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	2010-022742-25
Trial protocol	LV BE PT BG ES IT HU
Global end of trial date	03 May 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-P04832

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01499849
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, GSKClinicalSupportHD@gsk.com
Scientific contact	GSK Response Center, Tesaro, 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	11 August 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	03 May 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	Canada: 16
Country: Number of subjects enrolled	Mexico: 8
Country: Number of subjects enrolled	Peru: 46
Country: Number of subjects enrolled	Russian Federation: 81
Country: Number of subjects enrolled	Thailand: 116
Country: Number of subjects enrolled	United States: 71
Country: Number of subjects enrolled	Belarus: 17
Country: Number of subjects enrolled	Guatemala: 2
Country: Number of subjects enrolled	Romania: 21
Country: Number of subjects enrolled	Portugal: 14
Country: Number of subjects enrolled	Spain: 30
Country: Number of subjects enrolled	Belgium: 5
Country: Number of subjects enrolled	Bulgaria: 39
Country: Number of subjects enrolled	France: 13
Country: Number of subjects enrolled	Hungary: 13
Country: Number of subjects enrolled	Italy: 25
Country: Number of subjects enrolled	Latvia: 9
Worldwide total number of subjects	526
EEA total number of subjects	169

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)	392
From 65 to 84 years	132
85 years and over	2

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:

Overall Number of Baseline Participants only included the Modified Intent to Treat (MITT) population: 266 subjects were randomized to Rolapitant and 266 were randomized to control; 264 of those randomized to Rolapitant received study drug in Cycle 1; 262 of those who were randomized to control received study drug in Cycle 1.

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	264	262
Completed	42	40
Not completed	222	222
Consent withdrawn by subject	43	42
Physician decision	20	19
Adverse event, non-fatal	27	30
Other Reasons	26	29
Death	5	7

Lost to follow-up	6	3
Chemo completed or Change in Therapy	70	67
Disease Progression	11	10
Protocol deviation	11	11
Lack of efficacy	3	4

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	264	262	526
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	57.0	57.7	
standard deviation	± 10.08	± 11.15	-
Gender categorical Units: Subjects			
Female	110	112	222
Male	154	150	304
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	33	34	67
Not Hispanic or Latino	231	228	459
Unknown or Not Reported	0	0	0
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	2	0	2

Asian	61	56	117
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	2	3	5
White	178	179	357
More than one race	0	0	0
Unknown or Not Reported	21	24	45

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 emetic episodes 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	264[1]	262[2]		
Units: percentage of participants				
number (confidence interval 95%)	72.7 (66.9 to 78.0)	58.4 (52.2 to 64.4)		

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	526
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [3]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.3
upper limit	2.7

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	264[4]	262[5]		
Units: percentage of participants				
number (confidence interval 95%)	83.7 (78.7 to 88.0)	73.7 (67.9 to 78.9)		

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	526
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.005 [6]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.2
upper limit	2.8

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 rates 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	264[7]	262[8]		
Units: percentage of participants				
number (confidence interval 95%)	70.1 (64.2 to 75.5)	56.5 (50.2 to 62.6)		

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	526
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001 [9]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.3
upper limit	2.6

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.

Adverse event reporting additional description:

Safety analysis was based on actual treatment received in Cycle 1. 266 subjects were randomized to Rolapitant, among which 263 received Rolapitant in Cycle 1, hence Safety=263 for Rolapitant. 266 subjects were randomized to control, among which 263 received control in Cycle 1 (There was an error in treatment received), hence Safety=263 for control.

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	37 / 263 (14.07%)	54 / 263 (20.53%)	
number of deaths (all causes)	10	16	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bronchial carcinoma			
subjects affected / exposed	0 / 263 (0.00%)	1 / 263 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Gastrointestinal Stromal Cancer			

subjects affected / exposed	0 / 263 (0.00%)	1 / 263 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasm progression			
subjects affected / exposed	1 / 263 (0.38%)	0 / 263 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 263 (0.38%)	0 / 263 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Embolism			
subjects affected / exposed	0 / 263 (0.00%)	1 / 263 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hypotension			
subjects affected / exposed	0 / 263 (0.00%)	1 / 263 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orthostatic Hypotension			
subjects affected / exposed	0 / 263 (0.00%)	1 / 263 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Superior vena cava syndrome			
subjects affected / exposed	0 / 263 (0.00%)	1 / 263 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 263 (0.00%)	1 / 263 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Death			
subjects affected / exposed	0 / 263 (0.00%)	3 / 263 (1.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 3	
Disease progression			
subjects affected / exposed	1 / 263 (0.38%)	2 / 263 (0.76%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 1	
Fatigue			
subjects affected / exposed	0 / 263 (0.00%)	1 / 263 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	1 / 263 (0.38%)	0 / 263 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Malaise			
subjects affected / exposed	1 / 263 (0.38%)	1 / 263 (0.38%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multi-Organ Failure			
subjects affected / exposed	0 / 263 (0.00%)	2 / 263 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Non-cardiac chest pain			
subjects affected / exposed	1 / 263 (0.38%)	0 / 263 (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 / 263 (0.38%)	0 / 263 (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			

Anaphylactic reaction			
subjects affected / exposed	0 / 263 (0.00%)	1 / 263 (0.38%)	
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 respiratory failure			
subjects affected / exposed	0 / 263 (0.00%)	1 / 263 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Bronchopleural fistula			
subjects affected / exposed	1 / 263 (0.38%)	0 / 263 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydropneumothorax			
subjects affected / exposed	0 / 263 (0.00%)	1 / 263 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	1 / 263 (0.38%)	0 / 263 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	1 / 263 (0.38%)	0 / 263 (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	0 / 263 (0.00%)	1 / 263 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	2 / 263 (0.76%)	4 / 263 (1.52%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	

Respiratory distress			
subjects affected / exposed	0 / 263 (0.00%)	1 / 263 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	2 / 263 (0.76%)	0 / 263 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 263 (0.38%)	0 / 263 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	1 / 263 (0.38%)	0 / 263 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardio-respiratory arrest			
subjects affected / exposed	0 / 263 (0.00%)	1 / 263 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiomyopathy			
subjects affected / exposed	1 / 263 (0.38%)	0 / 263 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular tachycardia			
subjects affected / exposed	0 / 263 (0.00%)	1 / 263 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	2 / 263 (0.76%)	1 / 263 (0.38%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Convulsion			
subjects affected / exposed	1 / 263 (0.38%)	1 / 263 (0.38%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			
subjects affected / exposed	1 / 263 (0.38%)	2 / 263 (0.76%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Loss of consciousness			
subjects affected / exposed	0 / 263 (0.00%)	1 / 263 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	0 / 263 (0.00%)	1 / 263 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	0 / 263 (0.00%)	1 / 263 (0.38%)	
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			
Agranulocytosis			
subjects affected / exposed	0 / 263 (0.00%)	1 / 263 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Febrile neutropenia			
subjects affected / exposed	3 / 263 (1.14%)	2 / 263 (0.76%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	0 / 263 (0.00%)	2 / 263 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			

subjects affected / exposed	1 / 263 (0.38%)	0 / 263 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 263 (0.00%)	1 / 263 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer haemorrhage			
subjects affected / exposed	0 / 263 (0.00%)	1 / 263 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer perforation			
subjects affected / exposed	0 / 263 (0.00%)	1 / 263 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorder			
subjects affected / exposed	0 / 263 (0.00%)	1 / 263 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	1 / 263 (0.38%)	1 / 263 (0.38%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Impaired gastric emptying			
subjects affected / exposed	1 / 263 (0.38%)	0 / 263 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	0 / 263 (0.00%)	2 / 263 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Odynophagia			

subjects affected / exposed	0 / 263 (0.00%)	1 / 263 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal perforation			
subjects affected / exposed	1 / 263 (0.38%)	0 / 263 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	1 / 263 (0.38%)	0 / 263 (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	0 / 263 (0.00%)	5 / 263 (1.90%)	
occurrences causally related to treatment / all	0 / 0	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Renal Failure Acute			
subjects affected / exposed	2 / 263 (0.76%)	3 / 263 (1.14%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Hypercreatinaemia			
subjects affected / exposed	0 / 263 (0.00%)	1 / 263 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bacterial sepsis			
subjects affected / exposed	0 / 263 (0.00%)	1 / 263 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis bacterial			
subjects affected / exposed	1 / 263 (0.38%)	0 / 263 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Encephalitis Herpes			
subjects affected / exposed	0 / 263 (0.00%)	1 / 263 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocarditis			
subjects affected / exposed	1 / 263 (0.38%)	0 / 263 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			
subjects affected / exposed	0 / 263 (0.00%)	1 / 263 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infective exacerbation of bronchiectasis			
subjects affected / exposed	0 / 263 (0.00%)	1 / 263 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung abscess			
subjects affected / exposed	0 / 263 (0.00%)	1 / 263 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenic sepsis			
subjects affected / exposed	1 / 263 (0.38%)	0 / 263 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	5 / 263 (1.90%)	1 / 263 (0.38%)	
occurrences causally related to treatment / all	0 / 6	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Pseudomonal sepsis			
subjects affected / exposed	1 / 263 (0.38%)	0 / 263 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			

subjects affected / exposed	0 / 263 (0.00%)	1 / 263 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 263 (0.00%)	2 / 263 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	1 / 263 (0.38%)	0 / 263 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	2 / 263 (0.76%)	5 / 263 (1.90%)	
occurrences causally related to treatment / all	0 / 2	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 1	
Diabetes mellitus			
subjects affected / exposed	1 / 263 (0.38%)	0 / 263 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	0 / 263 (0.00%)	1 / 263 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malnutrition			
subjects affected / exposed	1 / 263 (0.38%)	0 / 263 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
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	187 / 263 (71.10%)	198 / 263 (75.29%)	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	28 / 263 (10.65%)	32 / 263 (12.17%)	
occurrences (all)	53	55	
Leukopenia			
subjects affected / exposed	18 / 263 (6.84%)	14 / 263 (5.32%)	
occurrences (all)	68	48	
Neutropenia			
subjects affected / exposed	33 / 263 (12.55%)	23 / 263 (8.75%)	
occurrences (all)	93	71	
Thrombocytopenia			
subjects affected / exposed	16 / 263 (6.08%)	12 / 263 (4.56%)	
occurrences (all)	24	40	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	35 / 263 (13.31%)	40 / 263 (15.21%)	
occurrences (all)	58	54	
Fatigue			
subjects affected / exposed	36 / 263 (13.69%)	30 / 263 (11.41%)	
occurrences (all)	52	40	
Mucosal inflammation			
subjects affected / exposed	17 / 263 (6.46%)	19 / 263 (7.22%)	
occurrences (all)	20	22	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	26 / 263 (9.89%)	29 / 263 (11.03%)	
occurrences (all)	31	31	
Diarrhoea			
subjects affected / exposed	20 / 263 (7.60%)	18 / 263 (6.84%)	
occurrences (all)	24	20	
Dyspepsia			
subjects affected / exposed	18 / 263 (6.84%)	8 / 263 (3.04%)	
occurrences (all)	24	10	

Nausea			
subjects affected / exposed	24 / 263 (9.13%)	35 / 263 (13.31%)	
occurrences (all)	29	48	
Stomatitis			
subjects affected / exposed	16 / 263 (6.08%)	14 / 263 (5.32%)	
occurrences (all)	21	15	
Vomiting			
subjects affected / exposed	9 / 263 (3.42%)	22 / 263 (8.37%)	
occurrences (all)	10	25	
Respiratory, thoracic and mediastinal disorders			
Hiccups			
subjects affected / exposed	16 / 263 (6.08%)	8 / 263 (3.04%)	
occurrences (all)	20	12	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	22 / 263 (8.37%)	23 / 263 (8.75%)	
occurrences (all)	24	26	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	30 / 263 (11.41%)	36 / 263 (13.69%)	
occurrences (all)	30	44	
Dehydration			
subjects affected / exposed	13 / 263 (4.94%)	15 / 263 (5.70%)	
occurrences (all)	15	15	

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