morning of Day 1: 3.0 mg/kg (up to 125 mg) PO 60 minutes prior to chemotherapy for participants 6 months to <12 years of age. On the morning of Days 2 and 3: 2.0 mg/kg (up to 80 mg) PO 60 minutes prior to chemotherapy (if applicable) for participants 6 months to <12 years of age

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

Dosage and administration details:

Day 1: Administered according to product label for pediatric usage or local standard of care.

Investigational medicinal product name	Emetogenic chemotherapy
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Any moderately emetic, highly emetic, or very highly emetic chemotherapeutic agent such as cyclophosphamide, doxorubicin, methotrexate, carboplatin, cisplatin, irinotecan, carmustine, ifosfamide, and streptozocin, or chemotherapeutics of a lower emetogenicity that were not previously tolerated. No chemotherapeutic agents were specified by the protocol, and many could potentially have been used.

Number of subjects in period 2^[1]	Open Label Aprepitant (Cycles 2-6)
Started	171
Treated	170
Completed	46
Not completed	125
Completed Chemotherapy Regimen	51
Consent withdrawn by subject	18
Physician decision	19
Adverse event, non-fatal	2

Did Not Respond To Chemotherapy Regimen	4
Did Not Meet Additional Criteria	25
Lost to follow-up	1
Lack of efficacy	1
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: Cycles 2-6 were optional and not required for the study. Following Cycle 1, 171 subjects elected to participate in the optional cycles (Cycles 2-6).

Baseline characteristics

Reporting groups

Reporting group title	Aprepitant Regimen
Reporting group description: Cycle 1: Participants 12 to 17 years of age, Day 1: aprepitant 125 mg capsule orally (PO) + ondansetron, Days 2 to 3: aprepitant 80 mg capsule PO. Participants 6 months to <12 years of age, Day 1: aprepitant powder for suspension (PFS), 3.0 mg/kg (up to 125 mg) + ondansetron, Days 2 to 3: aprepitant PFS, 2.0 mg/kg (up to 80 mg).	
Reporting group title	Control Regimen
Reporting group description: Cycle 1: Participants 12 to 17 years of age, Day 1: dose-matched placebo for aprepitant 125 mg capsule oral (PO) + ondansetron. Days 2 to 3: matching placebo for aprepitant 80 mg capsule PO. Participants 6 months to <12 years of age, Day 1: dose-matched placebo for PFS (3.0 mg/kg, up to 125 mg) + ondansetron. Days 2 to 3: dose-matched placebo for PFS (2.0 mg/kg, up to 80 mg).	

Reporting group values	Aprepitant Regimen	Control Regimen	Total
Number of subjects	155	152	307
Age categorical Units: Subjects			
Age continuous Units: months arithmetic mean standard deviation	97.4 ± 62.8	99.2 ± 60.8	-
Gender categorical Units: Subjects			
Female	69	71	140
Male	86	81	167
Not recorded	0	0	0

Subject analysis sets

Subject analysis set title	Aprepitant Regimen-Intent-to-treat (ITT) Population
Subject analysis set type	Intention-to-treat
Subject analysis set description: Aprepitant Regimen ITT population; consisting of all randomized patients who received at least one dose of Aprepitant.	
Subject analysis set title	Control Regimen-ITT Population
Subject analysis set type	Intention-to-treat
Subject analysis set description: Control Regimen ITT population; consisting of all randomized patients who received at least one dose of control.	

Reporting group values	Aprepitant Regimen-Intent-to-treat (ITT) Population	Control Regimen-ITT Population	
Number of subjects	152	150	
Age categorical Units: Subjects			

Age continuous			
Units: months			
arithmetic mean	97.7	99.4	
standard deviation	± 63.2	± 60.9	
Gender categorical			
Units: Subjects			
Female	68	71	
Male	84	79	
Not recorded	0	0	

End points

End points reporting groups

Reporting group title	Aprepitant Regimen
Reporting group description: Cycle 1: Participants 12 to 17 years of age, Day 1: aprepitant 125 mg capsule orally (PO) + ondansetron, Days 2 to 3: aprepitant 80 mg capsule PO. Participants 6 months to <12 years of age, Day 1: aprepitant powder for suspension (PFS), 3.0 mg/kg (up to 125 mg) + ondansetron, Days 2 to 3: aprepitant PFS, 2.0 mg/kg (up to 80 mg).	
Reporting group title	Control Regimen
Reporting group description: Cycle 1: Participants 12 to 17 years of age, Day 1: dose-matched placebo for aprepitant 125 mg capsule oral (PO) + ondansetron. Days 2 to 3: matching placebo for aprepitant 80 mg capsule PO. Participants 6 months to <12 years of age, Day 1: dose-matched placebo for PFS (3.0 mg/kg, up to 125 mg) + ondansetron. Days 2 to 3: dose-matched placebo for PFS (2.0 mg/kg, up to 80 mg).	
Reporting group title	Open Label Aprepitant (Cycles 2-6)
Reporting group description: Participants completing Cycle 1 from either the aprepitant or the control regimen who met eligibility criteria received open-label aprepitant administered in the same manner as in Cycle 1: Participants 12 to 17 years of age, Day 1: aprepitant 125 mg capsule PO + ondansetron, Days 2 to 3: aprepitant 80 mg capsule PO. Participants 6 months to <12 years of age, Day 1: aprepitant PFS, 3.0 mg/kg (up to 125 mg) + ondansetron, Days 2 to 3: aprepitant PFS, 2.0 mg/kg (up to 80 mg).	
Subject analysis set title	Aprepitant Regimen-Intent-to-treat (ITT) Population
Subject analysis set type	Intention-to-treat
Subject analysis set description: Aprepitant Regimen ITT population; consisting of all randomized patients who received at least one dose of Aprepitant.	
Subject analysis set title	Control Regimen-ITT Population
Subject analysis set type	Intention-to-treat
Subject analysis set description: Control Regimen ITT population; consisting of all randomized patients who received at least one dose of control.	

Primary: Percentage of Participants with a Complete Response in the Delayed Phase of Cycle 1

End point title	Percentage of Participants with a Complete Response in the Delayed Phase of Cycle 1
End point description: The Delayed Phase was defined as 25-120 hours after the start of chemotherapy. Complete response was defined as no vomiting or retching and no use of rescue medication in the delayed phase of Cycle 1.	
End point type	Primary
End point timeframe: 25 to 120 hours after the start of chemotherapy (Day 1)	

End point values	Aprepitant Regimen	Control Regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	152	150		
Units: P e r c e n t a g e of participants				
number (not applicable)	50.7	26		

Statistical analyses

Statistical analysis title	Complete Response in the Delayed Phase of Cycle 1
Statistical analysis description: Cochran-Mantel-Haenszel Analysis: Stratified by age group, use of dexamethasone as an anti-emetic, and receipt of very high risk emetogenic chemotherapy.	
Comparison groups	Aprepitant Regimen v Control Regimen
Number of subjects included in analysis	302
Analysis specification	Pre-specified
Analysis type	superiority ^[1]
P-value	< 0.01
Method	Cochran-Mantel-Haenszel

Notes:

[1] - The superiority hypotheses was evaluated by comparing the 1-tailed p-value to 0.025 and significance declared if this p-value was ≤ 0.025 .

Secondary: Percentage of Participants with a Complete Response in the Acute Phase of Cycle 1

End point title	Percentage of Participants with a Complete Response in the Acute Phase of Cycle 1
End point description: The Acute phase was defined as 0 to 24 hours after the start of chemotherapy. Complete response was defined as no vomiting or retching and no use of rescue medication in the Acute Phase of Cycle 1.	
End point type	Secondary
End point timeframe: 0 to 24 hours after initiation of chemotherapy (Day 1)	

End point values	Aprepitant Regimen	Control Regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	152	150		
Units: percentage of participants				
number (not applicable)	66.4	52		

Statistical analyses

Statistical analysis title	Complete Response in the Acute Phase of Cycle 1
Statistical analysis description: Cochran-Mantel-Haenszel analysis was stratified by age group, use of dexamethasone as an anti-emetic, and receipt of very high risk emetogenic chemotherapy.	
Comparison groups	Control Regimen v Aprepitant Regimen

Number of subjects included in analysis	302
Analysis specification	Pre-specified
Analysis type	superiority ^[2]
P-value	< 0.05
Method	Cochran-Mantel-Haenszel

Notes:

[2] - The superiority hypotheses was evaluated by comparing the 1-tailed p-value to 0.025 and significance declared if this p-value was ≤ 0.025 .

Secondary: Percentage of Participants with a Complete Response in the Overall Phase of Cycle 1

End point title	Percentage of Participants with a Complete Response in the Overall Phase of Cycle 1
-----------------	---

End point description:

The Overall Phase was defined as 0 to 120 hours after the start of chemotherapy. Complete Response was defined as no vomiting or retching and no use of rescue medication in the Overall Phase of Cycle 1.

End point type	Secondary
----------------	-----------

End point timeframe:

0 to 120 hours after initiation of chemotherapy (Day 1)

End point values	Aprepitant Regimen	Control Regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	152	150		
Units: percentage of participants				
number (not applicable)	40.1	20		

Statistical analyses

Statistical analysis title	Complete Response in the Overall Phase of Cycle 1
----------------------------	---

Statistical analysis description:

Cochran-Mantel-Haenszel Analysis: Stratified by age group, use of dexamethasone as an anti-emetic, and receipt of very high risk emetogenic chemotherapy.

Comparison groups	Aprepitant Regimen v Control Regimen
Number of subjects included in analysis	302
Analysis specification	Pre-specified
Analysis type	superiority ^[3]
P-value	< 0.01
Method	Cochran-Mantel-Haenszel

Notes:

[3] - The superiority hypotheses was evaluated by comparing the 1-tailed p-value to 0.025 and significance declared if this p-value was ≤ 0.025 .

Secondary: Percentage of Participants with No Vomiting in the Overall Phase of Cycle 1

End point title	Percentage of Participants with No Vomiting in the Overall Phase of Cycle 1
-----------------	---

End point description:

The Overall Phase was defined as 0 to 120 hours after the start of chemotherapy. No vomiting was defined as no emesis or retching or dry heaves in the Overall Phase of Cycle 1.

End point type	Secondary
----------------	-----------

End point timeframe:

0 to 120 hours after initiation of chemotherapy (Day 1)

End point values	Aprepitant Regimen	Control Regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	152	150		
Units: percentage of participants				
number (not applicable)	46.7	21.3		

Statistical analyses

Statistical analysis title	No Vomiting in the Overall Phase of Cycle 1
----------------------------	---

Statistical analysis description:

Cochran-Mantel-Haenszel Analysis: Stratified by age group, use of dexamethasone as an anti-emetic, and receipt of very high risk emetogenic chemotherapy.

Comparison groups	Aprepitant Regimen v Control Regimen
Number of subjects included in analysis	302
Analysis specification	Pre-specified
Analysis type	superiority ^[4]
P-value	< 0.01
Method	Cochran-Mantel-Haenszel

Notes:

[4] - The superiority hypotheses was evaluated by comparing the 1-tailed p-value to 0.025 and significance declared if this p-value was ≤ 0.025 .

Adverse events

Adverse events information

Timeframe for reporting adverse events:

14 days after the last dose of study drug (for maximum of 6 cycles, up to 6 months)

Adverse event reporting additional description:

Intent-to-treat (ITT) population: all randomized participants who received study medication.

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

Dictionary used

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

Dictionary version	16.0
--------------------	------

Reporting groups

Reporting group title	Aprepitant Regimen Cycle 1
-----------------------	----------------------------

Reporting group description:

Cycle 1: Participants 12 to 17 years of age, Day 1: aprepitant 125 mg capsule orally (PO) + ondansetron, Days 2 to 3: aprepitant 80 mg capsule PO. Participants 6 months to <12 years of age, Day 1: aprepitant powder for suspension (PFS), 3.0 mg/kg (up to 125 mg) + ondansetron, Days 2 to 3: aprepitant PFS, 2.0 mg/kg (up to 80 mg).

Reporting group title	Aprepitant Regimen Cycles 2-6
-----------------------	-------------------------------

Reporting group description:

Participants completing Cycle 1 from either the aprepitant or the control regimen who met eligibility criteria received open-label aprepitant administered in the same manner as in Cycle 1: Participants 12 to 17 years of age, Day 1: aprepitant 125 mg capsule orally (PO) + ondansetron, Days 2 to 3: aprepitant 80 mg capsule PO. Participants 6 months to <12 years of age, Day 1: aprepitant powder for suspension (PFS), 3.0 mg/kg (up to 125 mg) + ondansetron, Days 2 to 3: aprepitant PFS, 2.0 mg/kg (up to 80 mg).

Reporting group title	Control Regimen Cycle 1
-----------------------	-------------------------

Reporting group description:

Cycle 1: Participants 12 to 17 years of age, Day 1: dose-matched placebo for aprepitant 125 mg capsule oral (PO) + ondansetron. Days 2 to 3: matching placebo for aprepitant 80 mg capsule PO. Participants 6 months to <12 years of age, Day 1: dose-matched placebo for PFS (3.0 mg/kg, up to 125 mg) + ondansetron. Days 2 to 3: dose-matched placebo for PFS (2.0 mg/kg, up to 80 mg).

Serious adverse events	Aprepitant Regimen Cycle 1	Aprepitant Regimen Cycles 2-6	Control Regimen Cycle 1
Total subjects affected by serious adverse events			
subjects affected / exposed	46 / 152 (30.26%)	84 / 170 (49.41%)	41 / 150 (27.33%)
number of deaths (all causes)	1	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Epithelioid sarcoma			
subjects affected / exposed	0 / 152 (0.00%)	1 / 170 (0.59%)	0 / 150 (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
Neuroblastoma			

subjects affected / exposed	1 / 152 (0.66%)	0 / 170 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Osteosarcoma recurrent			
subjects affected / exposed	0 / 152 (0.00%)	1 / 170 (0.59%)	0 / 150 (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
Tumour haemorrhage			
subjects affected / exposed	0 / 152 (0.00%)	1 / 170 (0.59%)	0 / 150 (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
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 152 (0.00%)	1 / 170 (0.59%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Catheter site pain			
subjects affected / exposed	0 / 152 (0.00%)	1 / 170 (0.59%)	0 / 150 (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
Chills			
subjects affected / exposed	0 / 152 (0.00%)	1 / 170 (0.59%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mucosal inflammation			
subjects affected / exposed	2 / 152 (1.32%)	3 / 170 (1.76%)	2 / 150 (1.33%)
occurrences causally related to treatment / all	0 / 2	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain			
subjects affected / exposed	0 / 152 (0.00%)	1 / 170 (0.59%)	0 / 150 (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

Pyrexia			
subjects affected / exposed	0 / 152 (0.00%)	8 / 170 (4.71%)	2 / 150 (1.33%)
occurrences causally related to treatment / all	0 / 0	0 / 8	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombosis in device			
subjects affected / exposed	0 / 152 (0.00%)	1 / 170 (0.59%)	0 / 150 (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
Immune system disorders			
Anaphylactic shock			
subjects affected / exposed	1 / 152 (0.66%)	1 / 170 (0.59%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug hypersensitivity			
subjects affected / exposed	1 / 152 (0.66%)	0 / 170 (0.00%)	0 / 150 (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
Hypersensitivity			
subjects affected / exposed	1 / 152 (0.66%)	0 / 170 (0.00%)	0 / 150 (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
Reproductive system and breast disorders			
Menorrhagia			
subjects affected / exposed	0 / 152 (0.00%)	1 / 170 (0.59%)	0 / 150 (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
Respiratory, thoracic and mediastinal disorders			
Pulmonary oedema			
subjects affected / exposed	0 / 152 (0.00%)	1 / 170 (0.59%)	0 / 150 (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
Tracheal inflammation			

subjects affected / exposed	0 / 152 (0.00%)	1 / 170 (0.59%)	0 / 150 (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
Investigations			
Blood creatinine increased			
subjects affected / exposed	0 / 152 (0.00%)	1 / 170 (0.59%)	0 / 150 (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 clearance decreased			
subjects affected / exposed	1 / 152 (0.66%)	0 / 170 (0.00%)	0 / 150 (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
Electrocardiogram T wave inversion			
subjects affected / exposed	1 / 152 (0.66%)	0 / 170 (0.00%)	0 / 150 (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
Neutrophil count decreased			
subjects affected / exposed	1 / 152 (0.66%)	4 / 170 (2.35%)	2 / 150 (1.33%)
occurrences causally related to treatment / all	0 / 1	0 / 5	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Platelet count decreased			
subjects affected / exposed	2 / 152 (1.32%)	1 / 170 (0.59%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
White blood cell count decreased			
subjects affected / exposed	1 / 152 (0.66%)	0 / 170 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Postoperative wound complication			
subjects affected / exposed	0 / 152 (0.00%)	1 / 170 (0.59%)	0 / 150 (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

Toxicity to various agents subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 152 (0.00%) 0 / 0 0 / 0	2 / 170 (1.18%) 1 / 2 0 / 0	0 / 150 (0.00%) 0 / 0 0 / 0
Wound dehiscence subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 152 (0.00%) 0 / 0 0 / 0	2 / 170 (1.18%) 0 / 2 0 / 0	0 / 150 (0.00%) 0 / 0 0 / 0
Nervous system disorders Convulsion subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 152 (0.00%) 0 / 0 0 / 0	1 / 170 (0.59%) 0 / 1 0 / 0	0 / 150 (0.00%) 0 / 0 0 / 0
Headache subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 152 (0.00%) 0 / 0 0 / 0	1 / 170 (0.59%) 0 / 1 0 / 0	0 / 150 (0.00%) 0 / 0 0 / 0
Presyncope subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 152 (0.00%) 0 / 0 0 / 0	0 / 170 (0.00%) 0 / 0 0 / 0	1 / 150 (0.67%) 0 / 1 0 / 0
Blood and lymphatic system disorders Agranulocytosis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 152 (0.00%) 0 / 0 0 / 0	1 / 170 (0.59%) 0 / 1 0 / 0	0 / 150 (0.00%) 0 / 0 0 / 0
Anaemia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	2 / 152 (1.32%) 0 / 2 0 / 0	9 / 170 (5.29%) 0 / 11 0 / 0	3 / 150 (2.00%) 0 / 3 0 / 0
Bone marrow failure subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 152 (0.00%) 0 / 0 0 / 0	1 / 170 (0.59%) 0 / 1 0 / 0	1 / 150 (0.67%) 0 / 1 0 / 0

Febrile neutropenia			
subjects affected / exposed	23 / 152 (15.13%)	53 / 170 (31.18%)	22 / 150 (14.67%)
occurrences causally related to treatment / all	0 / 23	0 / 88	0 / 22
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukopenia			
subjects affected / exposed	0 / 152 (0.00%)	2 / 170 (1.18%)	0 / 150 (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
Neutropenia			
subjects affected / exposed	4 / 152 (2.63%)	4 / 170 (2.35%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 6	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			
subjects affected / exposed	3 / 152 (1.97%)	4 / 170 (2.35%)	6 / 150 (4.00%)
occurrences causally related to treatment / all	0 / 3	0 / 7	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 152 (0.00%)	3 / 170 (1.76%)	2 / 150 (1.33%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 152 (0.66%)	0 / 170 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Caecitis			
subjects affected / exposed	1 / 152 (0.66%)	0 / 170 (0.00%)	0 / 150 (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
Duodenitis			
subjects affected / exposed	0 / 152 (0.00%)	1 / 170 (0.59%)	0 / 150 (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
Gastritis erosive			

subjects affected / exposed	0 / 152 (0.00%)	1 / 170 (0.59%)	0 / 150 (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
Haematochezia			
subjects affected / exposed	0 / 152 (0.00%)	1 / 170 (0.59%)	0 / 150 (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
Intestinal obstruction			
subjects affected / exposed	0 / 152 (0.00%)	1 / 170 (0.59%)	0 / 150 (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
Oesophagitis			
subjects affected / exposed	0 / 152 (0.00%)	1 / 170 (0.59%)	0 / 150 (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
Stomatitis			
subjects affected / exposed	1 / 152 (0.66%)	1 / 170 (0.59%)	0 / 150 (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
Vomiting			
subjects affected / exposed	2 / 152 (1.32%)	8 / 170 (4.71%)	3 / 150 (2.00%)
occurrences causally related to treatment / all	0 / 2	0 / 9	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hepatotoxicity			
subjects affected / exposed	1 / 152 (0.66%)	0 / 170 (0.00%)	0 / 150 (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
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 152 (0.00%)	1 / 170 (0.59%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure acute			

subjects affected / exposed	0 / 152 (0.00%)	1 / 170 (0.59%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal tubular disorder			
subjects affected / exposed	0 / 152 (0.00%)	1 / 170 (0.59%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bacillus infection			
subjects affected / exposed	0 / 152 (0.00%)	0 / 170 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Balanoposthitis infective			
subjects affected / exposed	0 / 152 (0.00%)	1 / 170 (0.59%)	0 / 150 (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
Bronchitis			
subjects affected / exposed	0 / 152 (0.00%)	0 / 170 (0.00%)	1 / 150 (0.67%)
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 / 152 (0.00%)	1 / 170 (0.59%)	0 / 150 (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
Clostridium difficile infection			
subjects affected / exposed	1 / 152 (0.66%)	0 / 170 (0.00%)	0 / 150 (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
Cystitis			
subjects affected / exposed	0 / 152 (0.00%)	1 / 170 (0.59%)	0 / 150 (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
Device related infection			

subjects affected / exposed	2 / 152 (1.32%)	0 / 170 (0.00%)	0 / 150 (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
Enterobiasis			
subjects affected / exposed	0 / 152 (0.00%)	1 / 170 (0.59%)	0 / 150 (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
Enterococcal sepsis			
subjects affected / exposed	0 / 152 (0.00%)	1 / 170 (0.59%)	0 / 150 (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
Gastroenteritis clostridial			
subjects affected / exposed	0 / 152 (0.00%)	1 / 170 (0.59%)	0 / 150 (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
Gastrointestinal infection			
subjects affected / exposed	0 / 152 (0.00%)	1 / 170 (0.59%)	0 / 150 (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
Otitis media acute			
subjects affected / exposed	1 / 152 (0.66%)	0 / 170 (0.00%)	0 / 150 (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
Periorbital cellulitis			
subjects affected / exposed	1 / 152 (0.66%)	0 / 170 (0.00%)	0 / 150 (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
Pneumonia			
subjects affected / exposed	0 / 152 (0.00%)	1 / 170 (0.59%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postoperative wound infection			

subjects affected / exposed	0 / 152 (0.00%)	1 / 170 (0.59%)	0 / 150 (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
Sepsis			
subjects affected / exposed	1 / 152 (0.66%)	1 / 170 (0.59%)	0 / 150 (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
Upper respiratory tract infection			
subjects affected / exposed	0 / 152 (0.00%)	1 / 170 (0.59%)	0 / 150 (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
Urinary tract infection			
subjects affected / exposed	0 / 152 (0.00%)	3 / 170 (1.76%)	2 / 150 (1.33%)
occurrences causally related to treatment / all	0 / 0	0 / 5	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Varicella			
subjects affected / exposed	1 / 152 (0.66%)	0 / 170 (0.00%)	0 / 150 (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
Viral infection			
subjects affected / exposed	0 / 152 (0.00%)	1 / 170 (0.59%)	0 / 150 (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
Wound infection			
subjects affected / exposed	0 / 152 (0.00%)	2 / 170 (1.18%)	0 / 150 (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
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 152 (0.00%)	3 / 170 (1.76%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			

subjects affected / exposed	0 / 152 (0.00%)	4 / 170 (2.35%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	0 / 152 (0.00%)	1 / 170 (0.59%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypomagnesaemia			
subjects affected / exposed	0 / 152 (0.00%)	1 / 170 (0.59%)	0 / 150 (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
Hyponatraemia			
subjects affected / exposed	0 / 152 (0.00%)	0 / 170 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Aprepitant Regimen Cycle 1	Aprepitant Regimen Cycles 2-6	Control Regimen Cycle 1
Total subjects affected by non-serious adverse events			
subjects affected / exposed	106 / 152 (69.74%)	86 / 170 (50.59%)	109 / 150 (72.67%)
Investigations			
Haemoglobin decreased			
subjects affected / exposed	8 / 152 (5.26%)	14 / 170 (8.24%)	6 / 150 (4.00%)
occurrences (all)	9	27	7
Platelet count decreased			
subjects affected / exposed	10 / 152 (6.58%)	26 / 170 (15.29%)	15 / 150 (10.00%)
occurrences (all)	10	58	16
Neutrophil count decreased			
subjects affected / exposed	12 / 152 (7.89%)	32 / 170 (18.82%)	17 / 150 (11.33%)
occurrences (all)	12	83	19
White blood cell count decreased			
subjects affected / exposed	5 / 152 (3.29%)	12 / 170 (7.06%)	6 / 150 (4.00%)
occurrences (all)	5	15	6
Nervous system disorders			

Headache subjects affected / exposed occurrences (all)	11 / 152 (7.24%) 11	14 / 170 (8.24%) 15	7 / 150 (4.67%) 7
Blood and lymphatic system disorders			
Leukopenia subjects affected / exposed occurrences (all)	8 / 152 (5.26%) 9	13 / 170 (7.65%) 22	10 / 150 (6.67%) 11
Anaemia subjects affected / exposed occurrences (all)	24 / 152 (15.79%) 25	62 / 170 (36.47%) 134	35 / 150 (23.33%) 38
Thrombocytopenia subjects affected / exposed occurrences (all)	15 / 152 (9.87%) 15	38 / 170 (22.35%) 80	14 / 150 (9.33%) 16
Neutropenia subjects affected / exposed occurrences (all)	17 / 152 (11.18%) 17	39 / 170 (22.94%) 74	18 / 150 (12.00%) 20
General disorders and administration site conditions			
Mucosal inflammation subjects affected / exposed occurrences (all)	1 / 152 (0.66%) 1	11 / 170 (6.47%) 13	5 / 150 (3.33%) 5
Pyrexia subjects affected / exposed occurrences (all)	8 / 152 (5.26%) 8	22 / 170 (12.94%) 27	10 / 150 (6.67%) 10
Gastrointestinal disorders			
Abdominal pain subjects affected / exposed occurrences (all)	11 / 152 (7.24%) 15	17 / 170 (10.00%) 26	10 / 150 (6.67%) 15
Abdominal pain upper subjects affected / exposed occurrences (all)	0 / 152 (0.00%) 0	10 / 170 (5.88%) 12	1 / 150 (0.67%) 1
Constipation subjects affected / exposed occurrences (all)	3 / 152 (1.97%) 3	12 / 170 (7.06%) 15	6 / 150 (4.00%) 6
Diarrhoea subjects affected / exposed occurrences (all)	8 / 152 (5.26%) 11	16 / 170 (9.41%) 23	8 / 150 (5.33%) 8

Nausea			
subjects affected / exposed	13 / 152 (8.55%)	42 / 170 (24.71%)	17 / 150 (11.33%)
occurrences (all)	20	78	20
Stomatitis			
subjects affected / exposed	5 / 152 (3.29%)	12 / 170 (7.06%)	4 / 150 (2.67%)
occurrences (all)	6	16	4
Vomiting			
subjects affected / exposed	21 / 152 (13.82%)	59 / 170 (34.71%)	20 / 150 (13.33%)
occurrences (all)	31	152	21
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	9 / 152 (5.92%)	18 / 170 (10.59%)	5 / 150 (3.33%)
occurrences (all)	9	25	6
Epistaxis			
subjects affected / exposed	3 / 152 (1.97%)	10 / 170 (5.88%)	3 / 150 (2.00%)
occurrences (all)	3	15	3
Rhinorrhoea			
subjects affected / exposed	2 / 152 (1.32%)	11 / 170 (6.47%)	1 / 150 (0.67%)
occurrences (all)	2	11	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 July 2012	AMENDMENT 02: The primary reason for this amendment is to satisfy requirements proposed by the Food and Drug Administration (FDA) Written Request and to address the aprepitant Chemotherapy-Induced Nausea and Vomiting (CINV) Pediatric Research Equity Act (PREA) requirements. The minimum age requirement for eligibility has been changed to 6 months of age. Patients will be stratified into 4 age groups as follows: 12-17 years; 6 years to < 12 years; 2 years to <6 years; and 6 months to <2 years.
29 August 2012	AMENDMENT 03: Amendment 02 was immediately replaced with Amendment 03 after an error was discovered in the Cycle 1 Flow Chart.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported