Clinical trial results:
A Phase 3, Randomized, Double-Blind, Placebo-Controlled, Multi-Center Study to Assess the Efficacy and Safety of Lumateperone Monotherapy in the Treatment of Patients with Major Depressive Episodes Associated with Bipolar I or Bipolar II Disorder (Bipolar Depression) or Major Depressive Disorder

Summary

EudraCT number	2019-004440-29
Trial protocol	BG
Global end of trial date	30 November 2022

Results information

Result version number	v1 (current)
This version publication date	27 December 2023
First version publication date	27 December 2023

Trial information

Trial identification

Sponsor protocol code	ITI-007-403

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04285515
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Intra-Cellular Therapies, Inc.
Sponsor organisation address	430 East 29th Street, New York, United States, 10016
Public contact	ITI Clinical Trials, Intra-Cellular Therapies, Inc., +1 646-440-9333, ITCIClinicalTrials@itci-inc.com
Scientific contact	ITI Clinical Trials, Intra-Cellular Therapies, Inc., +1 646-440-9333, ITCIClinicalTrials@itci-inc.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	15 March 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 November 2022
Global end of trial reached?	Yes
Global end of trial date	30 November 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to confirm the efficacy of lumateperone 42 mg administered orally once daily compared with that of placebo as measured by mean change from baseline to Day 43 in the Montgomery-Åsberg Depression Rating Scale (MADRS) total score in patients with bipolar depression with mixed features or major depressive disorder with mixed features.

Protection of trial subjects:

The study was conducted in accordance with the ethical principles that have their origins in the Declaration of Helsinki. The study complied with the ICH Guidance on General Considerations for Clinical Trials and GCP, as well as CFR Part 312.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	07 February 2020
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	Bulgaria: 167
Country: Number of subjects enrolled	United States: 167
Country: Number of subjects enrolled	Ukraine: 37
Country: Number of subjects enrolled	Russian Federation: 78
Country: Number of subjects enrolled	Serbia: 39
Worldwide total number of subjects	488
EEA total number of subjects	167

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)	468
From 65 to 84 years	20
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The Screening phase begins once the Informed Consent Form is signed. Patients are evaluated during the screening period lasting up to 2 weeks.

Pre-assignment period milestones

Number of subjects started	731[1]
Number of subjects completed	488

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Screen Failure: 243

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Pre-assignment period includes all pts that are screened. Worldwide number enrolled are those patients that have been randomized.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Lumateperone 42mg

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Lumateperone
Investigational medicinal product code	
Other name	ITI-007
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Once daily oral administration

Investigational medicinal product name	Lumateperone
Investigational medicinal product code	
Other name	ITI-007
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Once oral daily administration

Arm title	Placebo

Arm description: -

Arm type	Placebo

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Once daily oral administration

Number of subjects in period 1	Lumateperone 42mg	Placebo
Started	243	245
Completed	211	217
Not completed	32	28
Physician decision	1	-
Consent withdrawn by subject	5	11
Adverse event, non-fatal	10	5
Other	1	3
Lost to follow-up	9	4
Lack of efficacy	2	3
Protocol deviation	4	2

Baseline characteristics

Reporting groups	
Reporting group title	Lumateperone 42mg
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Reporting group values	Lumateperone 42mg	Placebo	Total
Number of subjects	243	245	488
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	231	237	468
From 65-84 years	12	8	20
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	42.7	43.4	
standard deviation	± 14.58	± 13.84	-
Gender categorical Units: Subjects			
Female	151	150	301
Male	92	95	187

End points

End points reporting groups

Reporting group title	Lumateperone 42mg
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	
Subject analysis set title	Intent-to Treat
Subject analysis set type	Intention-to-treat

Subject analysis set description:

• Intent-to-Treat (ITT) Analysis Set contains all patients who were randomized before Protocol Amendment 2.0 and all patients who were randomized after Protocol Amendment 2.0, who received at least 1 dose of study drug and who had a nonmissing (predose) baseline assessment and at least 1 nonmissing postbaseline assessment of MADRS total score

Primary: Change from baseline to Day 43 in the Montgomery-Asberg Depression Rating Scale (MADRS) total score

End point title	Change from baseline to Day 43 in the Montgomery-Asberg Depression Rating Scale (MADRS) total score

End point description:

End point type	Primary

End point timeframe:

Baseline to Day 43

End point values	Lumateperone 42mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	211	219		
Units: unit(s)				
least squares mean (confidence interval 95%)	-17.7 (-18.92 to -16.42)	-12.1 (-13.34 to -10.86)		

Statistical analyses

Statistical analysis title	Primary Efficacy Analysis
Comparison groups	Lumateperone 42mg v Placebo
Number of subjects included in analysis	430
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-5.6

Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.25
upper limit	-3.88
Variability estimate	Standard error of the mean
Dispersion value	0.86

Secondary: Change from baseline to Day 43 in the Clinical Global Impression-Severity Scale (CGI-S) total score

End point title	Change from baseline to Day 43 in the Clinical Global Impression-Severity Scale (CGI-S) total score
End point description:	
End point type	Secondary
End point timeframe:	
Baseline to Day 43	

End point values	Lumateperone 42mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	211	219		
Units: Unit				
least squares mean (confidence interval 95%)	-1.7 (-1.89 to -1.61)	-1.1 (-1.26 to -0.98)		

Statistical analyses

Statistical analysis title	Key Secondary Efficacy Analysis
Comparison groups	Placebo v Lumateperone 42mg
Number of subjects included in analysis	430
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.82
upper limit	-0.44
Variability estimate	Standard error of the mean
Dispersion value	0.1

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the time the subject gives study-specific informed consent until the end of study procedures being completed.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.1

Reporting groups

Reporting group title	Lumateperone 42mg

Reporting group description:

Includes patients randomized to the Lumateperone 42 mg group and who received at least 1 dose of study drug.

Reporting group title	Placebo

Reporting group description:

Includes patients randomized to the Placebo group and who received at least 1 dose of study drug.

Serious adverse events	Lumateperone 42mg	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 240 (0.00%)	1 / 241 (0.41%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	0 / 240 (0.00%)	1 / 241 (0.41%)	
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	Lumateperone 42mg	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	84 / 240 (35.00%)	37 / 241 (15.35%)	
Nervous system disorders			
Headache			
subjects affected / exposed	37 / 240 (15.42%)	30 / 241 (12.45%)	
occurrences (all)	40	33	
Somnolence			

subjects affected / exposed	31 / 240 (12.92%)	4 / 241 (1.66%)	
occurrences (all)	31	4	
Dizziness			
subjects affected / exposed	28 / 240 (11.67%)	4 / 241 (1.66%)	
occurrences (all)	30	4	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	19 / 240 (7.92%)	5 / 241 (2.07%)	
occurrences (all)	19	5	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 November 2020	-The addition of patients with major depressive disorder (MDD) to the study population and the addition of the inclusion criterion for all patients to meet the Diagnostic and Statistical Manual of Mental Disorder, 5th Edition (DSM-5) criteria for mixed features specific to the Bipolar I or II diagnosis or MDD diagnosis. -Increase in sample size.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported