



Clinical trial results:

A Randomized, Double-blind, Active Comparator-Controlled Study to Evaluate the Long-term Safety and Tolerability of SEP-363856 in Subjects With Schizophrenia

Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2019-002259-40 |
| Trial protocol | RO |
| Global end of trial date | 30 December 2022 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 (current) |
| This version publication date | 31 December 2023 |
| First version publication date | 31 December 2023 |

Trial information

Trial identification

| | |
|-----------------------|------------|
| Sponsor protocol code | SEP361-304 |
|-----------------------|------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT04115319 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Sunovion Pharmaceuticals Inc. |
| Sponsor organisation address | 84 Waterford Drive, Marlboro, United States, 01752 |
| Public contact | CNS Medical Director, Sunovion Pharmaceuticals Inc., 01 18665036351, clinicaltrialdisclosure@sunovion.com |
| Scientific contact | CNS Medical Director, Sunovion Pharmaceuticals Inc., 01 18665036351, clinicaltrialdisclosure@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 | 30 December 2022 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 30 December 2022 |
| Global end of trial reached? | Yes |
| Global end of trial date | 30 December 2022 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To evaluate the long-term safety and tolerability of flexibly-dosed SEP-363856 (50, 75, and 100 mg/day) in clinically stable adult subjects with chronic schizophrenia by the incidence of overall adverse events (AEs), serious AEs (SAEs) and AEs leading to discontinuation.

Protection of trial subjects:

This study was conducted according to the protocol, ICH Good Clinical Practice (GCP), ICH guidelines and the ethical principles that have their origin in the Declaration of Helsinki

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 21 November 2019 |
| 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 | Russian Federation: 124 |
| Country: Number of subjects enrolled | Romania: 3 |
| Country: Number of subjects enrolled | Ukraine: 63 |
| Country: Number of subjects enrolled | United States: 113 |
| Worldwide total number of subjects | 303 |
| EEA total number of subjects | 3 |

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) | 302 |
| From 65 to 84 years | 1 |

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

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Informed consent will be obtained from subjects before any study procedures are performed. Subjects will be evaluated for eligibility during a Screening/Washout Period of up to 21 days, during which they will be tapered off all psychotropic medications in a manner that is consistent with labeling recommendations and conventional medical practices.

Period 1

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

Arms

| | |
|------------------------------|------------|
| Are arms mutually exclusive? | Yes |
| Arm title | SEP-363856 |

Arm description:

SEP-363856 50mg, 75mg, 100mg, flexibly dosed once daily capsule

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | SEP-3638 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

50mg, 75mg, 100mg, flexibly dosed once daily

| | |
|------------------|---------------|
| Arm title | Quetiapine XR |
|------------------|---------------|

Arm description:

Quetiapine XR, 400, 600, 800 mg, flexibly dosed once daily capsule

| | |
|--|-------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | Quetiapine XR |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

400, 600, 800 mg, flexibly dosed once daily

| Number of subjects in period 1 | SEP-363856 | Quetiapine XR |
|---------------------------------------|------------|---------------|
| Started | 201 | 102 |
| Completed | 105 | 57 |
| Not completed | 96 | 45 |
| Consent withdrawn by subject | 17 | 9 |
| Personal reasons | - | 1 |
| geopolitical conflict related | 2 | 1 |
| Adverse event, non-fatal | 48 | 21 |
| non compliance with study drug | 5 | 1 |
| deemed unsuitable for participation | 1 | - |
| Lost to follow-up | 6 | 7 |
| Covid 19 related | 1 | - |
| subject relocated | 5 | 2 |
| Lack of efficacy | 6 | 2 |
| Protocol deviation | 5 | 1 |

Baseline characteristics

Reporting groups

| | |
|--|---------------|
| Reporting group title | SEP-363856 |
| Reporting group description: SEP-363856 50mg, 75mg, 100mg, flexibly dosed once daily capsule | |
| Reporting group title | Quetiapine XR |
| Reporting group description: Quetiapine XR, 400, 600, 800 mg, flexibly dosed once daily capsule | |

| Reporting group values | SEP-363856 | Quetiapine XR | Total |
|--|------------|---------------|-------|
| Number of subjects | 201 | 102 | 303 |
| Age Categorical Units: Participants | | | |
| >= 12 to < 18 years | 0 | 0 | 0 |
| >=18 to < 65 years | 200 | 102 | 302 |
| >=65 years | 1 | 0 | 1 |
| < 12 years | 0 | 0 | 0 |
| Age Continuous Units: Years | | | |
| arithmetic mean | 40.3 | 38.4 | |
| standard deviation | ± 11.77 | ± 12.66 | - |
| Gender, Male/Female Units: Participants | | | |
| Female | 88 | 37 | 125 |
| Male | 113 | 65 | 178 |
| Race (NIH/OMB) Units: Subjects | | | |
| American Indian or Alaska Native | 2 | 0 | 2 |
| Asian | 2 | 0 | 2 |
| Black or African American | 47 | 28 | 75 |
| More than one race | 0 | 0 | 0 |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 |
| Other | 0 | 1 | 1 |
| Unknown or Not Reported | 0 | 0 | 0 |
| White | 150 | 73 | 223 |
| Ethnicity (NIH/OMB) Units: Subjects | | | |
| Hispanic or Latino | 8 | 4 | 12 |
| Not Hispanic or Latino | 193 | 98 | 291 |
| Unknown or Not Reported | 0 | 0 | 0 |
| Country Units: Subjects | | | |
| Romania | 2 | 1 | 3 |
| Russia | 83 | 41 | 124 |
| Ukraine | 42 | 21 | 63 |
| United States | 74 | 39 | 113 |

End points

End points reporting groups

| | |
|--|---------------|
| Reporting group title | SEP-363856 |
| Reporting group description: SEP-363856 50mg, 75mg, 100mg, flexibly dosed once daily capsule | |
| Reporting group title | Quetiapine XR |
| Reporting group description: Quetiapine XR, 400, 600, 800 mg, flexibly dosed once daily capsule | |

Primary: The incidence of overall Adverse Events (AEs), Serious Adverse Events (SAEs), and Adverse Events (AEs) leading to discontinuation

| | |
|--|--|
| End point title | The incidence of overall Adverse Events (AEs), Serious Adverse Events (SAEs), and Adverse Events (AEs) leading to discontinuation ^[1] |
| End point description: The incidence of AEs, SAEs, and AEs leading to discontinuation | |
| End point type | Primary |
| End point timeframe: 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: This outcome measure was not powered to have a statistical analysis.

| End point values | SEP-363856 | Quetiapine XR | | |
|---|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 201 | 102 | | |
| Units: participants | | | | |
| Any Adverse Events (AEs) | 153 | 77 | | |
| Serious Adverse Events (SAEs) | 16 | 0 | | |
| Adverse Events (AEs) leading to discontinuation | 48 | 21 | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

up to 395 days

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

Dictionary used

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

| | |
|--------------------|----|
| Dictionary version | 22 |
|--------------------|----|

Reporting groups

| | |
|-----------------------|---------------|
| Reporting group title | Quetiapine XR |
|-----------------------|---------------|

Reporting group description:

Quetiapine XR, 400, 600, 800 mg, flexibly dosed once daily capsule

| | |
|-----------------------|------------|
| Reporting group title | SEP-363856 |
|-----------------------|------------|

Reporting group description:

SEP-363856 50mg, 75mg, 100mg, flexibly dosed once daily capsule

| Serious adverse events | Quetiapine XR | SEP-363856 | |
|---|-----------------|------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 102 (0.00%) | 16 / 201 (7.96%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Injury, poisoning and procedural complications | | | |
| Fall | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 102 (0.00%) | 1 / 201 (0.50%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Limb injury | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 102 (0.00%) | 1 / 201 (0.50%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Multiple injuries | | | |
| alternative dictionary used: MedDRA 22.0 | | | |

| | | | |
|---|-----------------|------------------|--|
| subjects affected / exposed | 0 / 102 (0.00%) | 2 / 201 (1.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Cerebrovascular accident | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 102 (0.00%) | 1 / 201 (0.50%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| Suicide attempt | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 102 (0.00%) | 2 / 201 (1.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anxiety | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 102 (0.00%) | 1 / 201 (0.50%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Schizophrenia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 102 (0.00%) | 10 / 201 (4.98%) | |
| occurrences causally related to treatment / all | 0 / 0 | 3 / 10 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Corona virus infection | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 102 (0.00%) | 1 / 201 (0.50%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | Quetiapine XR | SEP-363856 | |
|---|-------------------|--------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 55 / 102 (53.92%) | 103 / 201 (51.24%) | |
| Investigations | | | |
| Weight decreased | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 102 (0.98%) | 11 / 201 (5.47%) | |
| occurrences (all) | 1 | 11 | |
| Weight increased | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 11 / 102 (10.78%) | 9 / 201 (4.48%) | |
| occurrences (all) | 11 | 9 | |
| Nervous system disorders | | | |
| Akathisia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 2 / 102 (1.96%) | 14 / 201 (6.97%) | |
| occurrences (all) | 2 | 15 | |
| Dizziness | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 5 / 102 (4.90%) | 16 / 201 (7.96%) | |
| occurrences (all) | 5 | 18 | |
| Headache | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 8 / 102 (7.84%) | 20 / 201 (9.95%) | |
| occurrences (all) | 8 | 29 | |
| Somnolence | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 21 / 102 (20.59%) | 12 / 201 (5.97%) | |
| occurrences (all) | 24 | 13 | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 9 / 102 (8.82%) | 5 / 201 (2.49%) | |
| occurrences (all) | 10 | 6 | |
| Gastrointestinal disorders | | | |

| | | | |
|--|--|--|--|
| <p>Constipation</p> <p>alternative dictionary used: MedDRA 22.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>12 / 102 (11.76%)</p> <p>16</p> | <p>7 / 201 (3.48%)</p> <p>8</p> | |
| <p>Nausea</p> <p>alternative dictionary used: MedDRA 22.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>4 / 102 (3.92%)</p> <p>5</p> | <p>13 / 201 (6.47%)</p> <p>13</p> | |
| <p>Psychiatric disorders</p> <p>Anxiety</p> <p>alternative dictionary used: MedDRA 22.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Insomnia</p> <p>alternative dictionary used: MedDRA 22.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Schizophrenia</p> <p>alternative dictionary used: MedDRA 22.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>10 / 102 (9.80%)</p> <p>12</p> <p>11 / 102 (10.78%)</p> <p>13</p> <p>6 / 102 (5.88%)</p> <p>6</p> | <p>27 / 201 (13.43%)</p> <p>41</p> <p>30 / 201 (14.93%)</p> <p>38</p> <p>21 / 201 (10.45%)</p> <p>23</p> | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-------------------|---|
| 16 September 2020 | Protocol Ver1.00 (28 June 2019) was amended: Added Phase of development to synopsis. Minor wording clarifications C-SSRS endpoint. Inclusion 5 was amended and 6,18 were added. Clarified that DSM-5 criteria must be met at screening. Added Sec10.7 for eligibility adjudication process to Sec10. Exclusion 2 subject's substance use disorder criteria were further restricted. Exclusion 10 part a & part g were updated to exclude subjects with unstable hypertension. Subjects with an ECG that has a centrally overall interpretation of abnormal, significant/potentially clinically significant must be discussed with Medical Monitor(MM). Exclusion 14 was added to require that specific blood pressure thresholds be met. Exclusion 15 was clarified: to indicate who determines clinical significance of abnormal lab values at Screening and to require that the MM approve retesting of clin lab tests and allow extensions to the screening period for technical issues. Exclusion 16 was clarified to always exclude subjects with a positive/indeterminate confirmatory test for hepatitis C. Simplified language for exclusion 21 for positive drug test at screening. Exception for subjects testing positive for cannabinoids at Screening was removed. Exclusion 22 made prior receipt of investigational drug product or device more restrictive. Clarified Other Safety Endpoint that suicidal ideation endpoint includes frequency and severity. Clarified the timing for obtaining consents. Added footnote to indicate a separate consent form is required for the duplicate subject check at screening. Clarified that pretreatment events and adverse events are determined programmatically. Clarified that the PANSS-IC form will be completed as part of PANSS. Sec 10.3 added clarification on collection of data. Clarification was made to allow antipsychotic medications to be reported in eCRF based on subject and caregiver input. Expectations on details of prior psychotropic medications were clarified. |
| 14 January 2021 | The protocol Version 2.00 dated 16 September 2020 is being amended as follows: Updated Exclusion Criteria #2 based on FDA feedback to make the criterion more specific while still maintaining the original intent of the criterion, which is to exclude subjects with a history of substantial substance use disorder that may result in significant confounding on diagnosis, presentation and/or treatment responsiveness. Updated Exclusion Criteria #22 based on FDA feedback to refine the restrictions on prior clinical trial participation to those that would meaningfully interfere with the conduct of the study. Updated frequency of Data Safety Monitoring Board (DSMB) to align with the DSMB charter. Update Sunovion Responsible Physician. Minor changes such as edits to the title page, headers, footers, and approval page of the document to reflect the new version number and document date have also been made. Updates to abbreviations for consistency, added phase of development, minor wording clarifications for readability, corrections to cross-references, and corrections to typographical errors have been made. Updates to the table of contents have also been made. These changes are not described within. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported