Clinical trial results:
A Randomized, Double-Blind, Placebo-Controlled Multicenter Study to Assess the Efficacy and Safety of Lumateperone as Adjunctive Therapy in the Treatment of Patients with Major Depressive Disorder

Summary

EudraCT number	2021-001192-17
Trial protocol	CZ SK BG HU
Global end of trial date	27 February 2024

Results information

Result version number	v1 (current)
This version publication date	13 November 2025
First version publication date	13 November 2025

Trial information

Trial identification

Sponsor protocol code	ITI-007-501

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04985942
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Intra-Cellular Therapies, Inc.
Sponsor organisation address	135 Route 202/206, Suite 6, Bedminster, NJ, United States, 07921
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	08 April 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 February 2024
Global end of trial reached?	Yes
Global end of trial date	27 February 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of lumateperone 42 mg administered once daily compared with placebo as adjunctive treatment to antidepressant therapy in subjects with Major Depressive Disorder (MDD) who have an inadequate response to ongoing antidepressant therapy (ADT) as measured by change from baseline to Day 43 in the Montgomery-Åsberg Depression Rating Scale (MADRS) total score.

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:

In order to meet eligibility criteria subjects must have had an inadequate response (less than 50% improvement) to one of the antidepressant therapies listed below as monotherapy treatment; having taken at least the minimum effective dose (per package insert) for at least 6 weeks duration. Patients would need to continue taking the antidepressant therapy throughout the 6 week double-blind treatment period:
a. citalopram/escitalopram
b. fluoxetine
c. paroxetine
d. sertraline
e. duloxetine
f. levomilnacipran/milnacipran (if locally approved for MDD)
g. venlafaxine/desvenlafaxine
h. bupropion
i. vilazodone
j. vortioxetine

Evidence for comparator: -

Actual start date of recruitment	27 July 2021
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	6 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 151
Country: Number of subjects enrolled	Slovakia: 39
Country: Number of subjects enrolled	Bulgaria: 109
Country: Number of subjects enrolled	Czechia: 105
Country: Number of subjects enrolled	Hungary: 16
Country: Number of subjects enrolled	India: 65

Worldwide total number of subjects	485
EEA total number of subjects	269

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)	478
From 65 to 84 years	7
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. Subjects are evaluated during the screening period lasting up to 2 weeks.

Pre-assignment period milestones

Number of subjects started	700[1]
Number of subjects completed	485

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Screen Failure: 215

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 subjects that were screened. Worldwide number enrolled are those subjects that were 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, Data analyst, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Lumateperone 42 mg + ADT

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:

Lumateperone 42 mg once daily oral administration

Arm title	Placebo + ADT

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:

Matching placebo capsule once daily oral administration

Number of subjects in period 1	Lumateperone 42 mg + ADT	Placebo + ADT
Started	242	243
Completed	220	232
Not completed	22	11
Consent withdrawn by subject	5	4
Adverse event, non-fatal	14	2
Lost to follow-up	2	1
Protocol deviation	1	1
Lack of efficacy	-	3

Baseline characteristics

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

Reporting group values	Lumateperone 42 mg + ADT	Placebo + ADT	Total
Number of subjects	242	243	485
Age categorical Units: Subjects			
Adults (18-64 years)	237	241	478
From 65-84 years	5	2	7
Age continuous Units: years			
arithmetic mean	44.9	45.1	
standard deviation	± 12.42	± 12.51	-
Gender categorical Units: Subjects			
Female	159	160	319
Male	83	83	166

End points

End points reporting groups

Reporting group title	Lumateperone 42 mg + ADT
Reporting group description: -	
Reporting group title	Placebo + ADT
Reporting group description: -	
Subject analysis set title	mITT
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
Modified Intent-to-Treat (mITT) Population includes all randomized subjects who received at least one dose of study drug and have a baseline MADRS total score, and who have at least one on-study drug, postbaseline 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 42 mg + ADT	Placebo + ADT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	239	242		
Units: MADRS Total Score				
least squares mean (confidence interval 95%)	-14.7 (-15.77 to -13.63)	-9.8 (-10.83 to -8.74)		

Statistical analyses

Statistical analysis title	Primary Efficacy Analysis
Comparison groups	Lumateperone 42 mg + ADT v Placebo + ADT
Number of subjects included in analysis	481
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Mixed Effects Model for Repeated Measure
Parameter estimate	LS Mean Difference
Point estimate	-4.9

Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.38
upper limit	-3.44
Variability estimate	Standard error of the mean
Dispersion value	0.75

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 42 mg + ADT	Placebo + ADT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	239	242		
Units: CGI-S Total Score				
least squares mean (confidence interval 95%)	-1.6 (-1.74 to -1.47)	-0.9 (-1.07 to -0.80)		

Statistical analyses

Statistical analysis title	Key Secondary Efficacy Analysis
Comparison groups	Lumateperone 42 mg + ADT v Placebo + ADT
Number of subjects included in analysis	481
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Mixed Effects Model for Repeated Measure
Parameter estimate	LS Mean Difference
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.85
upper limit	-0.48
Variability estimate	Standard error of the mean
Dispersion value	0.09

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	24.0

Reporting groups

Reporting group title	Lumateperone 42 mg + ADT

Reporting group description:

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

Reporting group title	Placebo + ADT

Reporting group description:

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

Serious adverse events	Lumateperone 42 mg + ADT	Placebo + ADT	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 241 (0.41%)	1 / 243 (0.41%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Joint dislocation			
subjects affected / exposed	0 / 241 (0.00%)	1 / 243 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 241 (0.41%)	0 / 243 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Lumateperone 42 mg + ADT	Placebo + ADT	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	92 / 241 (38.17%)	53 / 243 (21.81%)	
Nervous system disorders			
Tremor			
subjects affected / exposed	12 / 241 (4.98%)	1 / 243 (0.41%)	
occurrences (all)	13	1	
Headache			
subjects affected / exposed	38 / 241 (15.77%)	37 / 243 (15.23%)	
occurrences (all)	50	31	
Dizziness			
subjects affected / exposed	25 / 241 (10.37%)	15 / 243 (6.17%)	
occurrences (all)	27	19	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	23 / 241 (9.54%)	5 / 243 (2.06%)	
occurrences (all)	24	6	
Gastrointestinal disorders			
Dry Mouth			
subjects affected / exposed	26 / 241 (10.79%)	5 / 243 (2.06%)	
occurrences (all)	26	5	
Nausea			
subjects affected / exposed	12 / 241 (4.98%)	10 / 243 (4.12%)	
occurrences (all)	12	12	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 June 2021	Inclusion Criterion #2 was revised to lower maximum age of study eligibility from 75 years to 65 years; Inclusion Criterion #4 was modified to add ATRQ for confirmation of inadequate response to ADT by the Investigator; Removed "moderate CYP3A4 inhibitors" from prohibited medications; Clarified time period for AE and SAE reporting; Added estimand strategy for primary and key secondary efficacy objectives, revised analyses of primary, key secondary, and additional efficacy parameters to accommodate estimand strategy, and updated analysis populations.
20 August 2021	Exclusion Criterion #21e was modified to specify exclusion of patients with moderate or severe hepatic impairment; Added study stopping criteria; Added additional analyses of the primary efficacy parameter.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported