Clinical trial results:
A Multi-center, 2-Part Study to Evaluate the Pharmacokinetics Safety and Tolerability of Aprepitant in Pediatric Patients Undergoing Surgery

Summary

EudraCT number	2008-003178-17
Trial protocol	ES FI Outside EU/EEA
Global end of trial date	12 March 2013

Results information

Result version number	v1 (current)
This version publication date	16 February 2016
First version publication date	15 July 2015

Trial information

Trial identification

Sponsor protocol code	0869-148

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00819039
WHO universal trial number (UTN)	-
Other trial identifiers	MK-0869-148: Merck protocol number

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000144-PIP01-07
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	12 March 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	12 March 2013
Global end of trial reached?	Yes
Global end of trial date	12 March 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This two-part study will determine the appropriate dosing regimen of aprepitant for the prevention of postoperative nausea and vomiting (PONV) in pediatric participants 6 months to 17 years of age, by assessing pharmacokinetic parameters and monitoring safety and tolerability of administered doses. Part 1 will be an open label investigation of a single dose of aprepitant measuring pharmacokinetics at specified time points up to 48 hours after aprepitant dosing. Part 2 will be a double blind trial of participants randomized to receive either aprepitant or ondansetron.

Protection of trial subjects:

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

The following additional measure defined for this individual study was in place for the protection of trial subjects: Administration of post-surgery "rescue therapy" was to be allowed throughout the study for established nausea or vomiting. Recommended rescue medications were: 5-HT3 antagonists, phenothiazines, butyrophenones, benzamides, corticosteroids, benzodiazepines, and domperidone.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	26 January 2009
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Brazil: 20
Country: Number of subjects enrolled	Finland: 1
Country: Number of subjects enrolled	Mexico: 4
Country: Number of subjects enrolled	Russian Federation: 3
Country: Number of subjects enrolled	Spain: 36
Country: Number of subjects enrolled	Turkey: 30
Country: Number of subjects enrolled	United States: 4
Worldwide total number of subjects	98
EEA total number of subjects	37

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	27
Children (2-11 years)	47
Adolescents (12-17 years)	24
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:

Participants aged 6 months to 17 years who were scheduled to undergo surgery which would require a minimum post-surgical hospital stay of 48 hours for Part 1 and of 24 hours for Part 2 were screened for this study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Part 1: Oral Aprepitant

Arm description:

In Study Part 1, on Day 1, participants aged 6 months to <12 years received a single oral dose of aprepitant based on body surface area (BSA) up to the adult dose equivalent of 40 mg (24 mg/m^2) and participants aged 12 years to 17 years received a single oral dose of aprepitant at the equivalent adult dose (40 mg) for the control of post-operative nausea and vomiting (PONV).

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

Dosage and administration details:

In Part 1 on Day 1, participants aged 6 months to <12 years received a single dose of oral aprepitant based on body surface area (BSA) up to the adult dose equivalent of 40 mg (24 mg/m^2) and participants age 12 years to 17 years received an equivalent adult dose of oral aprepitant for PONV (40 mg).

Arm title	Part 2: Oral Aprepitant

Arm description:

In Study Part 2, on Day 1, participants aged 6 months to <12 years received a single oral dose of aprepitant based on BSA up to the adult dose equivalent of 40 mg (24 mg/m^2) and participants aged 12 years to 17 years received a single oral dose of aprepitant at the equivalent adult dose (40 mg) for the control of PONV.

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

Dosage and administration details:

In Part 1 on Day 1, participants aged 6 months to <12 years received a single dose of oral aprepitant based on body surface area (BSA) up to the adult dose equivalent of 40 mg (24 mg/m^2) and participants age 12 years to 17 years received an equivalent adult dose of oral aprepitant for PONV (40 mg).

Arm title	Part 2: Intravenous Ondansetron

Arm description:

In Study Part 2 on Day 1, participants aged 6 months to 17 years received a single intravenous dose of ondansetron based on participant weight for the control of PONV.

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

Dosage and administration details:

Participants received a single dose of intravenous ondansetron based on participant weight on Day 1

Number of subjects in period 1	Part 1: Oral Aprepitant	Part 2: Oral Aprepitant	Part 2: Intravenous Ondansetron
Started	46	27	25
Completed	44	27	24
Not completed	2	0	1
Physician decision	1	-	1
Protocol deviation	1	-	-

Baseline characteristics

Reporting groups	
Reporting group title	Part 1: Oral Aprepitant
Reporting group description:	
In Study Part 1, on Day 1, participants aged 6 months to <12 years received a single oral dose of aprepitant based on body surface area (BSA) up to the adult dose equivalent of 40 mg (24 mg/m^2) and participants aged 12 years to 17 years received a single oral dose of aprepitant at the equivalent adult dose (40 mg) for the control of post-operative nausea and vomiting (PONV).	
Reporting group title	Part 2: Oral Aprepitant
Reporting group description:	
In Study Part 2, on Day 1, participants aged 6 months to <12 years received a single oral dose of aprepitant based on BSA up to the adult dose equivalent of 40 mg (24 mg/m^2) and participants aged 12 years to 17 years received a single oral dose of aprepitant at the equivalent adult dose (40 mg) for the control of PONV.	
Reporting group title	Part 2: Intravenous Ondansetron
Reporting group description:	
In Study Part 2 on Day 1, participants aged 6 months to 17 years received a single intravenous dose of ondansetron based on participant weight for the control of PONV.	

Reporting group values	Part 1: Oral Aprepitant	Part 2: Oral Aprepitant	Part 2: Intravenous Ondansetron
Number of subjects	46	27	25
Age, Customized Units: Participants			
0.5 to <2 years	14	8	5
2 to <6 years	11	7	7
6 to <12 years	11	5	6
12 to 17 years	10	7	7
Gender, Male/Female Units: Participants			
Female	13	6	12
Male	33	21	13

Reporting group values	Total		
Number of subjects	98		
Age, Customized Units: Participants			
0.5 to <2 years	27		
2 to <6 years	25		
6 to <12 years	22		
12 to 17 years	24		
Gender, Male/Female Units: Participants			
Female	31		
Male	67		

End points

End points reporting groups

Reporting group title	Part 1: Oral Aprepitant

Reporting group description:

In Study Part 1, on Day 1, participants aged 6 months to <12 years received a single oral dose of aprepitant based on body surface area (BSA) up to the adult dose equivalent of 40 mg (24 mg/m^2) and participants aged 12 years to 17 years received a single oral dose of aprepitant at the equivalent adult dose (40 mg) for the control of post-operative nausea and vomiting (PONV).

Reporting group title	Part 2: Oral Aprepitant

Reporting group description:

In Study Part 2, on Day 1, participants aged 6 months to <12 years received a single oral dose of aprepitant based on BSA up to the adult dose equivalent of 40 mg (24 mg/m^2) and participants aged 12 years to 17 years received a single oral dose of aprepitant at the equivalent adult dose (40 mg) for the control of PONV.

Reporting group title	Part 2: Intravenous Ondansetron

Reporting group description:

In Study Part 2 on Day 1, participants aged 6 months to 17 years received a single intravenous dose of ondansetron based on participant weight for the control of PONV.

Subject analysis set title	Part 2: Oral Aprepitant
Subject analysis set type	Full analysis

Subject analysis set description:

In Study Part 2 on Day 1, participants aged 6 months to 17 years received a single oral dose of aprepitant for the control of PONV.

Primary: Area Under the Curve From 0-48 Hours (AUC0-48 hr) of Aprepitant Following a Single Oral Dose in Study Part 1

End point title	Area Under the Curve From 0-48 Hours (AUC0-48 hr) of Aprepitant Following a Single Oral Dose in Study Part 1[1][2]

End point description:

Blood samples of 0.5 mL were collected from participants for the analysis of AUC0-48 hr at specified time points: pre-dose, and 1, 2, 3, 4, 8, 12, 24, and 48 hours post aprepitant single dose.

End point type	Primary

End point timeframe:

Pre-dose, and 1, 2, 3, 4, 8, 12, 24, and 48 hours post-dose

Notes:

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

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Pharmacokinetic (PK) analyses were only conducted in Part 1 of this study. No PK analyses were conducted in Part 2 of this study.

End point values	Part 1: Oral Aprepitant			
Subject group type	Reporting group			
Number of subjects analysed	39[3]			
Units: hr*ug/ml				
arithmetic mean (standard deviation)				
6 months to <2 years (n=10)	5.97 (± 4.44)			
2 years to <6 years (n=8)	4.76 (± 3.55)			
6 years to <12 years (n=11)	6.16 (± 2.27)			
12 years to 17 years (n=10)	6.01 (± 2.53)			

Notes:

[3] - All participants who received ≥1 dose of study drug and for whom AUC0-48 hr data were available.

Statistical analyses

No statistical analyses for this end point

Primary: Maximum Plasma Concentration (Cmax) of Aprepitant Following a Single Oral Dose in Study Part 1

End point title	Maximum Plasma Concentration (Cmax) of Aprepitant Following a Single Oral Dose in Study Part 1[4][5]

End point description:

Blood samples were collected from participants for the analysis of Cmax up to 48 hours after dosing.

End point type	Primary

End point timeframe:

Up to 48 hours post-dose

Notes:

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

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: PK analyses were only conducted in Part 1 of this study. No PK analyses were conducted in Part 2 of this study.

End point values	Part 1: Oral Aprepitant			
Subject group type	Reporting group			
Number of subjects analysed	43[6]			
Units: ng/mL				
arithmetic mean (standard deviation)				
6 months to <2 years (n=11)	715 (± 445)			
2 years to <6 years (n=11)	586 (± 462)			
6 years to <12 years (n=11)	913 (± 294)			
12 years to 17 years (n=10)	520 (± 230)			

Notes:

[6] - All participants who received ≥1 dose of study drug and for whom Cmax data were available.

Statistical analyses

No statistical analyses for this end point

Primary: Time to Maximum Plasma Concentration (Tmax) of Aprepitant Following a Single Oral Dose in Study Part 1

End point title	Time to Maximum Plasma Concentration (Tmax) of Aprepitant Following a Single Oral Dose in Study Part 1[7][8]

End point description:

Blood samples were collected from participants for the analysis of Tmax up to 48 hours after dosing.

End point type	Primary

End point timeframe:

Up to 48 hours post-dose

Notes:

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

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: PK analyses were only conducted in Part 1 of this study. No PK analyses were conducted in Part 2 of this study.

End point values	Part 1: Oral Aprepitant			
Subject group type	Reporting group			
Number of subjects analysed	43[9]			
Units: Hours				
median (full range (min-max))				
6 months to <2 years (n=11)	3 (1 to 8)			
2 years to <6 years (n=11)	3 (1.03 to 12)			
6 years to <12 years (n=11)	2 (1 to 8)			
12 years to 17 years (n=10)	3.5 (1 to 11.98)			

Notes:

[9] - All participants who received ≥1 dose of study drug and for whom Tmax data were available.

Statistical analyses

No statistical analyses for this end point

Primary: Plasma Concentration of Aprepitant at 24 Hours (C24 hr) Following a Single Oral Dose in Study Part 1

End point title	Plasma Concentration of Aprepitant at 24 Hours (C24 hr) Following a Single Oral Dose in Study Part 1[10][11]

End point description:

Blood samples were collected from participants for the analysis of C24 hr at 24 hours after dosing.

End point type	Primary

End point timeframe:

24 hours post-dose

Notes:

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

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: PK analyses were only conducted in Part 1 of this study. No PK analyses were conducted in Part 2 of this study.

End point values	Part 1: Oral Aprepitant			
Subject group type	Reporting group			
Number of subjects analysed	42[12]			
Units: ng/mL				
arithmetic mean (standard deviation)				
6 months to <2 years (n=11)	31 (± 39.5)			
2 years to <6 years (n=11)	58.6 (± 54.3)			

6 years to <12 years (n=9)	51.1 (± 35.6)			
12 years to 17 years (n=10)	81.1 (± 59.8)			

Notes:

[12] - All participants who received ≥1 dose of study drug and for whom C24 hr data were available.

Statistical analyses

No statistical analyses for this end point

Primary: Plasma Concentration of Aprepitant at 48 Hours (C48 hr) Following a Single Oral Dose in Study Part 1

End point title	Plasma Concentration of Aprepitant at 48 Hours (C48 hr) Following a Single Oral Dose in Study Part 1[13][14]

End point description:

The mean plasma concentration of aprepitant was evaluated in participants at 48 hours following a single aprepitant oral dose. C48 hr values entered as zero (0) indicate that the mean and standard deviation were not reported since >50% of the measurements were below the lower level of quantitation (LLOQ).

End point type	Primary

End point timeframe:

48 hours post-dose

Notes:

[13] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: PK analyses were only conducted in Part 1 of this study. No PK analyses were conducted in Part 2 of this study.
[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: PK analyses were only conducted in Part 1 of this study. No PK analyses were conducted in Part 2 of this study.

End point values	Part 1: Oral Aprepitant			
Subject group type	Reporting group			
Number of subjects analysed	41[15]			
Units: ng/mL				
arithmetic mean (standard deviation)				
6 months to <2 years (n=11)	0 (± 0)			
2 years to <6 years (n=9)	0 (± 0)			
6 years to <12 years (n=11)	0 (± 0)			
12 years to 17 years (n=10)	7.25 (± 8.9)			

Notes:

[15] - All participants who received ≥1 dose of study drug and for whom C48 hr data were available.

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants Experiencing Adverse Events (AEs)

End point title	Number of Participants Experiencing Adverse Events (AEs)

End point description:

An AE was defined as any unfavorable and unintended change in the structure, function, or chemistry of the body temporally associated with the use of study drug, whether or not considered related to the use

of the product. Any worsening (i.e., any clinically significant adverse change in frequency and/or intensity) of a pre-existing condition which was temporally associated with the use of study drug, was also an AE.

End point type	Primary

End point timeframe:

Up to 21 days post-surgery

End point values	Part 1: Oral Aprepitant	Part 2: Oral Aprepitant	Part 2: Intravenous Ondansetron	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	46[16]	27[17]	25[18]	
Units: Participants				
number (not applicable)	20	12	7	

Notes:

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

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

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

Statistical analyses

Statistical analysis title	Treatment Comparison - Part 2

Statistical analysis description:

The treatment difference and 95% confidence interval (CI) between the aprepitant and ondansetron groups in Part 2 were calculated. The 95% CI was based on the Chan and Zhang method for difference in proportions of participants who experienced one or more AEs between aprepitant and ondansetron.

Comparison groups	Part 2: Oral Aprepitant v Part 2: Intravenous Ondansetron
Number of subjects included in analysis	52
Analysis specification	Pre-specified
Analysis type	other[19]
Parameter estimate	Mean difference (final values)
Point estimate	16.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.6
upper limit	42

Notes:

[19] - Estimation

Primary: Number of Participants Discontinuing Study Drug Due to AEs

End point title	Number of Participants Discontinuing Study Drug Due to AEs[20]

End point description:

An AE was defined as any unfavorable and unintended change in the structure, function, or chemistry of the body temporally associated with the use of study drug, whether or not considered related to the use of the product. Any worsening (i.e., any clinically significant adverse change in frequency and/or intensity) of a pre-existing condition which was temporally associated with the use of study drug, was also an AE.

End point type	Primary

End point timeframe:

Day 1

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 were performed on the number of participants discontinuing study drug due to an AE since no particpants in any treatment group discontinued study drug due to an AE.

End point values	Part 1: Oral Aprepitant	Part 2: Oral Aprepitant	Part 2: Intravenous Ondansetron	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	46[21]	27[22]	25[23]	
Units: Participants				
number (not applicable)	0	0	0	

Notes:

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

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

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

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With No Vomiting Up to 24 Hours Following Surgery in Study Part 2

End point title	Number of Participants With No Vomiting Up to 24 Hours Following Surgery in Study Part 2[24]

End point description:

No vomiting was defined as no emesis or retching or dry heaves (regardless of rescue therapy). The number of participants who experienced no vomiting up to 24 hours post-surgery is reported.

End point type	Secondary

End point timeframe:

Up to 24 hours post-surgery

Notes:

[24] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Efficacy analyses were only conducted in Part 2 of this study. No efficacy analyses were conducted in Part 1 of this study.

End point values	Part 2: Intravenous Ondansetron	Part 2: Oral Aprepitant		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	25[25]	25[26]		
Units: Participants				
number (not applicable)	20	20		

Notes:

[25] - Participants who received ≥1 study drug dose, underwent surgery & had ≥1 post-treatment assessment.
[26] - Participants who received ≥1 study drug dose, underwent surgery & had ≥1 post-treatment assessment.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Complete Response Up to 24 Hours

Following Surgery in Study Part 2

End point title	Number of Participants With Complete Response Up to 24 Hours Following Surgery in Study Part 2[27]

End point description:

Complete response was defined as no vomiting and no use of rescue medication in 0-24 hours post-surgery.

End point type	Secondary

End point timeframe:

Up to 24 hours post-surgery

Notes:

[27] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Efficacy analyses were only conducted in Part 2 of this study. No efficacy analyses were conducted in Part 1 of this study.

End point values	Part 2: Intravenous Ondansetron	Part 2: Oral Aprepitant		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	25[28]	25[29]		
Units: Participants				
number (not applicable)	20	19		

Notes:

[28] - Participants who received ≥1 study drug dose, underwent surgery & had ≥1 post-treatment assessment.
[29] - Participants who received ≥1 study drug dose, underwent surgery & had ≥1 post-treatment assessment.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With No Vomiting Up to 48 Hours Following Surgery in Study Part 2

End point title	Number of Participants With No Vomiting Up to 48 Hours Following Surgery in Study Part 2[30]

End point description:

No vomiting was defined as no emesis or retching or dry heaves (regardless of rescue therapy). The number of participants who experienced no vomiting up to 48 hours post-surgery is reported.

End point type	Secondary

End point timeframe:

Up to 48 hours post-surgery

Notes:

[30] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Efficacy analyses were only conducted in Part 2 of this study. No efficacy analyses were conducted in Part 1 of this study.

End point values	Part 2: Intravenous Ondansetron	Part 2: Oral Aprepitant		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	25[31]	25[32]		
Units: Participants				
number (not applicable)	20	18		

Notes:

[31] - Participants who received ≥1 study drug dose, underwent surgery & had ≥1 post-treatment assessment.
[32] - Participants who received ≥1 study drug dose, underwent surgery & had ≥1 post-treatment assessment.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Complete Response Up to 48 Hours Following Surgery in Study Part 2

End point title	Number of Participants With Complete Response Up to 48 Hours Following Surgery in Study Part 2[33]

End point description:

Complete response was defined as no vomiting and no use of rescue medication in 0-48 hours post-surgery.

End point type	Secondary

End point timeframe:

Up to 48 hours post-surgery

Notes:

[33] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Efficacy analyses were only conducted in Part 2 of this study. No efficacy analyses were conducted in Part 1 of this study.

End point values	Part 2: Intravenous Ondansetron	Part 2: Oral Aprepitant		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	25[34]	25[35]		
Units: Participants				
number (not applicable)	20	17		

Notes:

[34] - Participants who received ≥1 study drug dose, underwent surgery & had ≥1 post-treatment assessment.
[35] - Participants who received ≥1 study drug dose, underwent surgery & had ≥1 post-treatment assessment.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Vomiting Frequency in Study Part 2

End point title	Number of Participants With Vomiting Frequency in Study Part 2[36]

End point description:

A vomiting episode was defined as one or more continuous vomits (expulsion of stomach contents through the mouth) or retches (an attempt to vomit that was not productive of stomach contents also referred to as dry heaves). Distinct episodes were, by definition, separated by the absence of vomiting and retching for at least 1 minute.

End point type	Secondary

End point timeframe:

Up to 24 hours post-surgery

Notes:

[36] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Efficacy analyses were only conducted in Part 2 of this study. No efficacy analyses were conducted in Part 1 of this study.

End point values	Part 2: Intravenous Ondansetron	Part 2: Oral Aprepitant		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	25[37]	25[38]		
Units: Participants				
number (not applicable)				
No Vomiting	20	20		
1 Vomiting Episode	3	5		
2 Vomiting Episodes	1	0		
3 Vomiting Episodes	0	0		
>3 Vomiting Episodes	1	0		

Notes:

[37] - Participants who received ≥1 study drug dose, underwent surgery & had ≥1 post-treatment assessment.

[38] - Participants who received ≥1 study drug dose, underwent surgery & had ≥1 post-treatment assessment.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Up to Day 21 post-surgery	
Adverse event reporting additional description:	
The population consisted of all study participants who received at least one dose of study drug.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups	
Reporting group title	Part 2: Oral Aprepitant
Reporting group description:	
In Study Part 2, participants aged 6 months to 17 years received a single oral dose of aprepitant for the treatment of PONV on Day 1.	
Reporting group title	Part 1: Oral Aprepitant
Reporting group description:	
In Study Part 1, participants aged 6 months to 17 years received a single oral dose of aprepitant for the treatment of PONV on Day 1.	
Reporting group title	Part 2: Intravenous Ondansetron
Reporting group description:	
In Study Part 2, particpants aged 6 months to 17 years received a single intravenous dose of ondansetron for the treatment of PONV on Day 1.	

Serious adverse events	Part 2: Oral Aprepitant	Part 1: Oral Aprepitant	Part 2: Intravenous Ondansetron
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 27 (7.41%)	3 / 46 (6.52%)	0 / 25 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Anastomotic Complication			
subjects affected / exposed	0 / 27 (0.00%)	1 / 46 (2.17%)	0 / 25 (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			
Pneumonia			
subjects affected / exposed	1 / 27 (3.70%)	0 / 46 (0.00%)	0 / 25 (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
Incision Site Infection			

subjects affected / exposed	1 / 27 (3.70%)	2 / 46 (4.35%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
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	Part 2: Oral Aprepitant	Part 1: Oral Aprepitant	Part 2: Intravenous Ondansetron
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 27 (18.52%)	14 / 46 (30.43%)	4 / 25 (16.00%)
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 27 (0.00%)	3 / 46 (6.52%)	2 / 25 (8.00%)
occurrences (all)	0	3	2
Chest Pain			
subjects affected / exposed	2 / 27 (7.41%)	0 / 46 (0.00%)	2 / 25 (8.00%)
occurrences (all)	2	0	2
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	2 / 27 (7.41%)	3 / 46 (6.52%)	0 / 25 (0.00%)
occurrences (all)	3	4	0
Vomiting			
subjects affected / exposed	1 / 27 (3.70%)	10 / 46 (21.74%)	0 / 25 (0.00%)
occurrences (all)	5	20	0
Nausea			
subjects affected / exposed	0 / 27 (0.00%)	4 / 46 (8.70%)	0 / 25 (0.00%)
occurrences (all)	0	6	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 November 2012	Amendment 01: Per request of the United States Food and Drug Administration (US FDA), due to changes in the ondansetron label, expanded safety monitoring was implemented to include additional vital sign and electrolyte monitoring in all participants receiving ondansetron and post-dose electrocardiogram (ECG) for those participants with baseline electrolyte abnormalities. Another main change included: Participants may be discharged prior to 48 hours following the end of surgery. For these participants, the parent/guardian was required to record any vomiting episodes, use of rescue medication, use of pain medication, and/or adverse events from the time of discharge through 48 hours following the end of surgery. Site staff were to contact the participants/parent/guardian at 48 hours following the end of surgery to assess the occurrence of these events.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported