Clinical trial results:
A Phase 3, Multicenter, Randomized, Double-Blind, Active-Controlled Study of the Safety and Efficacy of Rolapitant for the Prevention of Chemotherapy-Induced Nausea and Vomiting (CINV) in Subjects Receiving Highly Emetogenic Chemotherapy (HEC)

Summary

EudraCT number	2010-022743-37
Trial protocol	HU ES CZ PL SK IT
Global end of trial date	24 February 2014

Results information

Result version number	v1 (current)
This version publication date	27 December 2019
First version publication date	27 December 2019

Trial information

Trial identification

Sponsor protocol code	TS-P04833

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01500213
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Tesaro
Sponsor organisation address	1000 Winter St North, Waltham, United States, 02451
Public contact	GSK Response Center, Tesaro, 1866 4357343, GSKClinicalSupportHD@gsk.com
Scientific contact	GSK Response Center, Tesaro, 1866 4357343, GSKClinicalSupportHD@gsk.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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	04 August 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	24 February 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine whether administration of rolapitant with granisetron and dexamethasone improves CINV in the delayed phase (>24 to 120 hours) of CINV compared with administration of placebo with granisetron and dexamethasone in subjects receiving HEC. The primary outcome will be based on complete response (defined as no emetic episodes and no rescue medication) in the delayed phase (>24 to 120 hours).

Protection of trial subjects:

NA

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	07 February 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	Poland: 79
Country: Number of subjects enrolled	Slovakia: 3
Country: Number of subjects enrolled	Spain: 71
Country: Number of subjects enrolled	Czech Republic: 24
Country: Number of subjects enrolled	Hungary: 37
Country: Number of subjects enrolled	Italy: 43
Country: Number of subjects enrolled	Brazil: 70
Country: Number of subjects enrolled	Georgia: 63
Country: Number of subjects enrolled	Korea, Republic of: 69
Country: Number of subjects enrolled	Mexico: 10
Country: Number of subjects enrolled	Taiwan: 4
Country: Number of subjects enrolled	Ukraine: 18
Country: Number of subjects enrolled	United States: 36
Country: Number of subjects enrolled	South Africa: 17
Worldwide total number of subjects	544
EEA total number of subjects	257

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)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	398
From 65 to 84 years	146
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This is a Phase 3, multicenter, randomized, parallel-group, double-blind, active-controlled study of rolapitant in subjects receiving HEC. All participants expected to complete Cycle 1 and will have the option of participating in up to five additional cycles.

Pre-assignment

Screening details:

MITT population: 278 participants were randomized to Rolapitant and 277 were randomized to control, 272 of those randomized to Rolapitant received study drug in C1; 274 of those who were randomized to control received study drug in C1, 1 Rolapitant subject and 1 control subject were from GCP-non-compliant sites.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Rolapitant + Granisetron + Dexamethasone

Arm description:

* Oral dose of rolapitant 180 mg (equivalent to 200 mg rolapitant hydrochloride monohydrate) 1–2 h before administration of chemotherapy
* Granisetron (10 µg/kg intravenously) about 30 min before chemotherapy
* Dexamethasone (20 mg orally) about 30 min before chemotherapy, and dexamethasone 8 mg orally twice daily on days 2–4

Arm type	Experimental
Investigational medicinal product name	Rolapitant
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Oral dose of rolapitant 180 mg (equivalent to 200 mg rolapitant hydrochloride monohydrate) 1–2 h before administration of chemotherapy

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

Dosage and administration details:

Granisetron (10 µg/kg intravenously) about 30 min before chemotherapy

Investigational medicinal product name	Dexamethasone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Dexamethasone (20 mg orally) about 30 min before chemotherapy, and dexamethasone 8 mg orally

twice daily on days 2–4

Arm title	Placebo + Granisetron + Dexamethasone

Arm description:

* Matching placebo 1–2 h before administration of chemotherapy
* Granisetron (10 µg/kg intravenously) about 30 min before chemotherapy
* Dexamethasone (20 mg orally) about 30 min before chemotherapy, and dexamethasone 8 mg orally twice daily on days 2–4

Arm type	Active comparator
Investigational medicinal product name	Matching Placebo for Rolapitant
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Matching placebo 1–2 h before administration of chemotherapy

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

Dosage and administration details:

Granisetron (10 µg/kg intravenously) about 30 min before chemotherapy

Investigational medicinal product name	Dexamethasone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Dexamethasone (20 mg orally) about 30 min before chemotherapy, and dexamethasone 8 mg orally twice daily on days 2–4

Number of subjects in period 1	Rolapitant + Granisetron + Dexamethasone	Placebo + Granisetron + Dexamethasone
Started	271	273
Completed	60	53
Not completed	211	220
Consent withdrawn by subject	26	35
Physician decision	12	10
Adverse event, non-fatal	35	34
Other Reasons	6	5
Death	7	3
Chemo Completed or Change in Therapy	84	81

Lost to follow-up	3	6
Disease Progression	13	21
Lack of efficacy	9	7
Protocol deviation	16	18

Baseline characteristics

Reporting groups

Reporting group title	Rolapitant + Granisetron + Dexamethasone

Reporting group description:

* Oral dose of rolapitant 180 mg (equivalent to 200 mg rolapitant hydrochloride monohydrate) 1–2 h before administration of chemotherapy
* Granisetron (10 µg/kg intravenously) about 30 min before chemotherapy
* Dexamethasone (20 mg orally) about 30 min before chemotherapy, and dexamethasone 8 mg orally twice daily on days 2–4

Reporting group title	Placebo + Granisetron + Dexamethasone

Reporting group description:

* Matching placebo 1–2 h before administration of chemotherapy
* Granisetron (10 µg/kg intravenously) about 30 min before chemotherapy
* Dexamethasone (20 mg orally) about 30 min before chemotherapy, and dexamethasone 8 mg orally twice daily on days 2–4

Reporting group values	Rolapitant + Granisetron + Dexamethasone	Placebo + Granisetron + Dexamethasone	Total
Number of subjects	271	273	544
Age categorical Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			0
Newborns (0-27 days)			0
Infants and toddlers (28 days-23 months)			0
Children (2-11 years)			0
Adolescents (12-17 years)			0
Adults (18-64 years)			0
From 65-84 years			0
85 years and over			0
Age continuous Units: years			
arithmetic mean	58.5	58.5	
standard deviation	± 10.05	± 9.25	-
Gender categorical Units: Subjects			
Female	88	87	175
Male	183	186	369
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	36	38	74
Not Hispanic or Latino	235	235	470
Unknown or Not Reported	0	0	0
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	2	8	10
Asian	34	41	75

Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	2	3	5
White	226	212	438
More than one race	0	0	0
Unknown or Not Reported	7	9	16

End points

End points reporting groups

Reporting group title	Rolapitant + Granisetron + Dexamethasone

Reporting group description:

* Oral dose of rolapitant 180 mg (equivalent to 200 mg rolapitant hydrochloride monohydrate) 1–2 h before administration of chemotherapy
* Granisetron (10 µg/kg intravenously) about 30 min before chemotherapy
* Dexamethasone (20 mg orally) about 30 min before chemotherapy, and dexamethasone 8 mg orally twice daily on days 2–4

Reporting group title	Placebo + Granisetron + Dexamethasone

Reporting group description:

* Matching placebo 1–2 h before administration of chemotherapy
* Granisetron (10 µg/kg intravenously) about 30 min before chemotherapy
* Dexamethasone (20 mg orally) about 30 min before chemotherapy, and dexamethasone 8 mg orally twice daily on days 2–4

Primary: No Emetic Episodes and No Rescue Medication

End point title	No Emetic Episodes and No Rescue Medication

End point description:

The primary objective of this study is to determine whether administration of rolapitant with granisetron and dexamethasone improves CINV in the delayed phase (>24 to 120 hours) of CINV compared with administration of placebo with granisetron and dexamethasone in subjects receiving HEC. The primary outcome will be based on complete response (defined as no emesis and no rescue medication) in the delayed phase (>24 to 120 hours).

End point type	Primary

End point timeframe:

>24 to 120 hours post chemotherapy

End point values	Rolapitant + Granisetron + Dexamethasone	Placebo + Granisetron + Dexamethasone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	271[1]	273[2]		
Units: percentage of participants				
number (confidence interval 95%)	70.1 (64.3 to 75.5)	61.9 (55.9 to 67.7)		

Notes:

[1] - MITT Population

[2] - MITT Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Cochran Mantel Haenszel (CMH) test was stratified by sex. Missing data were imputed as treatment failures.

Comparison groups	Rolapitant + Granisetron + Dexamethasone v Placebo +

	Granisetron + Dexamethasone
Number of subjects included in analysis	544
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.043 [3]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	1
upper limit	2.1

Notes:

[3] - To control for multiplicity, analyses were performed hierarchically. For the CR delayed the threshold for statistical significance was 0.05; no further adjustment for multiplicity were required for the primary endpoint.

Secondary: Acute Phase Response

End point title	Acute Phase Response

End point description:

To determine the effect of rolapitant on complete response rates in the acute (0 to 24 hours) phase of CINV.

End point type	Secondary

End point timeframe:

0 to 24 hours

End point values	Rolapitant + Granisetron + Dexamethasone	Placebo + Granisetron + Dexamethasone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	271[4]	273[5]		
Units: percentage of participants				
number (confidence interval 95%)	83.4 (78.4 to 87.6)	79.5 (74.2 to 84.1)		

Notes:

[4] - MITT Population

[5] - MITT Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Cochran Mantel Haenszel (CMH) test was stratified by sex. Missing data were imputed as treatment failures.

Comparison groups	Rolapitant + Granisetron + Dexamethasone v Placebo + Granisetron + Dexamethasone

Number of subjects included in analysis	544
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.233 [6]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.8
upper limit	2

Notes:

[6] - To control for multiplicity, analyses were performed hierarchically. CR-acute was tested only if the result for the primary endpoint, CR delayed, was statistically significant.

Secondary: Overall Response Rate

End point title	Overall Response Rate

End point description:

To determine the effect of rolapitant on complete response rate in the overall (0 to 120 hours) phase of CINV.

End point type	Secondary

End point timeframe:

0 to 120 hours

End point values	Rolapitant + Granisetron + Dexamethasone	Placebo + Granisetron + Dexamethasone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	271[7]	273[8]		
Units: percentage of participants				
number (confidence interval 95%)	67.5 (61.6 to 73.1)	60.4 (54.4 to 66.3)		

Notes:

[7] - MITT Population

[8] - MITT Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Cochran Mantel Haenszel (CMH) test was stratified by sex. Missing data were imputed as treatment failures.

Comparison groups	Rolapitant + Granisetron + Dexamethasone v Placebo + Granisetron + Dexamethasone

Number of subjects included in analysis	544
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.084 [9]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	1
upper limit	1.9

Notes:

[9] - To control for multiplicity, analyses were performed hierarchically. CR overall was tested only if both CR delayed and CR acute were statistically significant.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 6 cycles of treatment. Median number cycles=2; each cycle median duration = 21-22days. AEs that occur up to 30 days past last dose of treatment are included. Number of deaths (all causes) include those occurring > 30 days after last dose treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	15.0

Reporting groups

Reporting group title	Rolapitant + Granisetron + Dexamethasone

Reporting group description:

* Oral dose of rolapitant 180 mg (equivalent to 200 mg rolapitant hydrochloride monohydrate) 1–2 h before administration of chemotherapy
* Granisetron (10 µg/kg intravenously) about 30 min before chemotherapy
* Dexamethasone (20 mg orally) about 30 min before chemotherapy, and dexamethasone 8 mg orally twice daily on days 2–4

Reporting group title	Placebo + Granisetron + Dexamethasone

Reporting group description:

* Matching placebo 1–2 h before administration of chemotherapy
* Granisetron (10 µg/kg intravenously) about 30 min before chemotherapy
* Dexamethasone (20 mg orally) about 30 min before chemotherapy, and dexamethasone 8 mg orally twice daily on days 2–4

Serious adverse events	Rolapitant + Granisetron + Dexamethasone	Placebo + Granisetron + Dexamethasone	
Total subjects affected by serious adverse events			
subjects affected / exposed	80 / 272 (29.41%)	65 / 274 (23.72%)	
number of deaths (all causes)	12	11	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Leukoerythroblastosis			
subjects affected / exposed	0 / 272 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to central nervous system			
subjects affected / exposed	1 / 272 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Neoplasm malignant			

subjects affected / exposed	0 / 272 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Oral neoplasm			
subjects affected / exposed	1 / 272 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Tumour pain			
subjects affected / exposed	1 / 272 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Arterial occlusive disease			
subjects affected / exposed	0 / 272 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Axillary vein thrombosis			
subjects affected / exposed	1 / 272 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Circulatory collapse			
subjects affected / exposed	1 / 272 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Deep vein thrombosis			
subjects affected / exposed	3 / 272 (1.10%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage			
subjects affected / exposed	0 / 272 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			

subjects affected / exposed	1 / 272 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	3 / 272 (1.10%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Iliac artery occlusion			
subjects affected / exposed	0 / 272 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral arterial occlusive disease			
subjects affected / exposed	1 / 272 (0.37%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subclavian vein thrombosis			
subjects affected / exposed	1 / 272 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	5 / 272 (1.84%)	5 / 274 (1.82%)	
occurrences causally related to treatment / all	0 / 7	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 1	
Disease progression			
subjects affected / exposed	3 / 272 (1.10%)	2 / 274 (0.73%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 2	0 / 1	
Fatigue			
subjects affected / exposed	2 / 272 (0.74%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			

subjects affected / exposed	0 / 272 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-cardiac chest pain			
subjects affected / exposed	2 / 272 (0.74%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema			
subjects affected / exposed	1 / 272 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	0 / 272 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal pain			
subjects affected / exposed	1 / 272 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden death			
subjects affected / exposed	1 / 272 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 272 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute pulmonary oedema			
subjects affected / exposed	0 / 272 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Dyspnoea			
subjects affected / exposed	2 / 272 (0.74%)	2 / 274 (0.73%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Haemoptysis			
subjects affected / exposed	1 / 272 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pneumothorax			
subjects affected / exposed	1 / 272 (0.37%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	3 / 272 (1.10%)	2 / 274 (0.73%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood creatinine increased			
subjects affected / exposed	0 / 272 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutrophil count decreased			
subjects affected / exposed	0 / 272 (0.00%)	4 / 274 (1.46%)	
occurrences causally related to treatment / all	0 / 0	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Toxicity to various agents			
subjects affected / exposed	0 / 272 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			

subjects affected / exposed	1 / 272 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	3 / 272 (1.10%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	0 / 272 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiac failure			
subjects affected / exposed	0 / 272 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebral infarction			
subjects affected / exposed	1 / 272 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Convulsion			
subjects affected / exposed	1 / 272 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
subjects affected / exposed	1 / 272 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysarthria			
subjects affected / exposed	1 / 272 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic encephalopathy			

subjects affected / exposed	1 / 272 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Ischaemic stroke			
subjects affected / exposed	1 / 272 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Syncope			
subjects affected / exposed	1 / 272 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	0 / 272 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	4 / 272 (1.47%)	3 / 274 (1.09%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	12 / 272 (4.41%)	6 / 274 (2.19%)	
occurrences causally related to treatment / all	0 / 12	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukopenia			
subjects affected / exposed	0 / 272 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	5 / 272 (1.84%)	7 / 274 (2.55%)	
occurrences causally related to treatment / all	0 / 5	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			

subjects affected / exposed	1 / 272 (0.37%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	4 / 272 (1.47%)	2 / 274 (0.73%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	4 / 272 (1.47%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 6	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aphagia			
subjects affected / exposed	1 / 272 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	0 / 272 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	0 / 272 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocolitis			
subjects affected / exposed	0 / 272 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric haemorrhage			
subjects affected / exposed	1 / 272 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer perforation			

subjects affected / exposed	1 / 272 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 272 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Haematochezia			
subjects affected / exposed	1 / 272 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus paralytic			
subjects affected / exposed	1 / 272 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Melaena			
subjects affected / exposed	0 / 272 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	1 / 272 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophagitis			
subjects affected / exposed	1 / 272 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stomatitis			
subjects affected / exposed	2 / 272 (0.74%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			

subjects affected / exposed	1 / 272 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	2 / 272 (0.74%)	2 / 274 (0.73%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Biliary colic			
subjects affected / exposed	0 / 272 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			
subjects affected / exposed	1 / 272 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 272 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	2 / 272 (0.74%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Renal Failure Acute			
subjects affected / exposed	0 / 272 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 272 (0.00%)	2 / 274 (0.73%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Infections and infestations			
Device related infection			
subjects affected / exposed	0 / 272 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalitis Herpes			
subjects affected / exposed	0 / 272 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Gastroenteritis			
subjects affected / exposed	1 / 272 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	0 / 272 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Influenza			
subjects affected / exposed	0 / 272 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Klebsiella bacteraemia			
subjects affected / exposed	1 / 272 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infection			
subjects affected / exposed	1 / 272 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenic sepsis			
subjects affected / exposed	1 / 272 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parotitis			

subjects affected / exposed	1 / 272 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 272 (0.37%)	6 / 274 (2.19%)	
occurrences causally related to treatment / all	0 / 1	0 / 6	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pseudomonal sepsis			
subjects affected / exposed	0 / 272 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	3 / 272 (1.10%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 272 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Urinary tract infection			
subjects affected / exposed	0 / 272 (0.00%)	3 / 274 (1.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 272 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	3 / 272 (1.10%)	2 / 274 (0.73%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			

subjects affected / exposed	0 / 272 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			
subjects affected / exposed	1 / 272 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Hyponatraemia			
subjects affected / exposed	1 / 272 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypophagia			
subjects affected / exposed	0 / 272 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Rolapitant + Granisetron + Dexamethasone	Placebo + Granisetron + Dexamethasone	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	225 / 272 (82.72%)	211 / 274 (77.01%)	
Nervous system disorders			
Headache			
subjects affected / exposed	15 / 272 (5.51%)	12 / 274 (4.38%)	
occurrences (all)	17	16	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	30 / 272 (11.03%)	16 / 274 (5.84%)	
occurrences (all)	42	28	
Neutropenia			
subjects affected / exposed	39 / 272 (14.34%)	32 / 274 (11.68%)	
occurrences (all)	60	45	
General disorders and administration site conditions			

Asthenia			
subjects affected / exposed	52 / 272 (19.12%)	55 / 274 (20.07%)	
occurrences (all)	89	83	
Fatigue			
subjects affected / exposed	21 / 272 (7.72%)	28 / 274 (10.22%)	
occurrences (all)	26	32	
Mucosal inflammation			
subjects affected / exposed	21 / 272 (7.72%)	21 / 274 (7.66%)	
occurrences (all)	29	27	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	14 / 272 (5.15%)	9 / 274 (3.28%)	
occurrences (all)	19	9	
Constipation			
subjects affected / exposed	37 / 272 (13.60%)	40 / 274 (14.60%)	
occurrences (all)	47	47	
Diarrhoea			
subjects affected / exposed	34 / 272 (12.50%)	28 / 274 (10.22%)	
occurrences (all)	48	40	
Dyspepsia			
subjects affected / exposed	10 / 272 (3.68%)	14 / 274 (5.11%)	
occurrences (all)	12	16	
Nausea			
subjects affected / exposed	32 / 272 (11.76%)	35 / 274 (12.77%)	
occurrences (all)	52	61	
Vomiting			
subjects affected / exposed	14 / 272 (5.15%)	23 / 274 (8.39%)	
occurrences (all)	24	34	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	11 / 272 (4.04%)	14 / 274 (5.11%)	
occurrences (all)	11	16	
Hiccups			
subjects affected / exposed	25 / 272 (9.19%)	12 / 274 (4.38%)	
occurrences (all)	35	17	
Skin and subcutaneous tissue disorders			

Alopecia subjects affected / exposed occurrences (all)	20 / 272 (7.35%) 23	26 / 274 (9.49%) 29	
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	7 / 272 (2.57%) 9	15 / 274 (5.47%) 18	
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	39 / 272 (14.34%) 54	35 / 274 (12.77%) 47	
Hypomagnesaemia subjects affected / exposed occurrences (all)	16 / 272 (5.88%) 24	16 / 274 (5.84%) 25	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported