



Clinical trial results:

A Phase 2, Randomized, Multicenter, Placebo-Controlled, Double-Blind, Parallel-Group Study, with an Open-Label Extension to Evaluate the Efficacy, Safety, and Pharmacokinetics of E5501 in Subjects with Chronic Hepatitis C Virus Related Thrombocytopenia who are Potential Candidates for Antiviral Treatment

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2010-024479-20 |
| Trial protocol | DE BG |
| Global end of trial date | 01 May 2014 |

Results information

| | |
|--------------------------------|--|
| Result version number | v2 (current) |
| This version publication date | 25 March 2016 |
| First version publication date | 05 August 2015 |
| Version creation reason | <ul style="list-style-type: none">• Correction of full data set Results are being revised due to training issue with our staff and to reconcile the results to ensure consistency with ClinicalTrials.gov results. |

Trial information

Trial identification

| | |
|-----------------------|----------------|
| Sponsor protocol code | E5501-G000-203 |
|-----------------------|----------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01355289 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Eisai |
| Sponsor organisation address | 155 Tice Boulevard, Woodcliff Lake, United States, 07677 |
| Public contact | Medical Information, Eisai Limited, +44 08456761400, LmedInfo@eisai.net |
| Scientific contact | Medical Information, Eisai Limited, +44 08456761400, LmedInfo@eisai.net |

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 | 01 May 2014 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 01 May 2014 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of E5501 by measuring platelet response in subjects with chronic hepatitis C virus (HCV)-related thrombocytopenia who require antiviral treatment

Protection of trial subjects:

This study was conducted in accordance with standard operating procedures (SOPs) of the sponsor (or designee), which are designed to ensure adherence to Good Clinical Practice (GCP) guidelines as required by the following:

- Principles of the World Medical Association Declaration of Helsinki (World Medical Association, 2008)
- International Conference on Harmonisation (ICH) E6 Guideline for GCP (CPMP/ICH/135/95) of the European Agency for the Evaluation of Medicinal Products, Committee for Proprietary Medicinal Products, International Conference on Harmonisation of Pharmaceuticals for Human Use
- Title 21 of the United States (US) Code of Federal Regulations (US 21 CFR) regarding clinical studies, including Part 50 and Part 56 concerning informed subject consent and Institutional Review Board (IRB) regulations and applicable sections of US 21 CFR Part 312
- European Good Clinical Practice Directive 2005/28/EC and Clinical Trial Directive 2001/20/EC for studies conducted within any European Union (EU) country. All suspected unexpected serious adverse reactions were reported, as required, to the Competent Authorities of all involved EU member states.
- Article 14, Paragraph 3, and Article 80-2 of the Pharmaceutical Affairs Law (Law No. 145, 1960) for studies conducted in Japan, in addition to Japan's GCP Subject Information and Informed Consent.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 10 November 2011 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | Bulgaria: 3 |
| Country: Number of subjects enrolled | France: 3 |
| Country: Number of subjects enrolled | Germany: 5 |
| Country: Number of subjects enrolled | Israel: 9 |
| Country: Number of subjects enrolled | United States: 45 |

| | |
|------------------------------------|----|
| Worldwide total number of subjects | 65 |
| EEA total number of subjects | 11 |

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) | 60 |
| From 65 to 84 years | 5 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The Screening Period encompassed 14 days \pm 7 days. Prerandomization assessments took place in all participants who had provided informed consent.

Period 1

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

Arms

| | |
|------------------------------|----------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Placebo (Core Study) |

Arm description:

Placebo, was administered orally, once daily for up to 21 days.

| | |
|--|----------|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Once daily.

| | |
|------------------|---------------------------------|
| Arm title | Avatrombopag 10 mg (Core Study) |
|------------------|---------------------------------|

Arm description:

Avatrombopag 10 mg, was administered orally, once daily, preferably with food for up to 21 days.

| | |
|--|-------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | Avatrombopag |
| Investigational medicinal product code | E5501 |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

10 mg, tablet form, orally, once daily.

| | |
|------------------|---------------------------------|
| Arm title | Avatrombopag 20 mg (Core Study) |
|------------------|---------------------------------|

Arm description:

Avatrombopag 20 mg, was administered orally, once daily, preferably with food for up to 21 days.

| | |
|--|-------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | Avatrombopag |
| Investigational medicinal product code | E5501 |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:
20 mg, tablet form, orally, once daily.

| | |
|--|---------------------------------|
| Arm title | Avatrombopag 30 mg (Core Study) |
| Arm description: Avatrombopag 30 mg, was administered orally, once daily, preferably with food for up to 21 days. | |
| Arm type | Active comparator |
| Investigational medicinal product name | Avatrombopag |
| Investigational medicinal product code | E5501 |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:
30 mg, tablet form, orally, once daily.

| Number of subjects in period 1 | Placebo (Core Study) | Avatrombopag 10 mg (Core Study) | Avatrombopag 20 mg (Core Study) |
|---------------------------------------|----------------------|---------------------------------|---------------------------------|
| Started | 17 | 16 | 18 |
| Completed | 16 | 16 | 18 |
| Not completed | 1 | 0 | 0 |
| Adverse event, non-fatal | 1 | - | - |
| Not specified | - | - | - |
| Inadequate therapeutic effect | - | - | - |

| Number of subjects in period 1 | Avatrombopag 30 mg (Core Study) |
|---------------------------------------|---------------------------------|
| Started | 14 |
| Completed | 12 |
| Not completed | 2 |
| Adverse event, non-fatal | - |
| Not specified | 1 |
| Inadequate therapeutic effect | 1 |

Period 2

| | |
|------------------------------|-----------------------------|
| Period 2 title | Open Label Extension (OLE) |
| Is this the baseline period? | No |
| Allocation method | Non-randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|------------------|-------------------------------------|
| Arm title | Avatrombopag (Open Label Extension) |
|------------------|-------------------------------------|

Arm description:

Avatrombopag was initiated at a dose of 20 mg, once daily in the open label extension (OLE) period. The avatrombopag dose was titrated up or down in accordance with their individual response within the range of a minimum of 5 mg and a maximum of 50 mg for up to 48 weeks.

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | Avatrombopag |
| Investigational medicinal product code | E5501 |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

5-50 mg, tablet form, orally, once daily.

| Number of subjects in period 2 | Avatrombopag (Open Label Extension) |
|---------------------------------------|---|
| Started | 62 |
| Completed | 28 |
| Not completed | 34 |
| Adverse event, non-fatal | 1 |
| Not specified | 3 |
| Lost to follow-up | 1 |
| Lack of efficacy | 29 |

Baseline characteristics

Reporting groups

| | |
|--|---------------------------------|
| Reporting group title | Placebo (Core Study) |
| Reporting group description: Placebo, was administered orally, once daily for up to 21 days. | |
| Reporting group title | Avatrombopag 10 mg (Core Study) |
| Reporting group description: Avatrombopag 10 mg, was administered orally, once daily, preferably with food for up to 21 days. | |
| Reporting group title | Avatrombopag 20 mg (Core Study) |
| Reporting group description: Avatrombopag 20 mg, was administered orally, once daily, preferably with food for up to 21 days. | |
| Reporting group title | Avatrombopag 30 mg (Core Study) |
| Reporting group description: Avatrombopag 30 mg, was administered orally, once daily, preferably with food for up to 21 days. | |

| Reporting group values | Placebo (Core Study) | Avatrombopag 10 mg (Core Study) | Avatrombopag 20 mg (Core Study) |
|---|----------------------|---------------------------------|---------------------------------|
| Number of subjects | 17 | 16 | 18 |
| Age categorical Units: Subjects | | | |
| In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over | | | |
| Age continuous Units: years | | | |
| arithmetic mean | 50.2 | 55.3 | 54.9 |
| standard deviation | ± 7.96 | ± 8.06 | ± 7.38 |
| Gender categorical Units: Subjects | | | |
| Female | 3 | 4 | 5 |
| Male | 14 | 12 | 13 |

| Reporting group values | Avatrombopag 30 mg (Core Study) | Total | |
|--|---------------------------------|-------------|--|
| Number of subjects | 14 | 65 | |
| Age categorical Units: Subjects | | | |
| In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) | | 0 0 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 | 53.6 | | |
| standard deviation | ± 7.26 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 5 | 17 | |
| Male | 9 | 48 | |

End points

End points reporting groups

| | |
|---|-------------------------------------|
| Reporting group title | Placebo (Core Study) |
| Reporting group description: Placebo, was administered orally, once daily for up to 21 days. | |
| Reporting group title | Avatrombopag 10 mg (Core Study) |
| Reporting group description: Avatrombopag 10 mg, was administered orally, once daily, preferably with food for up to 21 days. | |
| Reporting group title | Avatrombopag 20 mg (Core Study) |
| Reporting group description: Avatrombopag 20 mg, was administered orally, once daily, preferably with food for up to 21 days. | |
| Reporting group title | Avatrombopag 30 mg (Core Study) |
| Reporting group description: Avatrombopag 30 mg, was administered orally, once daily, preferably with food for up to 21 days. | |
| Reporting group title | Avatrombopag (Open Label Extension) |
| Reporting group description: Avatrombopag was initiated at a dose of 20 mg, once daily in the open label extension (OLE) period. The avatrombopag dose was titrated up or down in accordance with their individual response within the range of a minimum of 5 mg and a maximum of 50 mg for up to 48 weeks. | |
| Subject analysis set title | Full Analysis Set |
| Subject analysis set type | Full analysis |
| Subject analysis set description: The full analysis set was the group of randomized participants. | |

Primary: Number of participants who achieved Platelet Response (greater than or equal to $100 \times 10^9/L$) by Day 21 of Treatment Period A1 of Core Study

| | |
|--|--|
| End point title | Number of participants who achieved Platelet Response (greater than or equal to $100 \times 10^9/L$) by Day 21 of Treatment Period A1 of Core Study |
| End point description: A responder was defined as a participant having a platelet count of greater than or equal to $100 \times 10^9/L$ by Day 21 starting from an average baseline platelet count of greater than $20 \times 10^9/L$ to less than or equal to $70 \times 10^9/L$. | |
| End point type | Primary |
| End point timeframe: Baseline to Day 21 | |

| End point values | Placebo (Core Study) | Avatrombopag 10 mg (Core Study) | Avatrombopag 20 mg (Core Study) | Avatrombopag 30 mg (Core Study) |
|-----------------------------|----------------------|---------------------------------|---------------------------------|---------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 17 | 16 | 18 | 14 |
| Units: Participants | | | | |
| number (not applicable) | | | | |
| Yes | 1 | 6 | 12 | 9 |
| No | 16 | 10 | 6 | 5 |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Difference of response rate (10 mg) vs placebo |
| Comparison groups | Avatrombopag 10 mg (Core Study) v Placebo (Core Study) |
| Number of subjects included in analysis | 33 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0236 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Median difference (final values) |
| Point estimate | 31.62 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 5.39 |
| upper limit | 57.84 |

| | |
|---|--|
| Statistical analysis title | Difference of response rate (20 mg) vs placebo |
| Comparison groups | Placebo (Core Study) v Avatrombopag 20 mg (Core Study) |
| Number of subjects included in analysis | 35 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0003 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Median difference (final values) |
| Point estimate | 60.78 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 36.3 |
| upper limit | 85.27 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Difference of response rate (30 mg) vs placebo |
| Comparison groups | Placebo (Core Study) v Avatrombopag 30 mg (Core Study) |

| | |
|---|----------------------------------|
| Number of subjects included in analysis | 31 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0003 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Median difference (final values) |
| Point estimate | 58.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 30.92 |
| upper limit | 85.88 |

Secondary: Change from Baseline of Local Platelet Count by Visit during Treatment Period A1 of Core Study

| | |
|------------------------|--|
| End point title | Change from Baseline of Local Platelet Count by Visit during Treatment Period A1 of Core Study |
| End point description: | Missing platelet counts were imputed using last observation carried forward (LOCF) approach for subjects who achieved platelet response at prior visits. |
| End point type | Secondary |
| End point timeframe: | Day 7 and Day 14 |

| End point values | Placebo (Core Study) | Avatrombopag 10 mg (Core Study) | Avatrombopag 20 mg (Core Study) | Avatrombopag 30 mg (Core Study) |
|--------------------------------------|----------------------|---------------------------------|---------------------------------|---------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 17 | 16 | 18 | 14 |
| Units: $\times 10^9/L$ | | | | |
| arithmetic mean (standard deviation) | | | | |
| Day 7 | -0.1 (\pm 7.15) | 19.8 (\pm 17.59) | 26.5 (\pm 22.06) | 30.9 (\pm 37.65) |
| Day 14 | -0.2 (\pm 13.79) | 29.2 (\pm 18.32) | 57.2 (\pm 31.39) | 55.4 (\pm 37.47) |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants who achieved Platelet Count greater than $30 \times 10^9/L$ from Baseline to Day 21 during Treatment Period A1 of Core Study

| | |
|------------------------|---|
| End point title | Number of Participants who achieved Platelet Count greater than $30 \times 10^9/L$ from Baseline to Day 21 during Treatment Period A1 of Core Study |
| End point description: | Blood draws were taken to monitor platelet counts. |
| End point type | Secondary |

End point timeframe:

Baseline to Day 21

| End point values | Placebo (Core Study) | Avatrombopag 10 mg (Core Study) | Avatrombopag 20 mg (Core Study) | Avatrombopag 30 mg (Core Study) |
|-----------------------------|----------------------|---------------------------------|---------------------------------|---------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 17 | 16 | 18 | 14 |
| Units: Participants | | | | |
| number (not applicable) | | | | |
| Yes | 1 | 9 | 16 | 11 |
| No | 16 | 7 | 2 | 3 |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Who Initiated Antiviral Treatment by Day 21 of Period A1 of Core Study

| | |
|-----------------|---|
| End point title | Number of Participants Who Initiated Antiviral Treatment by Day 21 of Period A1 of Core Study |
|-----------------|---|

End point description:

Blood draws were taken to monitor platelet counts during the first 21 days of study treatment. When a platelet count of greater than or equal to $100 \times 10^9/L$ was attained, antiviral treatment was initiated.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to Day 21

| End point values | Placebo (Core Study) | Avatrombopag 10 mg (Core Study) | Avatrombopag 20 mg (Core Study) | Avatrombopag 30 mg (Core Study) |
|-----------------------------|----------------------|---------------------------------|---------------------------------|---------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 17 | 16 | 18 | 14 |
| Units: Participants | | | | |
| number (not applicable) | | | | |
| Yes | 1 | 6 | 13 | 9 |
| No | 16 | 10 | 5 | 5 |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

For each participant, treatment emergent adverse events were collected from the first day of administration of study drug up to 30 days after the last dose of study drug or up to approximately 2.5 years.

Adverse event reporting additional description:

Safety Analysis Set was used which combines data of the Core and Extension Phase and includes subjects who had at least 1 dose of avatrombopag. Placebo treatment arm was excluded since not part of study design for the Extension Phase.

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 16.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-------------------------------------|
| Reporting group title | Avatrombopag (Open Label Extension) |
|-----------------------|-------------------------------------|

Reporting group description:

During the core study, participants were administered a fixed dose of Avatrombopag 10mg, 20mg, or 30mg, orally, once daily, preferably with food for up to 21 days. The participants initiated Open label extension with Avontrombopag 20 mg, once daily. The avotrambopag dose was titrated up or down in accordance with their individual response, within the range of a minimum of 5mg and a maximum of 50 mg for up to 48 weeks.

| | |
|-----------------------|----------------------|
| Reporting group title | Placebo (Core Study) |
|-----------------------|----------------------|

Reporting group description:

Placebo, was given orally for up to 21 days once daily.

| | |
|-----------------------|---------------------------------|
| Reporting group title | Avatrombopag 10 mg (Core Study) |
|-----------------------|---------------------------------|

Reporting group description:

Avatrombopag 10 mg, was administered orally, once daily, preferably with food for up to 21 days.

| | |
|-----------------------|---------------------------------|
| Reporting group title | Avatrombopag 20 mg (Core Study) |
|-----------------------|---------------------------------|

Reporting group description:

Avatrombopag 20 mg, was administered orally, once daily, preferably with food for up to 21 days.

| | |
|-----------------------|---------------------------------|
| Reporting group title | Avatrombopag 30 mg (Core Study) |
|-----------------------|---------------------------------|

Reporting group description:

Avatrombopag 30 mg, was administered orally, once daily, preferably with food for up to 21 days.

| Serious adverse events | Avatrombopag (Open Label Extension) | Placebo (Core Study) | Avatrombopag 10 mg (Core Study) |
|---|-------------------------------------|----------------------|---------------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 13 / 64 (20.31%) | 0 / 17 (0.00%) | 1 / 16 (6.25%) |
| number of deaths (all causes) | 1 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Nervous system disorders | | | |
| Paraesthesia | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 17 (0.00%) | 0 / 16 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 2 / 64 (3.13%) | 0 / 17 (0.00%) | 0 / 16 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Leukopenia | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 17 (0.00%) | 0 / 16 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neutropenia | | | |
| subjects affected / exposed | 2 / 64 (3.13%) | 0 / 17 (0.00%) | 0 / 16 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancytopenia | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 17 (0.00%) | 0 / 16 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Thrombocytopenia | | | |
| subjects affected / exposed | 2 / 64 (3.13%) | 0 / 17 (0.00%) | 1 / 16 (6.25%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 17 (0.00%) | 0 / 16 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Hepatic mass | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 17 (0.00%) | 0 / 16 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|----------------|----------------|----------------|
| Renal and urinary disorders | | | |
| Haematuria | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 17 (0.00%) | 0 / 16 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal failure acute | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 17 (0.00%) | 0 / 16 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Gastroenteritis | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 17 (0.00%) | 0 / 16 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary tract infection | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 17 (0.00%) | 0 / 16 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Hyperglycaemia | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 17 (0.00%) | 0 / 16 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hyperuricaemia | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 17 (0.00%) | 0 / 16 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | Avatrombopag 20 mg (Core Study) | Avatrombopag 30 mg (Core Study) | |
|---|---------------------------------|---------------------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 14 (7.14%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Nervous system disorders | | | |
| Paraesthesia | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 14 (7.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Leukopenia | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neutropenia | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pancytopenia | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Hepatic mass | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|----------------|----------------|--|
| Renal and urinary disorders | | | |
| Haematuria | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal failure acute | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Hyperglycaemia | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyperuricaemia | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 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 | Avatrombopag (Open Label Extension) | Placebo (Core Study) | Avatrombopag 10 mg (Core Study) |
|---|---|-------------------------|------------------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 55 / 64 (85.94%) | 6 / 17 (35.29%) | 11 / 16 (68.75%) |
| Vascular disorders | | | |

| | | | |
|--|------------------|-----------------|-----------------|
| Hot flush | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 17 (0.00%) | 1 / 16 (6.25%) |
| occurrences (all) | 0 | 0 | 1 |
| Pallor | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 17 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 8 / 64 (12.50%) | 0 / 17 (0.00%) | 1 / 16 (6.25%) |
| occurrences (all) | 9 | 0 | 2 |
| Chills | | | |
| subjects affected / exposed | 13 / 64 (20.31%) | 1 / 17 (5.88%) | 3 / 16 (18.75%) |
| occurrences (all) | 14 | 1 | 3 |
| Fatigue | | | |
| subjects affected / exposed | 16 / 64 (25.00%) | 0 / 17 (0.00%) | 1 / 16 (6.25%) |
| occurrences (all) | 17 | 0 | 1 |
| Influenza like illness | | | |
| subjects affected / exposed | 11 / 64 (17.19%) | 2 / 17 (11.76%) | 1 / 16 (6.25%) |
| occurrences (all) | 13 | 2 | 1 |
| Injection site erythema | | | |
| subjects affected / exposed | 6 / 64 (9.38%) | 0 / 17 (0.00%) | 1 / 16 (6.25%) |
| occurrences (all) | 7 | 0 | 1 |
| Irritability | | | |
| subjects affected / exposed | 7 / 64 (10.94%) | 0 / 17 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 7 | 0 | 0 |
| Oedema peripheral | | | |
| subjects affected / exposed | 6 / 64 (9.38%) | 0 / 17 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 6 | 0 | 0 |
| Pyrexia | | | |
| subjects affected / exposed | 9 / 64 (14.06%) | 1 / 17 (5.88%) | 0 / 16 (0.00%) |
| occurrences (all) | 13 | 1 | 0 |
| Chest discomfort | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 17 (0.00%) | 1 / 16 (6.25%) |
| occurrences (all) | 0 | 0 | 1 |
| Feeling cold | | | |

| | | | |
|---|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 17 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Feeling of body temperature change | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 17 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Injection site pruritus | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 17 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pain | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 17 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Reproductive system and breast disorders | | | |
| Spontaneous penile erection | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 17 (0.00%) | 1 / 16 (6.25%) |
| occurrences (all) | 0 | 0 | 1 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 9 / 64 (14.06%) | 0 / 17 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 10 | 0 | 0 |
| Dyspnoea | | | |
| subjects affected / exposed | 4 / 64 (6.25%) | 0 / 17 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 4 | 0 | 0 |
| Dyspnoea exertional | | | |
| subjects affected / exposed | 4 / 64 (6.25%) | 0 / 17 (0.00%) | 1 / 16 (6.25%) |
| occurrences (all) | 5 | 0 | 1 |
| Epistaxis | | | |
| subjects affected / exposed | 6 / 64 (9.38%) | 0 / 17 (0.00%) | 1 / 16 (6.25%) |
| occurrences (all) | 7 | 0 | 1 |
| Productive cough | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 17 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory tract congestion | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 17 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Upper-airway cough syndrome | | | |

| | | | |
|--|---------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 64 (0.00%) 0 | 0 / 17 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Psychiatric disorders | | | |
| Depression | | | |
| subjects affected / exposed | 5 / 64 (7.81%) | 0 / 17 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 6 | 0 | 0 |
| Insomnia | | | |
| subjects affected / exposed | 13 / 64 (20.31%) | 1 / 17 (5.88%) | 1 / 16 (6.25%) |
| occurrences (all) | 13 | 1 | 1 |
| Anxiety | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 17 (5.88%) | 1 / 16 (6.25%) |
| occurrences (all) | 0 | 1 | 1 |
| Food aversion | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 17 (0.00%) | 1 / 16 (6.25%) |
| occurrences (all) | 0 | 0 | 0 |
| Mood altered | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 17 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sleep disorder | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 17 (0.00%) | 1 / 16 (6.25%) |
| occurrences (all) | 0 | 0 | 1 |
| Investigations | | | |
| Staphylococcus test positive | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 17 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Weight decreased | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 17 (5.88%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Injury, poisoning and procedural complications | | | |
| Burns first degree | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 17 (0.00%) | 1 / 16 (6.25%) |
| occurrences (all) | 0 | 0 | 1 |
| Tooth fracture | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 17 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Congenital, familial and genetic disorders | | | |

| | | | |
|--|------------------------|---------------------|---------------------|
| Congenital lymphoedema subjects affected / exposed occurrences (all) | 0 / 64 (0.00%) 0 | 0 / 17 (0.00%) 0 | 1 / 16 (6.25%) 1 |
| Cardiac disorders | | | |
| Palpitations subjects affected / exposed occurrences (all) | 0 / 64 (0.00%) 0 | 1 / 17 (5.88%) 1 | 0 / 16 (0.00%) 0 |
| Tachycardia subjects affected / exposed occurrences (all) | 0 / 64 (0.00%) 0 | 0 / 17 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Nervous system disorders | | | |
| Dizziness subjects affected / exposed occurrences (all) | 4 / 64 (6.25%) 4 | 1 / 17 (5.88%) 1 | 0 / 16 (0.00%) 0 |
| Headache subjects affected / exposed occurrences (all) | 12 / 64 (18.75%) 16 | 1 / 17 (5.88%) 1 | 0 / 16 (0.00%) 0 |
| Disturbance in attention subjects affected / exposed occurrences (all) | 0 / 64 (0.00%) 0 | 0 / 17 (0.00%) 0 | 1 / 16 (6.25%) 1 |
| Dysgeusia subjects affected / exposed occurrences (all) | 0 / 64 (0.00%) 0 | 0 / 17 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Hypoaesthesia subjects affected / exposed occurrences (all) | 0 / 64 (0.00%) 0 | 0 / 17 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Mental impairment subjects affected / exposed occurrences (all) | 0 / 64 (0.00%) 0 | 0 / 17 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Sciatica subjects affected / exposed occurrences (all) | 0 / 64 (0.00%) 0 | 0 / 17 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Somnolence subjects affected / exposed occurrences (all) | 0 / 64 (0.00%) 0 | 0 / 17 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Syncope | | | |

| | | | |
|--|---------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 64 (0.00%) 0 | 0 / 17 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 21 / 64 (32.81%) | 0 / 17 (0.00%) | 2 / 16 (12.50%) |
| occurrences (all) | 26 | 0 | 3 |
| Leukopenia | | | |
| subjects affected / exposed | 14 / 64 (21.88%) | 0 / 17 (0.00%) | 1 / 16 (6.25%) |
| occurrences (all) | 14 | 0 | 2 |
| Lymphopenia | | | |
| subjects affected / exposed | 5 / 64 (7.81%) | 0 / 17 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 6 | 0 | 0 |
| Neutropenia | | | |
| subjects affected / exposed | 20 / 64 (31.25%) | 0 / 17 (0.00%) | 2 / 16 (12.50%) |
| occurrences (all) | 24 | 0 | 2 |
| Ear and labyrinth disorders | | | |
| Vertigo | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 17 (0.00%) | 1 / 16 (6.25%) |
| occurrences (all) | 0 | 0 | 1 |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 6 / 64 (9.38%) | 0 / 17 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 6 | 0 | 0 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 5 / 64 (7.81%) | 1 / 17 (5.88%) | 1 / 16 (6.25%) |
| occurrences (all) | 5 | 1 | 1 |
| Ascites | | | |
| subjects affected / exposed | 6 / 64 (9.38%) | 0 / 17 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 6 | 0 | 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 11 / 64 (17.19%) | 0 / 17 (0.00%) | 1 / 16 (6.25%) |
| occurrences (all) | 12 | 0 | 1 |
| Dyspepsia | | | |
| subjects affected / exposed | 4 / 64 (6.25%) | 0 / 17 (0.00%) | 2 / 16 (12.50%) |
| occurrences (all) | 4 | 0 | 2 |
| Haemorrhoids | | | |

| | | | |
|--|------------------|----------------|-----------------|
| subjects affected / exposed | 4 / 64 (6.25%) | 0 / 17 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 6 | 0 | 0 |
| Nausea | | | |
| subjects affected / exposed | 20 / 64 (31.25%) | 0 / 17 (0.00%) | 3 / 16 (18.75%) |
| occurrences (all) | 22 | 0 | 3 |
| Vomiting | | | |
| subjects affected / exposed | 8 / 64 (12.50%) | 0 / 17 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 10 | 0 | 0 |
| Abdominal distension | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 17 (5.88%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Anal pruritus | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 17 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Aphthous stomatitis | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 17 (5.88%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Constipation | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 17 (5.88%) | 1 / 16 (6.25%) |
| occurrences (all) | 0 | 1 | 1 |
| Flatulence | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 17 (5.88%) | 1 / 16 (6.25%) |
| occurrences (all) | 0 | 1 | 1 |
| Proctalgia | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 17 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hepatobiliary disorders | | | |
| Liver tenderness | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 17 (0.00%) | 1 / 16 (6.25%) |
| occurrences (all) | 0 | 0 | 1 |
| Skin and subcutaneous tissue disorders | | | |
| Pruritus | | | |
| subjects affected / exposed | 15 / 64 (23.44%) | 0 / 17 (0.00%) | 4 / 16 (25.00%) |
| occurrences (all) | 15 | 0 | 4 |
| Rash | | | |

| | | | |
|---|------------------|-----------------|-----------------|
| subjects affected / exposed | 12 / 64 (18.75%) | 2 / 17 (11.76%) | 1 / 16 (6.25%) |
| occurrences (all) | 14 | 2 | 1 |
| Rash macular | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 17 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Renal and urinary disorders | | | |
| Haematuria | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 17 (0.00%) | 1 / 16 (6.25%) |
| occurrences (all) | 0 | 0 | 1 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 17 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Muscle tightness | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 17 (5.88%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Muscular weakness | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 17 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infections and infestations | | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 4 / 64 (6.25%) | 0 / 17 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 4 | 0 | 0 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 4 / 64 (6.25%) | 0 / 17 (0.00%) | 2 / 16 (12.50%) |
| occurrences (all) | 5 | 0 | 2 |
| Abscess limb | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 17 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 17 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 17 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Metabolism and nutrition disorders | | | |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| Hyperuricaemia | | | |
| subjects affected / exposed | 4 / 64 (6.25%) | 1 / 17 (5.88%) | 0 / 16 (0.00%) |
| occurrences (all) | 5 | 1 | 0 |
| Hypertriglyceridaemia | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 17 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypokalaemia | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 17 (5.88%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

| Non-serious adverse events | Avatrombopag 20 mg (Core Study) | Avatrombopag 30 mg (Core Study) | |
|---|---------------------------------|---------------------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 12 / 18 (66.67%) | 11 / 14 (78.57%) | |
| Vascular disorders | | | |
| Hot flush | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 14 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Pallor | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 14 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 2 / 18 (11.11%) | 1 / 14 (7.14%) | |
| occurrences (all) | 2 | 1 | |
| Chills | | | |
| subjects affected / exposed | 3 / 18 (16.67%) | 1 / 14 (7.14%) | |
| occurrences (all) | 3 | 2 | |
| Fatigue | | | |
| subjects affected / exposed | 3 / 18 (16.67%) | 2 / 14 (14.29%) | |
| occurrences (all) | 4 | 2 | |
| Influenza like illness | | | |
| subjects affected / exposed | 4 / 18 (22.22%) | 3 / 14 (21.43%) | |
| occurrences (all) | 4 | 3 | |
| Injection site erythema | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 14 (0.00%) | |
| occurrences (all) | 1 | 0 | |

| | | | |
|---|-----------------|-----------------|--|
| Irritability | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 1 / 14 (7.14%) | |
| occurrences (all) | 1 | 1 | |
| Oedema peripheral | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 14 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Pyrexia | | | |
| subjects affected / exposed | 2 / 18 (11.11%) | 2 / 14 (14.29%) | |
| occurrences (all) | 2 | 2 | |
| Chest discomfort | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 14 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Feeling cold | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 14 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Feeling of body temperature change | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 14 (7.14%) | |
| occurrences (all) | 0 | 1 | |
| Injection site pruritus | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 14 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Pain | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 14 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Reproductive system and breast disorders | | | |
| Spontaneous penile erection | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 14 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 2 / 18 (11.11%) | 3 / 14 (21.43%) | |
| occurrences (all) | 2 | 3 | |
| Dyspnoea | | | |
| subjects affected / exposed | 2 / 18 (11.11%) | 0 / 14 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Dyspnoea exertional | | | |

| | | | |
|------------------------------|----------------|-----------------|--|
| subjects affected / exposed | 1 / 18 (5.56%) | 1 / 14 (7.14%) | |
| occurrences (all) | 1 | 1 | |
| Epistaxis | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 2 / 14 (14.29%) | |
| occurrences (all) | 0 | 2 | |
| Productive cough | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 1 / 14 (7.14%) | |
| occurrences (all) | 1 | 1 | |
| Respiratory tract congestion | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 14 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Upper-airway cough syndrome | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 14 (7.14%) | |
| occurrences (all) | 0 | 1 | |
| Psychiatric disorders | | | |
| Depression | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 14 (7.14%) | |
| occurrences (all) | 0 | 1 | |
| Insomnia | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 3 / 14 (21.43%) | |
| occurrences (all) | 0 | 3 | |
| Anxiety | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 1 / 14 (7.14%) | |
| occurrences (all) | 1 | 1 | |
| Food aversion | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 14 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Mood altered | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 14 (7.14%) | |
| occurrences (all) | 0 | 2 | |
| Sleep disorder | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 14 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Investigations | | | |
| Staphylococcus test positive | | | |

| | | | |
|--|----------------------|----------------------|--|
| subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 1 | 0 / 14 (0.00%) 0 | |
| Weight decreased subjects affected / exposed occurrences (all) | 0 / 18 (0.00%) 0 | 0 / 14 (0.00%) 0 | |
| Injury, poisoning and procedural complications Burns first degree subjects affected / exposed occurrences (all) | 0 / 18 (0.00%) 0 | 0 / 14 (0.00%) 0 | |
| Tooth fracture subjects affected / exposed occurrences (all) | 0 / 18 (0.00%) 0 | 1 / 14 (7.14%) 1 | |
| Congenital, familial and genetic disorders Congenital lymphoedema subjects affected / exposed occurrences (all) | 0 / 18 (0.00%) 0 | 0 / 14 (0.00%) 0 | |
| Cardiac disorders Palpitations subjects affected / exposed occurrences (all) | 0 / 18 (0.00%) 0 | 0 / 14 (0.00%) 0 | |
| Tachycardia subjects affected / exposed occurrences (all) | 0 / 18 (0.00%) 0 | 1 / 14 (7.14%) 1 | |
| Nervous system disorders Dizziness subjects affected / exposed occurrences (all) | 0 / 18 (0.00%) 0 | 1 / 14 (7.14%) 1 | |
| Headache subjects affected / exposed occurrences (all) | 3 / 18 (16.67%) 3 | 2 / 14 (14.29%) 3 | |
| Disturbance in attention subjects affected / exposed occurrences (all) | 0 / 18 (0.00%) 0 | 0 / 14 (0.00%) 0 | |
| Dysgeusia subjects affected / exposed occurrences (all) | 0 / 18 (0.00%) 0 | 1 / 14 (7.14%) 1 | |

| | | | |
|---|----------------------|----------------------|--|
| Hypoaesthesia subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 1 | 1 / 14 (7.14%) 1 | |
| Mental impairment subjects affected / exposed occurrences (all) | 0 / 18 (0.00%) 0 | 1 / 14 (7.14%) 1 | |
| Sciatica subjects affected / exposed occurrences (all) | 0 / 18 (0.00%) 0 | 1 / 14 (7.14%) 1 | |
| Somnolence subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 1 | 0 / 14 (0.00%) 0 | |
| Syncope subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 1 | 0 / 14 (0.00%) 0 | |
| Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) | 2 / 18 (11.11%) 2 | 1 / 14 (7.14%) 1 | |
| Leukopenia subjects affected / exposed occurrences (all) | 3 / 18 (16.67%) 3 | 1 / 14 (7.14%) 1 | |
| Lymphopenia subjects affected / exposed occurrences (all) | 0 / 18 (0.00%) 0 | 1 / 14 (7.14%) 1 | |
| Neutropenia subjects affected / exposed occurrences (all) | 4 / 18 (22.22%) 4 | 2 / 14 (14.29%) 2 | |
| Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all) | 0 / 18 (0.00%) 0 | 0 / 14 (0.00%) 0 | |
| Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all) | 0 / 18 (0.00%) 0 | 0 / 14 (0.00%) 0 | |
| Abdominal pain upper | | | |

| | | |
|-----------------------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 14 (0.00%) |
| occurrences (all) | 1 | 0 |
| Ascites | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 14 (7.14%) |
| occurrences (all) | 0 | 1 |
| Diarrhoea | | |
| subjects affected / exposed | 2 / 18 (11.11%) | 2 / 14 (14.29%) |
| occurrences (all) | 2 | 2 |
| Dyspepsia | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all) | 0 | 0 |
| Haemorrhoids | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 1 / 14 (7.14%) |
| occurrences (all) | 1 | 1 |
| Nausea | | |
| subjects affected / exposed | 4 / 18 (22.22%) | 2 / 14 (14.29%) |
| occurrences (all) | 4 | 2 |
| Vomiting | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 14 (0.00%) |
| occurrences (all) | 1 | 0 |
| Abdominal distension | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all) | 0 | 0 |
| Anal pruritus | | |
| subjects affected / exposed | 2 / 18 (11.11%) | 0 / 14 (0.00%) |
| occurrences (all) | 2 | 0 |
| Aphthous stomatitis | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all) | 0 | 0 |
| Constipation | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 14 (0.00%) |
| occurrences (all) | 1 | 0 |
| Flatulence | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 14 (0.00%) |
| occurrences (all) | 1 | 0 |
| Proctalgia | | |

| | | | |
|--|--|--|--|
| subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 1 | 0 / 14 (0.00%) 0 | |
| Hepatobiliary disorders Liver tenderness subjects affected / exposed occurrences (all) | 0 / 18 (0.00%) 0 | 0 / 14 (0.00%) 0 | |
| Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all) Rash subjects affected / exposed occurrences (all) Rash macular subjects affected / exposed occurrences (all) | 0 / 18 (0.00%) 0 2 / 18 (11.11%) 2 0 / 18 (0.00%) 0 | 2 / 14 (14.29%) 2 1 / 14 (7.14%) 1 1 / 14 (7.14%) 2 | |
| Renal and urinary disorders Haematuria subjects affected / exposed occurrences (all) | 0 / 18 (0.00%) 0 | 0 / 14 (0.00%) 0 | |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Muscle tightness subjects affected / exposed occurrences (all) Muscular weakness subjects affected / exposed occurrences (all) | 0 / 18 (0.00%) 0 0 / 18 (0.00%) 0 0 / 18 (0.00%) 0 | 1 / 14 (7.14%) 1 0 / 14 (0.00%) 0 1 / 14 (7.14%) 1 | |
| Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all) Upper respiratory tract infection | 1 / 18 (5.56%) 1 | 1 / 14 (7.14%) 1 | |

| | | | |
|------------------------------------|----------------|----------------|--|
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 14 (7.14%) | |
| occurrences (all) | 0 | 1 | |
| Abscess limb | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 14 (7.14%) | |
| occurrences (all) | 0 | 1 | |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 14 (7.14%) | |
| occurrences (all) | 0 | 1 | |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 14 (7.14%) | |
| occurrences (all) | 0 | 1 | |
| Metabolism and nutrition disorders | | | |
| Hyperuricaemia | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 1 / 14 (7.14%) | |
| occurrences (all) | 1 | 1 | |
| Hypertriglyceridaemia | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 14 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Hypokalaemia | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 14 (0.00%) | |
| occurrences (all) | 0 | 0 | |

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