



Clinical trial results:

A PHASE 1 OPEN-LABEL, MULTICENTER, SINGLE AND MULTIPLE ASCENDING DOSE STUDY TO EVALUATE PHARMACOKINETICS, SAFETY, AND TOLERABILITY OF LURASIDONE IN SUBJECTS 6 TO 17 YEARS OLD WITH SCHIZOPHRENIA SPECTRUM, BIPOLAR SPECTRUM, AUTISTIC SPECTRUM DISORDER, OR OTHER PSYCHIATRIC DISORDERS

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2013-001523-39 |
| Trial protocol | Outside EU/EEA |
| Global end of trial date | 06 May 2013 |

Results information

| | |
|--------------------------------|---|
| Result version number | v2 (current) |
| This version publication date | 11 July 2016 |
| First version publication date | 30 May 2014 |
| Version creation reason | • Correction of full data set Updating editorial discrepancies |

Trial information

Trial identification

| | |
|-----------------------|----------|
| Sponsor protocol code | D1050300 |
|-----------------------|----------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01620060 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Sunovion Pharmaceuticals Inc. |
| Sponsor organisation address | One Bridge Plaza North Suite 510, Fort Lee, NJ, United States, 07024 |
| Public contact | Yu-Yuan Chiu, Sunovion Pharmaceuticals Inc., 001 201228-8178, Yu-Yuan.Chiu@Sunovion.com |
| Scientific contact | Yu-Yuan Chiu, Sunovion Pharmaceuticals Inc., 001 201228-8178, Yu-Yuan.Chiu@Sunovion.com |

Notes:

Paediatric regulatory details

| | |
|--|---------------------|
| Is trial part of an agreed paediatric investigation plan (PIP) | Yes |
| EMA paediatric investigation plan number(s) | EMA-001230-PIP01-11 |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No | Yes |

| |
|--------------------------------|
| 1901/2006 apply to this trial? |
|--------------------------------|

Notes:

Results analysis stage

| | |
|--|--------------|
| Analysis stage | Final |
| Date of interim/final analysis | 04 June 2013 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 06 May 2013 |
| Global end of trial reached? | Yes |
| Global end of trial date | 06 May 2013 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To characterize the pharmacokinetics (PK) and assess safety and tolerability of single and multiple oral doses of 20, 40, 80, 120, or 160 mg/day lurasidone hydrochloride (HCl) in subjects 6 to 17 years old with schizophrenia spectrum, bipolar spectrum, autistic spectrum disorder, or other psychiatric disorders

Protection of trial subjects:

None

Background therapy: -

Evidence for comparator: -

| | |
|---|--------------|
| Actual start date of recruitment | 19 June 2012 |
| 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 | United States: 105 |
| Worldwide total number of subjects | 105 |
| EEA total number of subjects | 0 |

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) | 49 |
| Adolescents (12-17 years) | 56 |
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |

| | |
|-------------------|---|
| 85 years and over | 0 |
|-------------------|---|

Subject disposition

Recruitment

Recruitment details:

A Phase I, open-label, multicenter, United States only study. Pediatric subjects with schizophrenia spectrum, bipolar spectrum, autistic spectrum or other psychiatric disorders were enrolled. Study started enrollment on 19Jun2012.

Pre-assignment

Screening details:

All subjects received a single dose of lurasidone hydrochloride (HCl) followed by a 2-day washout period, then once-daily dosing of lurasidone hydrochloride for 7 days (20 mg through 120 mg lurasidone HCl cohort) or 9 days (160 mg lurasidone HCl cohort)

Period 1

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

Arms

| | |
|------------------------------|---------------------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | 20 mg Lurasidone hydrochloride cohort |

Arm description:

20 mg Lurasidone hydrochloride cohort

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

Dosage and administration details:

once daily

| | |
|------------------|--------------------------------------|
| Arm title | 40 mg cohort Lurasidone hydrochlorid |
|------------------|--------------------------------------|

Arm description:

40 mg Lurasidone hydrochloride cohort

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

Dosage and administration details:

once daily

| | |
|------------------|---------------------------------------|
| Arm title | 80 mg Lurasidone hydrochloride cohort |
|------------------|---------------------------------------|

Arm description:

80 mg Lurasidone hydrochloride cohort

| | |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

| | |
|--|--|
| Investigational medicinal product name | Lurasidone hydrochloride |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |
| Dosage and administration details: | |
| once daily | |
| Arm title | 120 mg Lurasidone hydrochloride cohort |
| Arm description: | |
| 120 mg Lurasidone hydrochloride cohort | |
| Arm type | Experimental |
| Investigational medicinal product name | Lurasidone hydrochloride |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |
| Dosage and administration details: | |
| once daily | |
| Arm title | 160 mg Lurasidone hydrochloride cohort |
| Arm description: | |
| 160 mg Lurasidone hydrochloride cohort | |
| Arm type | Experimental |
| Investigational medicinal product name | Lurasidone hydrochloride |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |
| Dosage and administration details: | |
| once daily | |

| Number of subjects in period 1 | 20 mg Lurasidone hydrochloride cohort | 40 mg cohort Lurasidone hydrochlorid | 80 mg Lurasidone hydrochloride cohort |
|--------------------------------------|---------------------------------------|--------------------------------------|---------------------------------------|
| | | | |
| Started | 20 | 25 | 19 |
| Completed | 19 | 21 | 18 |
| Not completed | 1 | 4 | 1 |
| Consent withdrawn by subject | - | - | - |
| Did not comply with Study procedures | 1 | - | - |
| Adverse event, non-fatal | - | 3 | 1 |
| family emergency | - | - | - |
| Per Sponsor Decision | - | - | - |
| Protocol deviation | - | 1 | - |

| Number of subjects in period 1 | 120 mg Lurasidone hydrochloride cohort | 160 mg Lurasidone hydrochloride cohort |
|--------------------------------|--|--|
| Started | 25 | 16 |

| | | |
|--------------------------------------|----|----|
| Completed | 18 | 14 |
| Not completed | 7 | 2 |
| Consent withdrawn by subject | - | 1 |
| Did not comply with Study procedures | - | - |
| Adverse event, non-fatal | 4 | 1 |
| family emergency | 1 | - |
| Per Sponsor Decision | 2 | - |
| Protocol deviation | - | - |

Baseline characteristics

Reporting groups

| | |
|------------------------------|--|
| Reporting group title | 20 mg Lurasidone hydrochloride cohort |
| Reporting group description: | 20 mg Lurasidone hydrochloride cohort |
| Reporting group title | 40 mg cohort Lurasidone hydrochlorid |
| Reporting group description: | 40 mg Lurasidone hydrochloride cohort |
| Reporting group title | 80 mg Lurasidone hydrochloride cohort |
| Reporting group description: | 80 mg Lurasidone hydrochloride cohort |
| Reporting group title | 120 mg Lurasidone hydrochloride cohort |
| Reporting group description: | 120 mg Lurasidone hydrochloride cohort |
| Reporting group title | 160 mg Lurasidone hydrochloride cohort |
| Reporting group description: | 160 mg Lurasidone hydrochloride cohort |

| Reporting group values | 20 mg Lurasidone hydrochloride cohort | 40 mg cohort Lurasidone hydrochlorid | 80 mg Lurasidone hydrochloride cohort |
|---------------------------------------|---------------------------------------|--------------------------------------|---------------------------------------|
| Number of subjects | 20 | 25 | 19 |
| Age categorical Units: Subjects | | | |
| 6-9 years old | 5 | 5 | 4 |
| 10-12 years old | 6 | 7 | 5 |
| 13-15 years old | 5 | 7 | 5 |
| 16-17 years old | 4 | 6 | 5 |
| Gender categorical Units: Subjects | | | |
| Female | 8 | 10 | 6 |
| Male | 12 | 15 | 13 |

| Reporting group values | 120 mg Lurasidone hydrochloride cohort | 160 mg Lurasidone hydrochloride cohort | Total |
|---------------------------------------|--|--|-------|
| Number of subjects | 25 | 16 | 105 |
| Age categorical Units: Subjects | | | |
| 6-9 years old | 6 | 0 | 20 |
| 10-12 years old | 5 | 6 | 29 |
| 13-15 years old | 8 | 6 | 31 |
| 16-17 years old | 6 | 4 | 25 |
| Gender categorical Units: Subjects | | | |
| Female | 8 | 5 | 37 |
| Male | 17 | 11 | 68 |

End points

End points reporting groups

| | |
|------------------------------|--|
| Reporting group title | 20 mg Lurasidone hydrochloride cohort |
| Reporting group description: | 20 mg Lurasidone hydrochloride cohort |
| Reporting group title | 40 mg cohort Lurasidone hydrochlorid |
| Reporting group description: | 40 mg Lurasidone hydrochloride cohort |
| Reporting group title | 80 mg Lurasidone hydrochloride cohort |
| Reporting group description: | 80 mg Lurasidone hydrochloride cohort |
| Reporting group title | 120 mg Lurasidone hydrochloride cohort |
| Reporting group description: | 120 mg Lurasidone hydrochloride cohort |
| Reporting group title | 160 mg Lurasidone hydrochloride cohort |
| Reporting group description: | 160 mg Lurasidone hydrochloride cohort |

Primary: Lurasidone Hydrochloride PK profile

| | |
|------------------------|---|
| End point title | Lurasidone Hydrochloride PK profile |
| End point description: | Primary PK parameters: C _{max} , AUC _{last} , and AUC _{0-∞} (Day 1), and C _{max} and AUC ₀₋₂₄ (Day 10 or Day 12) |
| End point type | Primary |
| End point timeframe: | Day 1 through Day 12 |

| End point values | 20 mg Lurasidone hydrochloride cohort | 40 mg cohort Lurasidone hydrochlorid | 80 mg Lurasidone hydrochloride cohort | 120 mg Lurasidone hydrochloride cohort |
|--|---------------------------------------|--------------------------------------|---------------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 20 | 25 | 19 | 25 |
| Units: ng/ml | | | | |
| arithmetic mean (standard deviation) | | | | |
| C _{max} ng/ml (Day 1) | 24.4 (± 14.1) | 38.3 (± 22.4) | 68.2 (± 37.5) | 0 (± 0) |
| C _{max} ng/ml (Day 10 or Day 12) | 30 (± 18) | 36.2 (± 17.5) | 80 (± 59.6) | 94.2 (± 46.6) |
| AUC ₀₋₂₄ ng.h/ml (Day 10 or Day 12) | 115 (± 72.2) | 154 (± 67.4) | 387 (± 194) | 494 (± 271) |
| AUC _{last} ng.h/ml (Day1) | 78 (± 44.9) | 140 (± 65.4) | 300 (± 140) | 0 (± 0) |
| AUC _{0-∞} ng.h/ml (Day 1) | 83.8 (± 48.3) | 153 (± 69.8) | 328 (± 163) | 0 (± 0) |

| End point values | 160 mg Lurasidone hydrochloride | | | |
|------------------|---------------------------------|--|--|--|
|------------------|---------------------------------|--|--|--|

| | cohort | | | |
|--------------------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 16 | | | |
| Units: ng/ml | | | | |
| arithmetic mean (standard deviation) | | | | |
| Cmax ng/ml (Day 1) | 0 (± 0) | | | |
| Cmax ng/ml (Day 10 or Day 12) | 99.7 (± 44.3) | | | |
| AUC0-24 ng.h/ml (Day 10 or Day 12) | 590 (± 227) | | | |
| AUClast ng.h/ml (Day1) | 0 (± 0) | | | |
| AUC0-∞ ng.h/ml (Day 1) | 0 (± 0) | | | |

Statistical analyses

| Statistical analysis title | Discriptive Summary |
|---|---|
| Comparison groups | 20 mg Lurasidone hydrochloride cohort v 40 mg cohort Lurasidone hydrochlorid v 80 mg Lurasidone hydrochloride cohort v 120 mg Lurasidone hydrochloride cohort v 160 mg Lurasidone hydrochloride cohort |
| Number of subjects included in analysis | 105 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 1 |
| Method | ANCOVA |
| Parameter estimate | Discriptive Summary |

Adverse events

Adverse events information

Timeframe for reporting adverse events:

June 19, 2012 through May 6, 2013

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

Dictionary used

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

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

Reporting groups

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|-----------------------|-------------------------------|
| Reporting group title | Lurasidone 20 mg oral tablets |
|-----------------------|-------------------------------|

Reporting group description:

Lurasidone 20 mg oral tablets

| | |
|-----------------------|-------------------------------|
| Reporting group title | Lurasidone 40 mg oral tablets |
|-----------------------|-------------------------------|

Reporting group description:

Lurasidone 40 mg oral tablets

| | |
|-----------------------|-------------------------------|
| Reporting group title | Lurasidone 80 mg oral tablets |
|-----------------------|-------------------------------|

Reporting group description:

Lurasidone 80 mg oral tablets

| | |
|-----------------------|--------------------------------|
| Reporting group title | Lurasidone 120 mg oral tablets |
|-----------------------|--------------------------------|

Reporting group description:

Lurasidone 120 mg oral tablets

| | |
|-----------------------|--------------------------------|
| Reporting group title | Lurasidone 160 mg oral tablets |
|-----------------------|--------------------------------|

Reporting group description:

Lurasidone 160 mg oral tablets

| Serious adverse events | Lurasidone 20 mg oral tablets | Lurasidone 40 mg oral tablets | Lurasidone 80 mg oral tablets |
|---|-------------------------------|-------------------------------|-------------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 25 (0.00%) | 2 / 19 (10.53%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Nervous system disorders | | | |
| Parkinsonism | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 25 (0.00%) | 1 / 19 (5.26%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dystonia | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 25 (0.00%) | 1 / 19 (5.26%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | Lurasidone 120 mg oral tablets | Lurasidone 160 mg oral tablets | |
|---|-----------------------------------|-----------------------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 25 (0.00%) | 0 / 16 (0.00%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Nervous system disorders | | | |
| Parkinsonism | | | |
| subjects affected / exposed | 0 / 25 (0.00%) | 0 / 16 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dystonia | | | |
| subjects affected / exposed | 0 / 25 (0.00%) | 0 / 16 (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: 3 %

| Non-serious adverse events | Lurasidone 20 mg oral tablets | Lurasidone 40 mg oral tablets | Lurasidone 80 mg oral tablets |
|---|----------------------------------|----------------------------------|----------------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 4 / 20 (20.00%) | 17 / 25 (68.00%) | 15 / 19 (78.95%) |
| Nervous system disorders | | | |
| Somnolence | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 11 / 25 (44.00%) | 7 / 19 (36.84%) |
| occurrences (all) | 0 | 27 | 17 |
| Sedation | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 3 / 25 (12.00%) | 5 / 19 (26.32%) |
| occurrences (all) | 0 | 5 | 9 |
| Dystonia | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 25 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrointestinal disorders | | | |
| Nausea | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 3 / 25 (12.00%) | 6 / 19 (31.58%) |
| occurrences (all) | 1 | 4 | 7 |
| Vomiting | | | |

| | | | |
|--|---------------------|----------------------|----------------------|
| subjects affected / exposed occurrences (all) | 0 / 20 (0.00%) 0 | 4 / 25 (16.00%) 4 | 4 / 19 (21.05%) 5 |
| Abdominal pain upper subjects affected / exposed occurrences (all) | 1 / 20 (5.00%) 1 | 0 / 25 (0.00%) 0 | 1 / 19 (5.26%) 1 |
| Psychiatric disorders Anxiety subjects affected / exposed occurrences (all) | 0 / 20 (0.00%) 0 | 0 / 25 (0.00%) 0 | 1 / 19 (5.26%) 1 |

| Non-serious adverse events | Lurasidone 120 mg oral tablets | Lurasidone 160 mg oral tablets | |
|--|-----------------------------------|-----------------------------------|--|
| Total subjects affected by non-serious adverse events subjects affected / exposed | 24 / 25 (96.00%) | 16 / 16 (100.00%) | |
| Nervous system disorders Somnolence subjects affected / exposed occurrences (all) | 16 / 25 (64.00%) 50 | 10 / 16 (62.50%) 10 | |
| Sedation subjects affected / exposed occurrences (all) | 7 / 25 (28.00%) 13 | 4 / 16 (25.00%) 8 | |
| Dystonia subjects affected / exposed occurrences (all) | 3 / 25 (12.00%) 4 | 2 / 16 (12.50%) 2 | |
| Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all) | 2 / 25 (8.00%) 2 | 6 / 16 (37.50%) 6 | |
| Vomiting subjects affected / exposed occurrences (all) | 5 / 25 (20.00%) 6 | 3 / 16 (18.75%) 3 | |
| Abdominal pain upper subjects affected / exposed occurrences (all) | 4 / 25 (16.00%) 4 | 0 / 16 (0.00%) 0 | |
| Psychiatric disorders Anxiety subjects affected / exposed occurrences (all) | 1 / 25 (4.00%) 1 | 4 / 16 (25.00%) 4 | |

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

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

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|------|
| None |
|------|

Notes: