



Clinical trial results: A Long-Term Study of SM-13496 in Patients with Bipolar I Disorder. Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2013-003039-31 |
| Trial protocol | LT SK |
| Global end of trial date | 17 February 2018 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 (current) |
| This version publication date | 03 May 2019 |
| First version publication date | 03 May 2019 |

Trial information

Trial identification

| | |
|-----------------------|----------|
| Sponsor protocol code | D1002002 |
|-----------------------|----------|

Additional study identifiers

| | |
|------------------------------------|------------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01986114 |
| WHO universal trial number (UTN) | - |
| Other trial identifiers | JapicCTI: 132319 |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Sumitomo Dainippon Pharma Co. Ltd. |
| Sponsor organisation address | 1-13-1 Kyobashi, Chuo-ku, Tokyo, Japan, 104-8356 |
| Public contact | Drug Development Division, Sumitomo Dainippon Pharmaceutical, cc@ds-pharma.co.jp |
| Scientific contact | Drug Development Division, Sumitomo Dainippon Pharmaceutical, cc@ds-pharma.co.jp |

Notes:

Paediatric regulatory details

| | |
|--|----|
| Is trial part of an agreed paediatric investigation plan (PIP) | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

Results analysis stage

| | |
|--|------------------|
| Analysis stage | Final |
| Date of interim/final analysis | 04 April 2018 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 08 February 2018 |
| Global end of trial reached? | Yes |
| Global end of trial date | 17 February 2018 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The study evaluates the long-term efficacy and safety of SM-13496 in patients with bipolar I disorder.

Protection of trial subjects:

This study was conducted in accordance with the protocol, ICH GCP, local regulations, and the ethical principles that had their origin in the Declaration of Helsinki. The study was conducted in accordance with applicable local law(s) and regulation(s).

Background therapy: -

Evidence for comparator: -

| | |
|---|-----------------|
| Actual start date of recruitment | 29 January 2014 |
| 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 | Japan: 199 |
| Country: Number of subjects enrolled | Malaysia: 11 |
| Country: Number of subjects enrolled | Philippines: 8 |
| Country: Number of subjects enrolled | Russian Federation: 129 |
| Country: Number of subjects enrolled | Taiwan: 7 |
| Country: Number of subjects enrolled | Ukraine: 117 |
| Country: Number of subjects enrolled | Lithuania: 9 |
| Country: Number of subjects enrolled | Slovakia: 15 |
| Worldwide total number of subjects | 495 |
| EEA total number of subjects | 24 |

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) | 474 |
| From 65 to 84 years | 21 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

The completers of the prior study (the placebo-controlled study; D1002001) whose most recent or current episode was depression, and newly recruited Japanese subjects whose most recent or current episode was mania, hypomania, or mixed could be enrolled in the present study.

Pre-assignment

Screening details:

For newly recruited Japanese subjects, the study consisted of the screening phase (1-14 days) and the treatment phase. SM-13496 was administered at a flexible dose (20-120 mg/day) for 28 weeks (outside Japan) or 52 weeks (in Japan).

Period 1

| | |
|------------------------------|--------------------------------|
| Period 1 title | Overall Study (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|-----------|-------------------|
| Arm title | SM-13496 20-120mg |
|-----------|-------------------|

Arm description:

once daily orally

SM-13496 (lurasidone HCl): SM-13496 20-120mg

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | SM-13496 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

SM-13496 20, 40, 60, 80, 100, or 120 mg/day, as 20 mg tablets, were administered orally once daily within 30 minutes after evening meal. For subjects who had completed the prior study, SM-13496 was administered at a dose of 60 mg/day (starting on Day 1) for the first week, and at a flexible dose within a range of 20 to 120 mg/day (starting on Day 8) thereafter. For subjects who had not participated in the prior study, SM-13496 was administered at a dose of 20 mg/day (starting on Day 1) for the first week, and at a flexible dose within a range of 20 to 120 mg/day (starting on Day 8) thereafter.

| Number of subjects in period 1 | SM-13496 20-120mg |
|--------------------------------|-------------------|
| Started | 495 |
| Completed | 339 |
| Not completed | 156 |
| Consent withdrawn by subject | 58 |
| Adverse event, non-fatal | 59 |
| Other reason | 7 |
| Lost to follow-up | 5 |
| Lack of efficacy | 23 |

| | |
|--------------------|---|
| Noncompliance | 3 |
| Protocol deviation | 1 |

Baseline characteristics

Reporting groups

Reporting group title SM-13496 20-120mg

Reporting group description:

once daily orally

SM-13496 (lurasidone HCl): SM-13496 20-120mg

| Reporting group values | SM-13496 20-120mg | Total | |
|--|-------------------|-------|--|
| Number of subjects | 495 | 495 | |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | |
| Newborns (0-27 days) | 0 | 0 | |
| Infants and toddlers (28 days-23 months) | 0 | 0 | |
| Children (2-11 years) | 0 | 0 | |
| Adolescents (12-17 years) | 0 | 0 | |
| Adults (18-64 years) | 474 | 474 | |
| From 65-84 years | 21 | 21 | |
| 85 years and over | 0 | 0 | |
| Age Continuous | | | |
| Units: years | | | |
| arithmetic mean | 42.6 | | |
| standard deviation | ± 12.78 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 259 | 259 | |
| Male | 236 | 236 | |
| Race (NIH/OMB) | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | |
| Asian | 225 | 225 | |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | |
| Black or African American | 0 | 0 | |
| White | 270 | 270 | |
| More than one race | 0 | 0 | |
| Unknown or Not Reported | 0 | 0 | |
| Region of Enrollment | | | |
| Units: Subjects | | | |
| Japan | 199 | 199 | |
| Philippines | 8 | 8 | |
| Taiwan | 7 | 7 | |
| Ukraine | 117 | 117 | |
| Malaysia | 11 | 11 | |
| Slovakia | 15 | 15 | |

| | | | |
|-----------|-----|-----|--|
| Lithuania | 9 | 9 | |
| Russia | 129 | 129 | |

Subject analysis sets

| | |
|----------------------------|---------------------------------------|
| Subject analysis set title | SM-13496 20-120mg (Overall, 28 weeks) |
| Subject analysis set type | Safety analysis |

Subject analysis set description:
once daily orally

SM-13496 (lurasidone HCl): SM-13496 20-120mg flexibly dosed up to 28 weeks

| | |
|----------------------------|-------------------------------------|
| Subject analysis set title | SM-13496 20-120mg (Japan, 52 weeks) |
| Subject analysis set type | Safety analysis |

Subject analysis set description:
once daily orally

SM-13496 (lurasidone HCl): SM-13496 20-120mg flexibly dosed up to 52 weeks

| Reporting group values | SM-13496 20-120mg (Overall, 28 weeks) | SM-13496 20-120mg (Japan, 52 weeks) | |
|---|---------------------------------------|-------------------------------------|--|
| Number of subjects | 495 | 199 | |
| 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 | 42.6 | 41.6 | |
| standard deviation | ± 12.78 | ± 11.97 | |
| Gender categorical Units: Subjects | | | |
| Female | 259 | 97 | |
| Male | 236 | 102 | |
| Race (NIH/OMB) Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | |
| Asian | 225 | 199 | |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | |
| Black or African American | 0 | 0 | |
| White | 270 | 0 | |
| More than one race | 0 | 0 | |
| Unknown or Not Reported | 0 | 0 | |

| | | | |
|----------------------|-----|-----|--|
| Region of Enrollment | | | |
| Units: Subjects | | | |
| Japan | 199 | 199 | |
| Philippines | 8 | 0 | |
| Taiwan | 7 | 0 | |
| Ukraine | 117 | 0 | |
| Malaysia | 11 | 0 | |
| Slovakia | 15 | 0 | |
| Lithuania | 9 | 0 | |
| Russia | 129 | 0 | |

End points

End points reporting groups

| | |
|-----------------------|-------------------|
| Reporting group title | SM-13496 20-120mg |
|-----------------------|-------------------|

Reporting group description:
once daily orally

SM-13496 (lurasidone HCl): SM-13496 20-120mg

| | |
|----------------------------|---------------------------------------|
| Subject analysis set title | SM-13496 20-120mg (Overall, 28 weeks) |
|----------------------------|---------------------------------------|

| | |
|---------------------------|-----------------|
| Subject analysis set type | Safety analysis |
|---------------------------|-----------------|

Subject analysis set description:
once daily orally

SM-13496 (lurasidone HCl): SM-13496 20-120mg flexibly dosed up to 28 weeks

| | |
|----------------------------|-------------------------------------|
| Subject analysis set title | SM-13496 20-120mg (Japan, 52 weeks) |
|----------------------------|-------------------------------------|

| | |
|---------------------------|-----------------|
| Subject analysis set type | Safety analysis |
|---------------------------|-----------------|

Subject analysis set description:
once daily orally

SM-13496 (lurasidone HCl): SM-13496 20-120mg flexibly dosed up to 52 weeks

Primary: Incidence of adverse events (AEs) and adverse drug reactions (ADRs)

| | |
|-----------------|--|
| End point title | Incidence of adverse events (AEs) and adverse drug reactions (ADRs) ^[1] |
|-----------------|--|

End point description:

The number of subjects with at least one adverse events and adverse drug reactions

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:
28, 52 weeks

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The number of subjects with at least one AE or ADR for each preferred term (PT) and system organ class (SOC) were summarized for all subjects. Detailed results are reported in the Adverse events section.

| End point values | SM-13496 20-120mg (Overall, 28 weeks) | SM-13496 20-120mg (Japan, 52 weeks) | | |
|-----------------------------|--|-------------------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 495 | 199 | | |
| Units: subjects | 352 | 169 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from long term study baseline to LOCF Endpoint in the Montgomery-Asberg Depression Rating Scale (MADRS) score

| | |
|-----------------|--|
| End point title | Change from long term study baseline to LOCF Endpoint in the Montgomery-Asberg Depression Rating Scale (MADRS) score |
|-----------------|--|

End point description:

Montgomery-Asberg Depression Rating Scale (MADRS) is a clinician-rated assessment of a subject's level of depression.

The MADRS total score ranges from a minimum of 0 to a maximum of 60. For the MADRS total score, low scores indicate a better outcome and high scores indicate a worse outcome. When change from baseline is considered, a negative (decrease in score) value is considered a better outcome, and a positive (increase in score) value is considered a worse outcome.

The MADRS contains ten (10) items. The total score is computed as the sum of the scores for the 10 items.

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

End point timeframe:

Baseline, 52 weeks and each month

| | | | | |
|--------------------------------------|---------------------------------------|-------------------------------------|--|--|
| End point values | SM-13496 20-120mg (Overall, 28 weeks) | SM-13496 20-120mg (Japan, 52 weeks) | | |
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 494 | 198 | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | -4.4 (\pm 12.09) | 1.1 (\pm 12.58) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from long term study baseline to LOCF Endpoint in the Young Mania Rating Scale (YMRS) total score.

| | |
|-----------------|---|
| End point title | Change from long term study baseline to LOCF Endpoint in the Young Mania Rating Scale (YMRS) total score. |
|-----------------|---|

End point description:

YMRS (Young Mania Rating Scale) is a clinician-rated assessment of the severity of mania in subjects with a diagnosis of bipolar disorder.

The YMRS total score ranges from a minimum of 0 to a maximum of 60. For the YMRS total score, low scores indicate a better outcome and high scores indicate a worse outcome. When change from baseline is considered, a negative (decrease in score) value is considered a better outcome, and a positive (increase in score) value is considered a worse outcome.

The YMRS contains eleven (11) items. The total score is computed as the sum of the scores for the 11 items.

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

End point timeframe:

Baseline, 52 weeks and each month

| End point values | SM-13496 20-120mg (Overall, 28 weeks) | SM-13496 20-120mg (Japan, 52 weeks) | | |
|--------------------------------------|---------------------------------------|-------------------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 494 | 198 | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | -1.0 (± 4.54) | -2.0 (± 6.73) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Rate of recurrence/relapse of any mood event from clinical stability of bipolar disorder.

| | |
|--|---|
| End point title | Rate of recurrence/relapse of any mood event from clinical stability of bipolar disorder. |
| End point description: The number of subjects who experienced recurrence/relapse of any mood event from clinical stability of bipolar disorder. | |
| End point type | Secondary |
| End point timeframe: Baseline to 52 weeks | |

| End point values | SM-13496 20-120mg (Overall, 28 weeks) | SM-13496 20-120mg (Japan, 52 weeks) | | |
|-----------------------------|---------------------------------------|-------------------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 495 | 199 | | |
| Units: subjects | | | | |
| With relapse or recurrence | 14 | 18 | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse event data was collected for 28 weeks (outside Japan) and 52 weeks (Japan).

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 19.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|---------------------------------------|
| Reporting group title | SM-13496 20-120mg (Overall, 28 weeks) |
|-----------------------|---------------------------------------|

Reporting group description:

once daily orally

SM-13496 (lurasidone HCl): SM-13496 20-120mg flexibly dosed up to 28 weeks

| | |
|-----------------------|-------------------------------------|
| Reporting group title | SM-13496 20-120mg (Japan, 52 weeks) |
|-----------------------|-------------------------------------|

Reporting group description:

once daily orally

SM-13496 (lurasidone HCl): SM-13496 20-120mg flexibly dosed up to 52 weeks

| Serious adverse events | SM-13496 20-120mg (Overall, 28 weeks) | SM-13496 20-120mg (Japan, 52 weeks) | |
|---|---------------------------------------|-------------------------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 19 / 495 (3.84%) | 12 / 199 (6.03%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Investigations | | | |
| Blood potassium decreased | | | |
| subjects affected / exposed | 1 / 495 (0.20%) | 1 / 199 (0.50%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Glucose urine present | | | |
| subjects affected / exposed | 1 / 495 (0.20%) | 1 / 199 (0.50%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Weight decreased | | | |
| subjects affected / exposed | 1 / 495 (0.20%) | 1 / 199 (0.50%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|-----------------|-----------------|--|
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Uterine cancer | | | |
| subjects affected / exposed | 0 / 495 (0.00%) | 1 / 199 (0.50%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Pelvic fracture | | | |
| subjects affected / exposed | 1 / 495 (0.20%) | 1 / 199 (0.50%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Akathisia | | | |
| subjects affected / exposed | 1 / 495 (0.20%) | 1 / 199 (0.50%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychomotor hyperactivity | | | |
| subjects affected / exposed | 1 / 495 (0.20%) | 1 / 199 (0.50%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Disease progression | | | |
| subjects affected / exposed | 8 / 495 (1.62%) | 3 / 199 (1.51%) | |
| occurrences causally related to treatment / all | 2 / 8 | 2 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| Alcoholism | | | |
| subjects affected / exposed | 1 / 495 (0.20%) | 1 / 199 (0.50%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hallucination, auditory | | | |
| subjects affected / exposed | 1 / 495 (0.20%) | 0 / 199 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hallucination, visual | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 495 (0.20%) | 0 / 199 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mania | | | |
| subjects affected / exposed | 1 / 495 (0.20%) | 1 / 199 (0.50%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Suicidal ideation | | | |
| subjects affected / exposed | 1 / 495 (0.20%) | 0 / 199 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Suicide attempt | | | |
| subjects affected / exposed | 3 / 495 (0.61%) | 1 / 199 (0.50%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Lumbar spinal stenosis | | | |
| subjects affected / exposed | 1 / 495 (0.20%) | 1 / 199 (0.50%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Urinary tract infection | | | |
| subjects affected / exposed | 1 / 495 (0.20%) | 0 / 199 (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 | | | |
| Diabetes mellitus | | | |
| subjects affected / exposed | 0 / 495 (0.00%) | 1 / 199 (0.50%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lactic acidosis | | | |
| subjects affected / exposed | 0 / 495 (0.00%) | 1 / 199 (0.50%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | SM-13496 20-120mg (Overall, 28 weeks) | SM-13496 20-120mg (Japan, 52 weeks) | |
|---|---------------------------------------|-------------------------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 250 / 495 (50.51%) | 137 / 199 (68.84%) | |
| Investigations | | | |
| Weight increased | | | |
| subjects affected / exposed | 31 / 495 (6.26%) | 17 / 199 (8.54%) | |
| occurrences (all) | 31 | 17 | |
| Nervous system disorders | | | |
| Akathisia | | | |
| subjects affected / exposed | 91 / 495 (18.38%) | 60 / 199 (30.15%) | |
| occurrences (all) | 104 | 64 | |
| Headache | | | |
| subjects affected / exposed | 37 / 495 (7.47%) | 16 / 199 (8.04%) | |
| occurrences (all) | 46 | 19 | |
| Parkinsonism | | | |
| subjects affected / exposed | 34 / 495 (6.87%) | 15 / 199 (7.54%) | |
| occurrences (all) | 43 | 25 | |
| Somnolence | | | |
| subjects affected / exposed | 41 / 495 (8.28%) | 24 / 199 (12.06%) | |
| occurrences (all) | 44 | 24 | |
| Dystonia | | | |
| subjects affected / exposed | 13 / 495 (2.63%) | 10 / 199 (5.03%) | |
| occurrences (all) | 15 | 11 | |
| General disorders and administration site conditions | | | |
| Disease progression | | | |
| subjects affected / exposed | 16 / 495 (3.23%) | 10 / 199 (5.03%) | |
| occurrences (all) | 17 | 11 | |
| Gastrointestinal disorders | | | |
| Nausea | | | |

| | | | |
|--|-------------------------|-------------------------|--|
| subjects affected / exposed occurrences (all) | 35 / 495 (7.07%) 38 | 24 / 199 (12.06%) 25 | |
| Diarrhoea subjects affected / exposed occurrences (all) | 14 / 495 (2.83%) 15 | 10 / 199 (5.03%) 11 | |
| Vomiting subjects affected / exposed occurrences (all) | 17 / 495 (3.43%) 21 | 13 / 199 (6.53%) 13 | |
| Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all) | 51 / 495 (10.30%) 63 | 53 / 199 (26.63%) 72 | |

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