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
Ukarine	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			

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

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