Clinical trial results:
An Open-label, Multicenter Trial to Assess the Safety and Tolerability of Lumateperone as Adjunctive Therapy in the Treatment of Patients with Major Depressive Disorder

Summary

EudraCT number	2021-001172-41
Trial protocol	CZ SK HU BG PL SE FI
Global end of trial date	23 October 2024

Results information

Result version number	v1 (current)
This version publication date	14 November 2025
First version publication date	14 November 2025

Trial information

Trial identification

Sponsor protocol code	ITI-007-503

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05061719
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	09 December 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 October 2024
Global end of trial reached?	Yes
Global end of trial date	23 October 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety and tolerability of lumateperone 42 mg administered orally once daily for approximately 26 weeks as adjunctive treatment to antidepressant therapy (ADT) in patients with major depressive disorder (MDD).

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:

Subjects continued to take one of the following antidepressants as monotherapy treatment that they had taken in the Lead-In Study:
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	26 September 2021
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	India: 53
Country: Number of subjects enrolled	Poland: 147
Country: Number of subjects enrolled	Slovakia: 32
Country: Number of subjects enrolled	Sweden: 2
Country: Number of subjects enrolled	Bulgaria: 159
Country: Number of subjects enrolled	Czechia: 95
Country: Number of subjects enrolled	Germany: 25
Country: Number of subjects enrolled	Hungary: 15
Country: Number of subjects enrolled	United States: 225
Country: Number of subjects enrolled	Argentina: 56

Worldwide total number of subjects	809
EEA total number of subjects	475

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)	796
From 65 to 84 years	13
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The Screening phase began once the Informed Consent Form was signed. Subjects enrolled in this open-label safety study had to have completed 1 of 2 double-blind lead-in studies.

Pre-assignment period milestones

Number of subjects started	812[1]
Number of subjects completed	809

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Consent withdrawn by subject: 2
Reason: Number of subjects	Lost to follow-up: 1

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 are screened. Worldwide number enrolled are those subjects that have been enrolled.

Period 1

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

Arms

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

Number of subjects in period 1	Lumateperone 42 mg + ADT
Started	809
Completed	684
Not completed	125
Adverse event, serious fatal	1
Consent withdrawn by subject	41
Adverse event, non-fatal	60

Pregnancy	1
Subjects discontinued due to site closure	2
Lost to follow-up	5
Lack of efficacy	7
Protocol deviation	8

Baseline characteristics

Reporting groups	
Reporting group title	Lumateperone 42 mg + ADT

Reporting group description: -

Reporting group values	Lumateperone 42 mg + ADT	Total	
Number of subjects	809	809	
Age categorical Units: Subjects			
Adults (18-64 years)	796	796	
From 65-84 years	13	13	
Age continuous Units: years			
arithmetic mean	46.2		
standard deviation	± 12.22	-	
Gender categorical Units: Subjects			
Female	549	549	
Male	260	260	

End points

End points reporting groups

Reporting group title	Lumateperone 42 mg + ADT

Reporting group description: -

Primary: The Number and Percentage of Subjects Reporting Treatment Emergent Adverse Events

End point title	The Number and Percentage of Subjects Reporting Treatment Emergent Adverse Events[1]

End point description:

548 out of 809 subjects (67.74%) reported at least 1 TEAE

End point type	Primary

End point timeframe:

26 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: As this was an open-label safety study there was no comparison to placebo or other treatment. The Primary outcome was number and percentage of of subjects that reported a TEAE.

End point values	Lumateperone 42 mg + ADT			
Subject group type	Reporting group			
Number of subjects analysed	809			
Units: Number of subjects reporting TEAEs				
number (not applicable)	548			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in one of the 6 Week Double-blind Lead-in Studies to the End of the Open-Label Treatment Period in the Montgomery-Åsberg Depression Rating Scale

End point title	Change From Baseline in one of the 6 Week Double-blind Lead-in Studies to the End of the Open-Label Treatment Period in the Montgomery-Åsberg Depression Rating Scale

End point description:

End point type	Secondary

End point timeframe:

Up to 32 weeks

End point values	Lumateperone 42 mg + ADT			
Subject group type	Reporting group			
Number of subjects analysed	809			
Units: MADRS Total Score				
arithmetic mean (standard deviation)	-21.7 (± 8.39)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in one of the 6 Week Double-blind Lead-in Studies to the End of the Open-Label Treatment Period in the Clinical Global Impression Scale-Severity

End point title	Change From Baseline in one of the 6 Week Double-blind Lead-in Studies to the End of the Open-Label Treatment Period in the Clinical Global Impression Scale-Severity

End point description:

End point type	Secondary

End point timeframe:

Up to 32 weeks

End point values	Lumateperone 42 mg + ADT			
Subject group type	Reporting group			
Number of subjects analysed	809			
Units: CGI-S Total Score				
arithmetic mean (standard deviation)	-2.5 (± 1.19)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From signing ICF until end of study procedures (~28 weeks), including 26 weeks of open-label treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	Lumateperone 42 mg + ADT

Reporting group description: -

Serious adverse events	Lumateperone 42 mg + ADT		
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 809 (0.99%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	1		
Injury, poisoning and procedural complications			
Alcohol poisoning			
subjects affected / exposed	1 / 809 (0.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Contusion			
subjects affected / exposed	1 / 809 (0.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Spinal compression fracture			
subjects affected / exposed	1 / 809 (0.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Postmenopausal haemorrhage			

subjects affected / exposed	1 / 809 (0.12%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Biliary colic			
subjects affected / exposed	1 / 809 (0.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	2 / 809 (0.25%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Infections and infestations			
Helicobacter gastritis			
subjects affected / exposed	1 / 809 (0.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Lumateperone 42 mg + ADT		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	322 / 809 (39.80%)		
Nervous system disorders			
Dizziness			
subjects affected / exposed	86 / 809 (10.63%)		
occurrences (all)	91		
Headache			
subjects affected / exposed	134 / 809 (16.56%)		
occurrences (all)	182		
Somnolence			
subjects affected / exposed	58 / 809 (7.17%)		
occurrences (all)	60		
Gastrointestinal disorders			

Diarrhoea subjects affected / exposed occurrences (all)	50 / 809 (6.18%) 62		
Dry mouth subjects affected / exposed occurrences (all)	65 / 809 (8.03%) 65		
Nausea subjects affected / exposed occurrences (all)	62 / 809 (7.66%) 84		
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	42 / 809 (5.19%) 46		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 August 2021	Verified Clinical Trials (VCT) was used to monitor for patient participation in other clinical trials; Added Study Stopping Criteria and clarified study discontinuation and patient-level stopping criteria; Clarified the definition of TEAEs to be reported during the OLTP; Updated study drug supply and storage information.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported