



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