



Clinical trial results:

A Multicenter, Open-Label, Flexible-Dose Extension Study of Lurasidone Adjunctive to Lithium or Divalproex in Subjects with Bipolar I Disorder (PERSIST EXTENSION STUDY)

Summary

| | |
|--------------------------|-------------------|
| EudraCT number | 2011-004789-14 |
| Trial protocol | HU CZ SK BG PL HR |
| Global end of trial date | 01 July 2015 |

Results information

| | |
|--------------------------------|----------------|
| Result version number | v1 (current) |
| This version publication date | 19 August 2016 |
| First version publication date | 19 August 2016 |

Trial information

Trial identification

| | |
|-----------------------|----------|
| Sponsor protocol code | D1050308 |
|-----------------------|----------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01575561 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Sunovion Pharmaceuticals Inc. |
| Sponsor organisation address | One Bridge Plaza Suite 510, Fort Lee, New Jersey, United States, NJ 07024 |
| Public contact | Rob Goldman, Sunovion Pharmaceuticals Inc., +1 201-228-8319, Robert.Goldman@sunovion.com |
| Scientific contact | Rob Goldman, Sunovion Pharmaceuticals Inc., +1 201-228-8319, Robert.Goldman@sunovion.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 | 27 May 2016 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 01 July 2015 |
| Global end of trial reached? | Yes |
| Global end of trial date | 01 July 2015 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The main objective of the trial was to evaluate the longer term safety, tolerability, and effectiveness of lurasidone, flexibly dosed at 20, 40, 60 or 80 mg/day in subjects with bipolar disorder who had either completed double-blind treatment or experienced a protocol-specified recurrence of any mood event during the Double-blind Phase in Study D1050296 (EudraCT No.: 2011-000986-10).

Protection of trial subjects:

The study was conducted according to the protocol, International Conference on Harmonisation (ICH) Good Clinical Practice (GCP), ICH guidelines, and the ethical principles that have their origin in the Declaration of Helsinki. The study was conducted in accordance with applicable local law(s) and regulation(s).

Use of nonprescription pain medications (eg, aspirin) was allowed during the study provided these medications did not have a propensity for psychotropic effects and did not interfere with the evaluation of study medication.

Background therapy:

Prior and Concomitant Therapy:

Potent inducers or inhibitors of the CYP3A4 enzyme system and any medications that consistently prolong the QTc interval were prohibited during the study. The use of herbal supplements or other complementary or alternative medications was not permitted during the study.

Initiation of new psychotherapeutic interventions was permitted during the study. Subjects who participated in ongoing psychotherapy treatment during Study D1050296 were permitted to continue it during the study.

Psychotropic Medications:

Subjects may have been treated with benzodiazepines, or antidepressants (no CYP3A4 inhibitors/inducers), at the discretion of Investigator (Inv.) Monoamine oxidase (MAO) inhibitors and other antipsychotic medications (exception: lurasidone) were prohibited.

Benzotropine (up to 6 mg/day) was permitted for movement disorders: if it was not available or if inadequate response or intolerability, the following medications were used to treat acute extrapyramidal symptoms (EPS): biperiden (up to 16 mg/day), trihexyphenidyl (up to 15 mg/day) or diphenhydramine (up to 100 mg/day). Propranolol (up to 120 mg/day) was permitted as needed for akathisia.

Use of lorazepam, or equivalent benzodiazepine, was permitted at the discretion of Inv. (up to 6 mg/day) for intolerable anxiety/agitation. Oral benzodiazepines or rapid-acting IM injection were used sparingly (only when clinically required per Investigator judgment). Zolpidem (≤ 10 mg/day), zolpidem controlled release (≤ 12.5 mg/day), eszopiclone (≤ 3 mg/day), zaleplon (≤ 20 mg/day), and temazepam (≤ 30 mg/day) may have been used at bedtime for insomnia. Hypnotic agents were used max. once nightly and not in combination.

If lorazepam or zolpidem or other medications not available, a similar agent at equivalent doses was permitted as specified by the Medical Monitor (MM) and/or the Operations Manual. Opiates were allowed rarely for a limited period of time with prior authorization from MM.

Evidence for comparator:

Not applicable (Intervention Model: Single Group Assignment)

| | |
|---|--------------|
| Actual start date of recruitment | 12 June 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 | France: 8 |
| Country: Number of subjects enrolled | Hungary: 21 |
| Country: Number of subjects enrolled | Japan: 13 |
| Country: Number of subjects enrolled | Poland: 37 |
| Country: Number of subjects enrolled | Russian Federation: 42 |
| Country: Number of subjects enrolled | Serbia: 35 |
| Country: Number of subjects enrolled | Slovakia: 5 |
| Country: Number of subjects enrolled | Chile: 17 |
| Country: Number of subjects enrolled | Czech Republic: 40 |
| Country: Number of subjects enrolled | United States: 95 |
| Country: Number of subjects enrolled | Argentina: 30 |
| Country: Number of subjects enrolled | Bulgaria: 34 |
| Worldwide total number of subjects | 377 |
| EEA total number of subjects | 145 |

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) | 360 |
| From 65 to 84 years | 17 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Subjects who had either completed double-blind treatment or experienced a protocol-specified recurrence of any mood event during the Double-blind Phase in study D1050296 had the option to participate in this study. Subjects who had at least entered the Open-label Phase of Study D1050296 when the Sponsor stopped the study were also eligible.

Pre-assignment

Screening details:

Of the 428 subjects who either completed the double-blind phase of the D1050296 study or had a recurrence of a mood event, 372 continued into this extension study: a total of 5 subjects who were receiving open-label study medication when the D1050296 study was stopped by the Sponsor also continued into this study.

338 subjects completed this study

Period 1

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

Blinding implementation details:

Not applicable: Open-Label Extension Study

Arms

| | |
|--|--|
| Arm title | Lurasidone + lithium / valproate |
| Arm description: - | |
| Arm type | Experimental |
| Investigational medicinal product name | Lurasidone Hydrochloride |
| Investigational medicinal product code | SM-13496 |
| Other name | CAS Number: 367514-88-3, EV Substance code: SUB34204 |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects were initially treated with open-label lurasidone 40 mg/day (Day 1). Dose adjustment of study drug (20, 40, 60 or 80 mg/day) was to occur at the regularly scheduled visits and in increments/decrements of 1 dose level. If dose adjustment was required in between regular study visits, the subject came in for an unscheduled visit and returned all used/unused medication kits at the time of dose adjustment. Dose reductions for tolerability or safety purposes were permitted to occur starting on the second day of extension study treatment (Day 2). These dose reductions may have occurred more frequently than the regular study visits and at more than 1 dose level at a time (maximum of 2 dose levels at a time) to optimize effectiveness and tolerability, based on Investigator judgment. Subjects were treated with open-label lithium or divalproex for the duration of the study and were treated with the same drug (either lithium or divalproex) they received in the D1050296 study.

| | |
|---------------------------------------|----------------------------------|
| Number of subjects in period 1 | Lurasidone + lithium / valproate |
| Started | 377 |
| Completed | 338 |
| Not completed | 39 |
| Consent withdrawn by subject | 11 |
| Administrative | 1 |

| | |
|--------------------------|---|
| Adverse event, non-fatal | 9 |
| Lost to follow-up | 6 |
| Lack of efficacy | 8 |
| Protocol deviation | 4 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|----------------------------------|
| Reporting group title | Lurasidone + lithium / valproate |
|-----------------------|----------------------------------|

Reporting group description: -

| Reporting group values | Lurasidone + lithium / valproate | Total | |
|----------------------------------|----------------------------------|-------|--|
| Number of subjects | 377 | 377 | |
| Age categorical | | | |
| Units: Subjects | | | |
| Between 18 and 64 years | 360 | 360 | |
| ≥ 65 years | 17 | 17 | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 45.5 | | |
| standard deviation | ± 12.27 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 206 | 206 | |
| Male | 171 | 171 | |
| Race | | | |
| Units: Subjects | | | |
| White | 327 | 327 | |
| Black or African American | 28 | 28 | |
| Asian | 15 | 15 | |
| American Indian or Alaska Native | 1 | 1 | |
| Other | 6 | 6 | |
| Ethnicity | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 62 | 62 | |
| Not Hispanic or Latino | 315 | 315 | |
| Region on Enrollment | | | |
| Units: Subjects | | | |
| North America/ US | 95 | 95 | |
| South America/ Argentina | 30 | 30 | |
| Europe/ Bulgaria | 34 | 34 | |
| South America/ Chile | 17 | 17 | |
| Europe/ Czech Republic | 40 | 40 | |
| Europe/ France | 8 | 8 | |
| Europe/ Hungary | 21 | 21 | |
| Asia/ Japan | 13 | 13 | |
| Europe/ Poland | 37 | 37 | |
| Europe/ Russia | 42 | 42 | |
| Europe/ Serbia | 35 | 35 | |
| Europe/ Slovakia | 5 | 5 | |

End points

End points reporting groups

| | |
|--------------------------------|----------------------------------|
| Reporting group title | Lurasidone + lithium / valproate |
| Reporting group description: - | |

Primary: Number of subjects with treatment emergent AEs, SAEs, and TEAEs leading to discontinuation

| | |
|-----------------|---|
| End point title | Number of subjects with treatment emergent AEs, SAEs, and TEAEs leading to discontinuation ^[1] |
|-----------------|---|

End point description:

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

End point timeframe:

During 12 weeks treatment period

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: This is the extension study of Study D1050296 (EudraCT No.: 2011-000986-10): every subject took lurasidone during this extension study, and thus only one treatment group is reported and no statistical analyses could be performed.

| End point values | Lurasidone + lithium / valproate | | | |
|---|----------------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 377 | | | |
| Units: Subjects | | | | |
| At least 1 TEAE | 155 | | | |
| At least 1 TEAE potentially related to study drug | 69 | | | |
| Deaths | 0 | | | |
| At least 1 treatment-emergent SAE (TESAE) | 14 | | | |
| At least 1 TESAE related to study drug | 1 | | | |
| At least one TEAE leading to discontinuation | 9 | | | |

| | |
|----------------------------|---|
| Attachments (see zip file) | DB750001/Cardiac Safety Data Review Meeting Summary - |
|----------------------------|---|

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to Week 12 (LOCF) in the MADRS total score

| | |
|-----------------|---|
| End point title | Change from baseline to Week 12 (LOCF) in the MADRS total score |
|-----------------|---|

End point description:

The MADRS consists of 10 items, each rated on a Likert scale, from 0="Normal" to 6="Most Severe".

The MADRS total score is calculated as the sum of the 10 items. The MADRS total score ranges from 0 to 60. Higher scores are associated with greater severity.

| | |
|--------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Week 12 (LOCF) | |

| | | | | |
|--------------------------------------|----------------------------------|--|--|--|
| End point values | Lurasidone + lithium / valproate | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 375 | | | |
| Units: Score | | | | |
| arithmetic mean (standard deviation) | -1.9 (± 6.82) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to Week 12 (LOCF) in the CGI-BP-S score

| | |
|-----------------|--|
| End point title | Change from baseline to Week 12 (LOCF) in the CGI-BP-S score |
|-----------------|--|

End point description:

The CGI-BP-S overall score is a single value, clinician-rated assessment of overall bipolar illness severity and ranges from 1= 'Normal, not at all ill' to 7= 'Among the most extremely ill patients'. A higher score is associated with greater illness severity.

The CGI-BP-S mania score is a single value, clinician-rated assessment of mania illness severity and ranges from 1= 'Normal, not at all ill' to 7= 'Among the most extremely ill patients'. A higher score is associated with greater illness severity.

The CGI-BP-S depression score is a single value, clinician-rated assessment of depression illness severity and ranges from 1= 'Normal, not at all ill' to 7= 'Among the most extremely ill patients'. A higher score is associated with greater illness severity.

| | |
|--------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Week 12 (LOCF) | |

| | | | | |
|--------------------------------------|----------------------------------|--|--|--|
| End point values | Lurasidone + lithium / valproate | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 375 | | | |
| Units: Score | | | | |
| arithmetic mean (standard deviation) | | | | |
| CGI-BP-S Overall Score | -0.31 (± 1.068) | | | |
| CGI-BP-S Mania Score | -0.13 (± 0.807) | | | |
| CGI-BP-S Depression Score | -0.27 (± 0.969) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to Week 12 (LOCF) in the YMRS total score

| | |
|-----------------|--|
| End point title | Change from baseline to Week 12 (LOCF) in the YMRS total score |
|-----------------|--|

End point description:

The YMRS is an 11 item instrument used to assess the severity of mania in subjects with a diagnosis of bipolar disorder. Ratings are based on patient self reporting, combined with clinician observation (accorded greater score). The YMRS total score is calculated as the sum of the 11 items. The YMRS total score ranges from 0 to 60. Higher scores are associated with greater severity of mania.

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

End point timeframe:

Baseline, Week 12 (LOCF)

| | | | | |
|--------------------------------------|----------------------------------|--|--|--|
| End point values | Lurasidone + lithium / valproate | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 375 | | | |
| Units: Score | | | | |
| arithmetic mean (standard deviation) | -1 (± 5.17) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to Week 12 (LOCF) in the QIDS-SR16 total score

| | |
|-----------------|---|
| End point title | Change from baseline to Week 12 (LOCF) in the QIDS-SR16 total score |
|-----------------|---|

End point description:

The QIDS-SR16 is a 16-item self-report measure of depressive symptomatology which uses a computerized assessment interface for administration. The scoring system for the QIDS-SR16 converts responses to 16 separate items into nine DSM-IV symptom criterion domains. The nine domains comprise: depressed mood (Item 5); concentration/decision making (Item 10); self outlook (Item 11); suicidal ideation (Item 12); decreased interest (Item 13); decreased energy (Item 14); sleep disturbance (initial, middle, and late insomnia or hypersomnia) (highest score of Items 1 to 4); appetite/weight disturbance (highest score of Items 6 to 9); and psychomotor disturbance (highest score of Items 15 and 16). The QIDS-SR16 total score is calculated as the sum of the 9 domain scores. The QIDS-SR16 total score ranges from 0 to 27 with a high score indicating more severe symptoms.

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

End point timeframe:

Baseline, Week 12 (LOCF)

| | | | | |
|--------------------------------------|----------------------------------|--|--|--|
| End point values | Lurasidone + lithium / valproate | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 351 | | | |
| Units: Score | | | | |
| arithmetic mean (standard deviation) | -1 (\pm 3.23) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to Week 12 (LOCF) in the PANSS-P score

| | |
|--|---|
| End point title | Change from baseline to Week 12 (LOCF) in the PANSS-P score |
| End point description: | |
| The PANSS-P is a subset of items in the PANSS, an interview-based measure of the severity of psychopathology in adults with psychotic disorders. The measure contains seven questions to assess delusions, conceptual disorganization, hallucinations behavior, excitement, grandiosity, suspiciousness/persecution, and hostility. An anchored Likert scale from 1-7, where values of 2 and above indicate the presence of progressively more severe symptoms, is used to score each item. The PANSS-P subscale score is the sum of the 7 items and ranges from 7 through 49. A higher score is associated with greater illness severity. | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Week 12 (LOCF) | |

| | | | | |
|--------------------------------------|----------------------------------|--|--|--|
| End point values | Lurasidone + lithium / valproate | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 359 | | | |
| Units: Score | | | | |
| arithmetic mean (standard deviation) | -0.2 (\pm 1.16) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to Week 12 (LOCF) in the SDS total score

| | | |
|--|---|--|
| End point title | Change from baseline to Week 12 (LOCF) in the SDS total score | |
| End point description: | | |
| The SDS is a composite of three self-rated items designed to measure the extent to which three major | | |

sectors in the patient's life are impaired by depressive symptoms. The SDS total score is calculated as the sum of the 3 items. The SDS total score ranges from 0 to 30. Higher scores are associated with greater severity of global functional impairments. If a subject has not worked/studied at all during the past week for reasons unrelated to the disorder, the SDS total score will be set to missing.

| | |
|--------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Week 12 (LOCF) | |

| | | | | |
|--------------------------------------|----------------------------------|--|--|--|
| End point values | Lurasidone + lithium / valproate | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 297 | | | |
| Units: Score | | | | |
| arithmetic mean (standard deviation) | -1.4 (\pm 5.98) | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

12 weeks

Adverse event reporting additional description:

Safety population was used for all safety analyses and summaries. Summaries of adverse events were limited to treatment-emergent adverse events, which were defined as adverse events with a start date on or after the first study dose date, through 7 days post last study dose date for non-serious adverse events (AE), or 14 days for serious AEs (SAEs)

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 15.0 |
|--------------------|------|

Reporting groups

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|-----------------------|----------------------------------|
| Reporting group title | Lurasidone + lithium / valproate |
|-----------------------|----------------------------------|

Reporting group description: -

| Serious adverse events | Lurasidone + lithium / valproate | | |
|---|----------------------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 14 / 377 (3.71%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Basal cell carcinoma | | | |
| subjects affected / exposed | 1 / 377 (0.27%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Injury, poisoning and procedural complications | | | |
| Craniocerebral injury | | | |
| subjects affected / exposed | 1 / 377 (0.27%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Femur fracture | | | |
| subjects affected / exposed | 1 / 377 (0.27%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Intentional overdose | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 377 (0.27%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Overdose | | | |
| subjects affected / exposed | 1 / 377 (0.27%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vascular disorders | | | |
| Accelerated hypertension | | | |
| subjects affected / exposed | 1 / 377 (0.27%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood and lymphatic system disorders | | | |
| Anaemia megaloblastic | | | |
| subjects affected / exposed | 1 / 377 (0.27%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Psychiatric disorders | | | |
| Depression | | | |
| subjects affected / exposed | 4 / 377 (1.06%) | | |
| occurrences causally related to treatment / all | 1 / 4 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Mania | | | |
| subjects affected / exposed | 2 / 377 (0.53%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Bipolar disorder | | | |
| subjects affected / exposed | 1 / 377 (0.27%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Emotional distress | | | |
| subjects affected / exposed | 1 / 377 (0.27%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|-----------------|--|--|
| Panic attack | | | |
| subjects affected / exposed | 1 / 377 (0.27%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Persecutory delusion | | | |
| subjects affected / exposed | 1 / 377 (0.27%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

Frequency threshold for reporting non-serious adverse events: 2 %

| Non-serious adverse events | Lurasidone + lithium / valproate | | |
|---|----------------------------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 51 / 377 (13.53%) | | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 15 / 377 (3.98%) | | |
| occurrences (all) | 18 | | |
| Akathisia | | | |
| subjects affected / exposed | 12 / 377 (3.18%) | | |
| occurrences (all) | 13 | | |
| Gastrointestinal disorders | | | |
| Nausea | | | |
| subjects affected / exposed | 8 / 377 (2.12%) | | |
| occurrences (all) | 9 | | |
| Psychiatric disorders | | | |
| Insomnia | | | |
| subjects affected / exposed | 11 / 377 (2.92%) | | |
| occurrences (all) | 12 | | |
| Infections and infestations | | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 13 / 377 (3.45%) | | |
| occurrences (all) | 14 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---------------|--|
| 19 March 2012 | Protocol Amendment 1, 19 March 2012, implemented the following changes: <ul style="list-style-type: none">- Data and Safety Monitoring Board (DSMB) did not monitor this study, therefore this information was removed.- Contact information was updated.- Because Concomitant medication review and Adverse event (AE) monitoring were performed in the last visit of Study D1050296, these assessments were removed from the Visit 1E (Day 1) visit.- Wording concerning concomitant psychotropic medications was updated for clarity.- Collection of the Health Services Utilization Questionnaire (HSUQ) assessment was updated. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

| |
|------|
| None |
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Notes: