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 Moderately Emetogenic Chemotherapy (MEC)

Summary

EudraCT number	2010-022746-24
Trial protocol	HU LV ES BE CZ PL BG SK PT IT
Global end of trial date	19 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-P04834

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01500226
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	30 June 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	19 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 MEC. 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	13 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: 26
Country: Number of subjects enrolled	Portugal: 4
Country: Number of subjects enrolled	Slovakia: 7
Country: Number of subjects enrolled	Spain: 80
Country: Number of subjects enrolled	Belgium: 24
Country: Number of subjects enrolled	Bulgaria: 57
Country: Number of subjects enrolled	Czech Republic: 25
Country: Number of subjects enrolled	France: 5
Country: Number of subjects enrolled	Hungary: 89
Country: Number of subjects enrolled	Italy: 38
Country: Number of subjects enrolled	Latvia: 20
Country: Number of subjects enrolled	Belarus: 24
Country: Number of subjects enrolled	Georgia: 67
Country: Number of subjects enrolled	Korea, Republic of: 45
Country: Number of subjects enrolled	Mexico: 15
Country: Number of subjects enrolled	Peru: 48
Country: Number of subjects enrolled	Romania: 60
Country: Number of subjects enrolled	Russian Federation: 76
Country: Number of subjects enrolled	Thailand: 76

Country: Number of subjects enrolled	Taiwan: 45
Country: Number of subjects enrolled	Ukraine: 9
Country: Number of subjects enrolled	United States: 445
Country: Number of subjects enrolled	South Africa: 47
Worldwide total number of subjects	1332
EEA total number of subjects	435

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)	965
From 65 to 84 years	364
85 years and over	3

Subject disposition

Recruitment

Recruitment details:

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

Pre-assignment

Screening details:

684 subjects were randomized to Rolapitant and 685 were randomized to control; 670 of those randomized to Rolapitant received study drug in C1; 674 of those who were randomized to control received study drug in C1. 4 Rolapitant subject and 8 control subject were from GCP-non-compliant sites. MITT = 666 Rolapitant and 666 control

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 200mg rolapitant hydrochloride monohydrate) 1–2 h before administration of chemotherapy.
* Granisetron (2 mg orally) about 30 min before chemotherapy. Subsequently, granisetron 2mg was administered orally to all patients once daily on days 2–3
* Dexamethasone (20 mg orally) about 30 min before chemotherapy.

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

Dosage and administration details:

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

Investigational medicinal product name	Granisetron
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Granisetron (2 mg orally) about 30 min before chemotherapy. Subsequently, granisetron 2mg was administered orally to all patients once daily on days 2–3

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.

Arm title	Placebo + Granisetron + Dexamethasone

Arm description:

* Matching placebo 1–2 h before administration of chemotherapy
* Granisetron (2 mg orally) about 30 min before chemotherapy. Subsequently, granisetron 2mg was administered orally to all patients once daily on days 2–3
* Dexamethasone (20 mg orally) about 30 min before chemotherapy

Arm type	Placebo
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	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Granisetron (2 mg orally) about 30 min before chemotherapy. Subsequently, granisetron 2mg was administered orally to all patients once daily on days 2–3

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.

Number of subjects in period 1	Rolapitant + Granisetron + Dexamethasone	Placebo + Granisetron + Dexamethasone
Started	666	666
Completed	185	189
Not completed	481	477
Consent withdrawn by subject	87	89
Physician decision	17	15
Other Reasons	15	15
Adverse event, non-fatal	31	38
Death	12	4
Chemo Completed or Change in Therapy	235	232

Lost to follow-up	9	5
Disease Progression	16	14
Protocol deviation	45	35
Lack of efficacy	14	30

Baseline characteristics

Reporting groups

Reporting group title	Rolapitant + Granisetron + Dexamethasone

Reporting group description:

* Oral dose of rolapitant 180 mg (equivalent to 200mg rolapitant hydrochloride monohydrate) 1–2 h before administration of chemotherapy.
* Granisetron (2 mg orally) about 30 min before chemotherapy. Subsequently, granisetron 2mg was administered orally to all patients once daily on days 2–3
* Dexamethasone (20 mg orally) about 30 min before chemotherapy.

Reporting group title	Placebo + Granisetron + Dexamethasone

Reporting group description:

* Matching placebo 1–2 h before administration of chemotherapy
* Granisetron (2 mg orally) about 30 min before chemotherapy. Subsequently, granisetron 2mg was administered orally to all patients once daily on days 2–3
* Dexamethasone (20 mg orally) about 30 min before chemotherapy

Reporting group values	Rolapitant + Granisetron + Dexamethasone	Placebo + Granisetron + Dexamethasone	Total
Number of subjects	666	666	1332
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	56.7	56.6	
standard deviation	± 11.65	± 12.01	-
Gender categorical Units: Subjects			
Female	531	536	1067
Male	135	130	265
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	77	70	147
Not Hispanic or Latino	584	593	1177
Unknown or Not Reported	5	3	8
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	7	6	13
Asian	92	84	176

Native Hawaiian or Other Pacific Islander	1	2	3
Black or African American	24	29	53
White	508	512	1020
More than one race	0	0	0
Unknown or Not Reported	34	33	67

End points

End points reporting groups

Reporting group title	Rolapitant + Granisetron + Dexamethasone

Reporting group description:

* Oral dose of rolapitant 180 mg (equivalent to 200mg rolapitant hydrochloride monohydrate) 1–2 h before administration of chemotherapy.
* Granisetron (2 mg orally) about 30 min before chemotherapy. Subsequently, granisetron 2mg was administered orally to all patients once daily on days 2–3
* Dexamethasone (20 mg orally) about 30 min before chemotherapy.

Reporting group title	Placebo + Granisetron + Dexamethasone

Reporting group description:

* Matching placebo 1–2 h before administration of chemotherapy
* Granisetron (2 mg orally) about 30 min before chemotherapy. Subsequently, granisetron 2mg was administered orally to all patients once daily on days 2–3
* Dexamethasone (20 mg orally) about 30 min before chemotherapy

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 MEC. 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	666[1]	666[2]		
Units: percentage of participants				
number (confidence interval 95%)	71.3 (67.7 to 74.7)	61.6 (57.7 to 65.3)		

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	1332
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [3]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.2
upper limit	2

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	666[4]	666[5]		
Units: percentage of participants				
number (confidence interval 95%)	83.5 (80.4 to 86.2)	80.3 (77.1 to 83.3)		

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	1332
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.143 [6]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.9
upper limit	1.6

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	666[7]	666[8]		
Units: percentage of participants				
number (confidence interval 95%)	68.6 (64.9 to 72.1)	57.8 (54.0 to 61.6)		

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	1332
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [9]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.3
upper limit	2

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 (2 mg orally) about 30 min before chemotherapy. Subsequently, granisetron 2mg was administered orally to all patients once daily on days 2–3
* Dexamethasone (20 mg orally) about 30 min before chemotherapy

684 subjects were randomized to Rolapitant
670 of those randomized to Rolapitant received rolapitant in C1
Safety = 670 Rolapitant

Reporting group title	Placebo + Granisetron + Dexamethasone

Reporting group description:

* Matching placebo 1–2 h before administration of chemotherapy
* Granisetron (2 mg orally) about 30 min before chemotherapy. Subsequently, granisetron 2mg was administered orally to all patients once daily on days 2–3
* Dexamethasone (20 mg orally) about 30 min before chemotherapy

685 subjects were randomized to control
674 of those who were randomized to control received control in C1
Safety = 674 control

Serious adverse events	Rolapitant + Granisetron + Dexamethasone	Placebo + Granisetron + Dexamethasone	
Total subjects affected by serious adverse events			
subjects affected / exposed	89 / 670 (13.28%)	103 / 674 (15.28%)	
number of deaths (all causes)	16	8	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases to central nervous system			
subjects affected / exposed	1 / 670 (0.15%)	0 / 674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to peritoneum			

subjects affected / exposed	0 / 670 (0.00%)	1 / 674 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Neoplasm progression			
subjects affected / exposed	1 / 670 (0.15%)	2 / 674 (0.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 2	
Vascular disorders			
Aortic aneurysm			
subjects affected / exposed	0 / 670 (0.00%)	1 / 674 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deep vein thrombosis			
subjects affected / exposed	3 / 670 (0.45%)	0 / 674 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Embolism			
subjects affected / exposed	1 / 670 (0.15%)	0 / 674 (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	1 / 670 (0.15%)	3 / 674 (0.45%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombosis			
subjects affected / exposed	0 / 670 (0.00%)	1 / 674 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venous thrombosis limb			
subjects affected / exposed	0 / 670 (0.00%)	1 / 674 (0.15%)	
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	1 / 670 (0.15%)	0 / 674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			
subjects affected / exposed	1 / 670 (0.15%)	0 / 674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disease progression			
subjects affected / exposed	1 / 670 (0.15%)	1 / 674 (0.15%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			
subjects affected / exposed	0 / 670 (0.00%)	1 / 674 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multi-Organ Failure			
subjects affected / exposed	0 / 670 (0.00%)	1 / 674 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pyrexia			
subjects affected / exposed	4 / 670 (0.60%)	1 / 674 (0.15%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 670 (0.00%)	1 / 674 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Vaginal haemorrhage			
subjects affected / exposed	1 / 670 (0.15%)	0 / 674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	1 / 670 (0.15%)	0 / 674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 670 (0.00%)	2 / 674 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	1 / 670 (0.15%)	2 / 674 (0.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea Exertional			
subjects affected / exposed	1 / 670 (0.15%)	0 / 674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoptysis			
subjects affected / exposed	1 / 670 (0.15%)	0 / 674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Hypoxia			
subjects affected / exposed	0 / 670 (0.00%)	1 / 674 (0.15%)	
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	0 / 670 (0.00%)	1 / 674 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	1 / 670 (0.15%)	0 / 674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pneumothorax			
subjects affected / exposed	0 / 670 (0.00%)	1 / 674 (0.15%)	
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	5 / 670 (0.75%)	4 / 674 (0.59%)	
occurrences causally related to treatment / all	0 / 5	0 / 4	
deaths causally related to treatment / all	0 / 1	0 / 0	
Respiratory distress			
subjects affected / exposed	3 / 670 (0.45%)	0 / 674 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Respiratory failure			
subjects affected / exposed	2 / 670 (0.30%)	2 / 674 (0.30%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 2	
Psychiatric disorders			
Mental status changes			
subjects affected / exposed	1 / 670 (0.15%)	0 / 674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 670 (0.15%)	0 / 674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 670 (0.15%)	0 / 674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
C-reactive protein increased			
subjects affected / exposed	0 / 670 (0.00%)	1 / 674 (0.15%)	
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	3 / 670 (0.45%)	4 / 674 (0.59%)	
occurrences causally related to treatment / all	0 / 6	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Radius fracture			
subjects affected / exposed	1 / 670 (0.15%)	0 / 674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal fracture			
subjects affected / exposed	0 / 670 (0.00%)	1 / 674 (0.15%)	
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	0 / 670 (0.00%)	2 / 674 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	2 / 670 (0.30%)	4 / 674 (0.59%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	1 / 670 (0.15%)	0 / 674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardio-respiratory arrest			
subjects affected / exposed	2 / 670 (0.30%)	0 / 674 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Palpitations			
subjects affected / exposed	1 / 670 (0.15%)	0 / 674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Ventricular tachycardia			
subjects affected / exposed	0 / 670 (0.00%)	1 / 674 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericarditis			
subjects affected / exposed	1 / 670 (0.15%)	0 / 674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebral haematoma			
subjects affected / exposed	1 / 670 (0.15%)	0 / 674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	1 / 670 (0.15%)	0 / 674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Headache			
subjects affected / exposed	2 / 670 (0.30%)	0 / 674 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoaesthesia			
subjects affected / exposed	1 / 670 (0.15%)	0 / 674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuropathy peripheral			
subjects affected / exposed	1 / 670 (0.15%)	0 / 674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Partial seizures			
subjects affected / exposed	1 / 670 (0.15%)	0 / 674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Posterior reversible encephalopathy			

syndrome			
subjects affected / exposed	1 / 670 (0.15%)	0 / 674 (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	1 / 670 (0.15%)	0 / 674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 670 (0.30%)	5 / 674 (0.74%)	
occurrences causally related to treatment / all	0 / 3	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	14 / 670 (2.09%)	25 / 674 (3.71%)	
occurrences causally related to treatment / all	0 / 15	0 / 27	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukopenia			
subjects affected / exposed	1 / 670 (0.15%)	1 / 674 (0.15%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	7 / 670 (1.04%)	13 / 674 (1.93%)	
occurrences causally related to treatment / all	0 / 7	0 / 17	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
subjects affected / exposed	0 / 670 (0.00%)	1 / 674 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	1 / 670 (0.15%)	1 / 674 (0.15%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			

Abdominal pain			
subjects affected / exposed	0 / 670 (0.00%)	1 / 674 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	2 / 670 (0.30%)	2 / 674 (0.30%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			
subjects affected / exposed	0 / 670 (0.00%)	1 / 674 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enteritis			
subjects affected / exposed	0 / 670 (0.00%)	1 / 674 (0.15%)	
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 / 670 (0.00%)	1 / 674 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 670 (0.00%)	1 / 674 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	3 / 670 (0.45%)	1 / 674 (0.15%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jejunal perforation			
subjects affected / exposed	1 / 670 (0.15%)	0 / 674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine perforation			

subjects affected / exposed	1 / 670 (0.15%)	0 / 674 (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 / 670 (0.00%)	2 / 674 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	0 / 670 (0.00%)	3 / 674 (0.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 2	
Skin and subcutaneous tissue disorders			
Skin erosion			
subjects affected / exposed	0 / 670 (0.00%)	1 / 674 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin ulcer			
subjects affected / exposed	1 / 670 (0.15%)	0 / 674 (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			
Hydronephrosis			
subjects affected / exposed	0 / 670 (0.00%)	1 / 674 (0.15%)	
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	0 / 670 (0.00%)	1 / 674 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal Failure Acute			
subjects affected / exposed	1 / 670 (0.15%)	2 / 674 (0.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Renal Failure Chronic			

subjects affected / exposed	1 / 670 (0.15%)	0 / 674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 670 (0.15%)	0 / 674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Catheter site infection			
subjects affected / exposed	1 / 670 (0.15%)	0 / 674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	2 / 670 (0.30%)	2 / 674 (0.30%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile colitis			
subjects affected / exposed	1 / 670 (0.15%)	0 / 674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection			
subjects affected / exposed	0 / 670 (0.00%)	1 / 674 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related sepsis			
subjects affected / exposed	1 / 670 (0.15%)	0 / 674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea infectious			
subjects affected / exposed	0 / 670 (0.00%)	1 / 674 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			

subjects affected / exposed	2 / 670 (0.30%)	1 / 674 (0.15%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fungaemia			
subjects affected / exposed	0 / 670 (0.00%)	1 / 674 (0.15%)	
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 / 670 (0.15%)	0 / 674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lobar Pneumonia			
subjects affected / exposed	0 / 670 (0.00%)	1 / 674 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Mucosal infection			
subjects affected / exposed	1 / 670 (0.15%)	0 / 674 (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	4 / 670 (0.60%)	2 / 674 (0.30%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 1	
Oral fungal infection			
subjects affected / exposed	1 / 670 (0.15%)	0 / 674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic infection			
subjects affected / exposed	0 / 670 (0.00%)	1 / 674 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peridiverticular Abscess			

subjects affected / exposed	1 / 670 (0.15%)	0 / 674 (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	4 / 670 (0.60%)	4 / 674 (0.59%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative wound infection			
subjects affected / exposed	1 / 670 (0.15%)	1 / 674 (0.15%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			
subjects affected / exposed	1 / 670 (0.15%)	0 / 674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	0 / 670 (0.00%)	1 / 674 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	4 / 670 (0.60%)	0 / 674 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	1 / 670 (0.15%)	1 / 674 (0.15%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	2 / 670 (0.30%)	2 / 674 (0.30%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			

subjects affected / exposed	6 / 670 (0.90%)	4 / 674 (0.59%)	
occurrences causally related to treatment / all	0 / 6	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus inadequate control			
subjects affected / exposed	1 / 670 (0.15%)	0 / 674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypovolaemia			
subjects affected / exposed	0 / 670 (0.00%)	1 / 674 (0.15%)	
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	540 / 670 (80.60%)	542 / 674 (80.42%)	
Nervous system disorders			
Dizziness			
subjects affected / exposed	69 / 670 (10.30%)	71 / 674 (10.53%)	
occurrences (all)	83	86	
Dysgeusia			
subjects affected / exposed	29 / 670 (4.33%)	38 / 674 (5.64%)	
occurrences (all)	31	39	
Headache			
subjects affected / exposed	82 / 670 (12.24%)	109 / 674 (16.17%)	
occurrences (all)	99	132	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	67 / 670 (10.00%)	50 / 674 (7.42%)	
occurrences (all)	110	88	
Leukopenia			
subjects affected / exposed	37 / 670 (5.52%)	31 / 674 (4.60%)	
occurrences (all)	68	93	
Neutropenia			

subjects affected / exposed	96 / 670 (14.33%)	84 / 674 (12.46%)	
occurrences (all)	178	168	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	78 / 670 (11.64%)	78 / 674 (11.57%)	
occurrences (all)	97	104	
Fatigue			
subjects affected / exposed	179 / 670 (26.72%)	183 / 674 (27.15%)	
occurrences (all)	294	259	
Mucosal inflammation			
subjects affected / exposed	41 / 670 (6.12%)	30 / 674 (4.45%)	
occurrences (all)	54	36	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	34 / 670 (5.07%)	31 / 674 (4.60%)	
occurrences (all)	41	37	
Constipation			
subjects affected / exposed	114 / 670 (17.01%)	138 / 674 (20.47%)	
occurrences (all)	142	167	
Diarrhoea			
subjects affected / exposed	92 / 670 (13.73%)	101 / 674 (14.99%)	
occurrences (all)	123	131	
Dyspepsia			
subjects affected / exposed	46 / 670 (6.87%)	42 / 674 (6.23%)	
occurrences (all)	50	50	
Nausea			
subjects affected / exposed	76 / 670 (11.34%)	97 / 674 (14.39%)	
occurrences (all)	101	137	
Stomatitis			
subjects affected / exposed	40 / 670 (5.97%)	46 / 674 (6.82%)	
occurrences (all)	50	57	
Vomiting			
subjects affected / exposed	14 / 670 (2.09%)	39 / 674 (5.79%)	
occurrences (all)	14	48	
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed	35 / 670 (5.22%)	37 / 674 (5.49%)	
occurrences (all)	39	46	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	157 / 670 (23.43%)	172 / 674 (25.52%)	
occurrences (all)	170	185	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	32 / 670 (4.78%)	55 / 674 (8.16%)	
occurrences (all)	37	59	
Musculoskeletal and connective tissue disorders			
Bone pain			
subjects affected / exposed	42 / 670 (6.27%)	40 / 674 (5.93%)	
occurrences (all)	57	68	
Arthralgia			
subjects affected / exposed	25 / 670 (3.73%)	34 / 674 (5.04%)	
occurrences (all)	30	39	
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	57 / 670 (8.51%)	45 / 674 (6.68%)	
occurrences (all)	63	58	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	92 / 670 (13.73%)	87 / 674 (12.91%)	
occurrences (all)	116	106	
Dehydration			
subjects affected / exposed	25 / 670 (3.73%)	37 / 674 (5.49%)	
occurrences (all)	26	46	
Hypomagnesaemia			
subjects affected / exposed	41 / 670 (6.12%)	28 / 674 (4.15%)	
occurrences (all)	54	36	

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