



Clinical trial results:

A 26-week, Multicenter, Open-label, Extension Study of Aripiprazole Intramuscular Depot (OPC-14597, Lu AF41155) in Patients with Schizophrenia

Summary

EudraCT number	2012-003806-28
Trial protocol	LV
Global end of trial date	17 February 2014

Results information

Result version number	v1 (current)
This version publication date	09 April 2016
First version publication date	09 April 2016

Trial information

Trial identification

Sponsor protocol code	31-12-297
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01683058
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Otsuka Pharmaceutical Development & Commercialization, Inc.
Sponsor organisation address	2440 Research Boulevard, Rockville, Maryland, United States, 20850
Public contact	Timothy Peters-Strickland, Otsuka Pharmaceutical Development & Commercialization, +1 609-249-6559, Tim.Peters-Strickland@otsuka-us.com
Scientific contact	Timothy Peters-Strickland, Otsuka Pharmaceutical Development & Commercialization, +1 609-249-6559, Tim.Peters-Strickland@otsuka-us.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	10 May 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	17 February 2014
Global end of trial reached?	Yes
Global end of trial date	17 February 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this open-label trial was to evaluate the safety and tolerability of aripiprazole intramuscular (IM) depot administered for 26 weeks to participants with schizophrenia.

Protection of trial subjects:

The trial was conducted in compliance with the protocol, International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) Consolidated Guideline, and the applicable local laws and regulatory requirements of the countries in which the trial was conducted, copies of the protocol, amendments, and informed consent form (ICF) were reviewed and approved by the governing institutional review board (IRB) or independent ethics committee (IEC) for each investigational site or country, as appropriate, prior to trial start or prior to implementation of the amendment at that site or country.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	10 January 2013
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	Latvia: 1
Country: Number of subjects enrolled	United States: 68
Country: Number of subjects enrolled	Croatia: 5
Worldwide total number of subjects	74
EEA total number of subjects	6

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)	74

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A multicenter, open-label, single-arm rollover trial designed to demonstrate the safety of aripiprazole intramuscular (IM) depot [400 or 300 milligrams (mg)] for the acute treatment of participants with schizophrenia, who met completion criteria in the registration trial 2012-003805-86. 74 participants were enrolled in this trial.

Pre-assignment

Screening details:

Participants entered this trial after completing the Week 12/Early Termination (ET) visit of trial 2012-003805-86 as it served as the Baseline evaluations for this trial.

Period 1

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

Blinding implementation details:

This was an open-label trial.

Arms

Arm title	Aripiprazole IM Depot 400/300 mg
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Arm description:

All participants in this trial received aripiprazole IM depot 400/300 mg every 4 weeks for 24 weeks.

Arm type	Experimental
Investigational medicinal product name	Aripiprazole
Investigational medicinal product code	OPC-14597, Lu AF41155
Other name	Abilify
Pharmaceutical forms	Powder and suspension for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

All participants received aripiprazole IM depot 400 mg/ 300 mg every 4 weeks for 24 weeks.

Number of subjects in period 1	Aripiprazole IM Depot 400/300 mg
Started	74
Completed	45
Not completed	29
Consent withdrawn by subject	7
Met withdrawal criteria	5
Adverse event	6
Lost to follow-up	9
Lack of efficacy	2

Baseline characteristics

Reporting groups

Reporting group title	Aripiprazole IM Depot 400/300 mg
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Reporting group description:

All participants in this trial received aripiprazole IM depot 400/300 mg every 4 weeks for 24 weeks.

Reporting group values	Aripiprazole IM Depot 400/300 mg	Total	
Number of subjects	74	74	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	74	74	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	43		
standard deviation	± 11.7	-	
Gender categorical			
Units: Subjects			
Female	18	18	
Male	56	56	

End points

End points reporting groups

Reporting group title	Aripiprazole IM Depot 400/300 mg
Reporting group description:	
All participants in this trial received aripiprazole IM depot 400/300 mg every 4 weeks for 24 weeks.	

Primary: Percentage of participants reporting treatment emergent adverse events (TEAEs)

End point title	Percentage of participants reporting treatment emergent adverse events (TEAEs) ^[1]
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End point description:

A TEAE was defined as an AE that began after the first injection or was continuous from Baseline for serious AEs, drug-related AEs and AEs resulting in death were also reported. In safety analysis, all enrolled participants took at least one injection of aripiprazole IM depot 400/300mg in the IM depot treatment period.

End point type	Primary
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End point timeframe:

Baseline to Week 24

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: No statistical analysis was planned for Percentage of participants reporting treatment emergent adverse events (TEAEs), severe TEAEs, discontinued investigational medicinal product (IMP) due to AEs, serious TEAEs and outcome of death

End point values	Aripiprazole IM Depot 400/300 mg			
Subject group type	Reporting group			
Number of subjects analysed	74			
Units: percentage of participants				
number (not applicable)				
Participants with TEAEs	66.2			
Participants with serious TEAEs	6.8			
Participants with severe TEAEs	6.8			
Participants discontinued IMP due to AEs	8.1			
Deaths	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from Baseline in suicidal ideation intensity total score by the Columbia Suicide Severity Rating Scale (C-SSRS)

End point title	Mean change from Baseline in suicidal ideation intensity total score by the Columbia Suicide Severity Rating Scale (C-SSRS)
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End point description:

Data collected from C-SSRS were mapped into C-CASA. The Columbia Classification Algorithm of Suicide Assessment (C-CASA) method and C-SSRS(text in parentheses as said below) were mapped as; 1=

completed suicide(completed suicide); 2= suicide attempt(actual attempt); 3= preparatory actions toward imminent suicidal behavior (interrupted attempt, aborted attempt and preparatory acts/behavior); 4= suicidal ideation(wish to die, active suicidal thought, active suicidal thought with method, active suicidal thought with intent, active suicidal thought with plan/intent); 5= self-injurious behavior, intent unknown; 6= not enough information: death; 7= non-suicidal self-injurious behavior(nonsuicidal self-injurious behavior); 8= other accident; psychiatric/medical; 9= not enough information/non-death. C-CASA category 5, 6, 8 and 9 are not applicable. For each item, each participant received an intensity score from 0(none) to 5(worst). Suicidal ideation intensity total score range from 0 to 25.

End point type	Secondary
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End point timeframe:

Baseline to Week 24

End point values	Aripiprazole IM Depot 400/300 mg			
Subject group type	Reporting group			
Number of subjects analysed	74			
Units: Units on a scale				
arithmetic mean (standard deviation)				
Week 4 (N= 69)	-0.1 (± 2.3)			
Week 8 (N= 61)	-0.1 (± 2.2)			
Week 12 (N= 57)	-0.3 (± 2)			
Week 16 (N= 52)	0.7 (± 4.7)			
Week 20 (N= 44)	0.3 (± 2)			
Week 24 (N= 45)	0 (± 0)			
Last Visit (N= 71)	0.6 (± 4.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from Baseline by Week by Extrapyramidal Symptoms (EPS) evaluated using the Simpson-Angus Scale (SAS)

End point title	Mean change from Baseline by Week by Extrapyramidal Symptoms (EPS) evaluated using the Simpson-Angus Scale (SAS)
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End point description:

The EPS rating scales included SAS total score (range 10-50) was the sum of the rating scores for 10 items from the SAS panel. This scale consists of a list of 10 symptoms, each to be rated on a 5-point scale of severity. For each symptom, the rating which best described the patient's condition were, 1= gait; 2= arm dropping; 3= shoulder shaking; 4= elbow rigidity; 5= wrist rigidity; 6= head rotation; 8= tremor; 9= salivation; 10= akathisia.

End point type	Secondary
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End point timeframe:

Baseline to Week 24

End point values	Aripiprazole IM Depot 400/300 mg			
Subject group type	Reporting group			
Number of subjects analysed	72			
Units: Units on a scale				
arithmetic mean (standard deviation)				
Week 12 (N= 66)	0.19 (± 1.51)			
Week 24 (N= 70)	0.04 (± 1.62)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from Baseline by Week by EPS evaluated using the Abnormal Involuntary Movement Scale (AIMS)

End point title	Mean change from Baseline by Week by EPS evaluated using the Abnormal Involuntary Movement Scale (AIMS)
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End point description:

EPS rating scale included the AIMS movement rating score (range 0-28) was the sum of the rating scores for facial and oral movements (i.e., item 1 - 4), extremity movements (i.e. item 5 - 6), and trunk movements (i.e. item 7). The symptoms for facial and oral movements were 1= muscles of facial expression, 2= lips and perioral area, 3= jaw and 4=tongue; extremity movements were, 5= upper (arms, wrists, hands, fingers), lower (legs, knees, ankles, toes), 7= neck, shoulders, hips). This scale consisted of 10 items, each to be rated on a 4-point scale of severity, and 2 questions to be answered by yes or no. To complete the scale, the patient was observed unobtrusively at rest (e.g., in waiting room). The chair used for this examination was hard, firm one without arms.

End point type	Secondary
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End point timeframe:

Baseline to Week 24

End point values	Aripiprazole IM Depot 400/300 mg			
Subject group type	Reporting group			
Number of subjects analysed	73			
Units: Units on a scale				
arithmetic mean (standard deviation)				
Week 12 (N= 65)	-0.06 (± 0.81)			
Week 24 (N= 70)	0.07 (± 1.28)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from Baseline by Week by EPS evaluated using Barnes Akathisia Rating Scale (BARS)

End point title	Mean change from Baseline by Week by EPS evaluated using
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End point description:

The BARS global score (range 0-5) was derived from the global clinical assessment of akathisia from the BARS panel were, 0= absent; 1= questionable; 2= mild akathisia; 3= moderate akathisia; 4= marked akathisia; 5= severe akathisia. Participants were observed while they were seated and then standing (for a minimum of 2 minutes in each position). Symptoms were observed in other situations (e.g., while engaged in neutral conversation, engaged in activity on the ward) was also rated.

End point type

Secondary

End point timeframe:

Baseline to Week 24

End point values	Aripiprazole IM Depot 400/300 mg			
Subject group type	Reporting group			
Number of subjects analysed	73			
Units: Units on a scale				
arithmetic mean (standard deviation)				
Week 12 (N= 65)	0.19 (± 0.73)			
Week 24 (N= 70)	0.14 (± 0.91)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change in body temperature from Baseline in all participants.

End point title

Mean change in body temperature from Baseline in all participants.

End point description:

The body temperature, which is a vital sign parameter was one of the parameters to measure the safety and tolerability of individual participants. Last visit was defined as the last assessment visit in the treatment phase (scheduled or unscheduled visit).

End point type

Secondary

End point timeframe:

Baseline to last visit

End point values	Aripiprazole IM Depot 400/300 mg			
Subject group type	Reporting group			
Number of subjects analysed	74			
Units: °C				
arithmetic mean (standard deviation)				
Week 4 (N= 69)	0.1 (± 0.4)			
Week 8 (N= 61)	0 (± 0.4)			
Week 12 (N= 58)	0 (± 0.4)			
Week 16 (N= 53)	0 (± 0.3)			

Week 20 (N= 44)	0.1 (± 0.4)			
Week 24 (N= 45)	0.1 (± 0.4)			
Last visit (N= 72)	0 (± 0.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change in supine heart rate from Baseline in all participants.

End point title	Mean change in supine heart rate from Baseline in all participants.
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End point description:

The heart rate supine, which is a vital sign parameter was one of the parameters to measure the safety and tolerability of individual participants. Last visit was defined as the last assessment visit in the treatment phase (scheduled or unscheduled visit).

End point type	Secondary
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End point timeframe:

Baseline to last visit

End point values	Aripiprazole IM Depot 400/300 mg			
Subject group type	Reporting group			
Number of subjects analysed	74			
Units: beats per minute				
arithmetic mean (standard deviation)				
Week 4 (N= 69)	3.8 (± 10.9)			
Week 8 (N= 61)	2.3 (± 11.2)			
Week 12 (N= 58)	1.3 (± 10.8)			
Week 16 (N= 53)	4.7 (± 12)			
Week 20 (N= 44)	3.6 (± 9.8)			
Week 24 (N= 45)	1.7 (± 12.7)			
Last visit (N= 72)	3.4 (± 12.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change in supine systolic blood pressure (BP) from Baseline in all participants.

End point title	Mean change in supine systolic blood pressure (BP) from Baseline in all participants.
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End point description:

The systolic supine BP, which is a vital sign parameter was one of the parameters to measure the safety and tolerability of individual participants. Last visit was defined as the last assessment visit in the treatment phase (scheduled or unscheduled visit).

End point type	Secondary
End point timeframe:	
Baseline to last visit	

End point values	Aripiprazole IM Depot 400/300 mg			
Subject group type	Reporting group			
Number of subjects analysed	74			
Units: mmHg				
arithmetic mean (standard deviation)				
Week 4 (N= 69)	1.9 (± 12.8)			
Week 8 (N= 61)	1.3 (± 12.2)			
Week 12 (N= 58)	-0.2 (± 12.4)			
Week 16 (N= 53)	2 (± 12.4)			
Week 20 (N= 44)	4.8 (± 12.8)			
Week 24 (N= 45)	0.7 (± 11.3)			
Last visit (N= 72)	0.4 (± 13.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change in supine diastolic BP from Baseline in all participants.

End point title	Mean change in supine diastolic BP from Baseline in all participants.
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End point description:

The diastolic supine BP, which is a vital sign parameter was one of the parameters to measure the safety and tolerability of individual participants. Last visit was defined as the last assessment visit in the treatment phase (scheduled or unscheduled visit).

End point type	Secondary
End point timeframe:	
Baseline to last visit	

End point values	Aripiprazole IM Depot 400/300 mg			
Subject group type	Reporting group			
Number of subjects analysed	74			
Units: mmHg				
arithmetic mean (standard deviation)				
Week 4 (N= 69)	0.1 (± 8.6)			
Week 8 (N= 61)	-1.3 (± 8.1)			
Week 12 (N= 58)	-0.9 (± 7.7)			
Week 16 (N= 53)	0.3 (± 8.6)			
Week 20 (N= 44)	0 (± 9.6)			

Week 24 (N= 45)	0.4 (± 9.7)			
Last visit (N= 72)	0.5 (± 9.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change in sitting heart rate from Baseline in all participants.

End point title	Mean change in sitting heart rate from Baseline in all participants.
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End point description:

The heart rate sitting, which is a vital sign parameter was one of the parameters to measure the safety and tolerability of individual participants. Orthostatic assessments of blood pressure and heart rate were made after the participant was supine for at least 5 minutes and again after the participant was sitting for approximately 2 minutes. Last visit was defined as the last assessment visit in the treatment phase (scheduled or unscheduled visit).

End point type	Secondary
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End point timeframe:

Baseline to last visit

End point values	Aripiprazole IM Depot 400/300 mg			
Subject group type	Reporting group			
Number of subjects analysed	74			
Units: beats per minute				
arithmetic mean (standard deviation)				
Week 4 (N= 69)	1.2 (± 9.1)			
Week 8 (N= 61)	1.4 (± 10.1)			
Week 12 (N= 58)	-1.1 (± 10.8)			
Week 16 (N= 53)	4.3 (± 12)			
Week 20 (N= 44)	3.3 (± 10.1)			
Week 24 (N= 45)	0.6 (± 13.6)			
Last visit (N= 72)	1.9 (± 13)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change in sitting systolic BP from Baseline in all participants.

End point title	Mean change in sitting systolic BP from Baseline in all participants.
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End point description:

The systolic sitting BP, which is a vital sign parameter was one of the parameters to measure the safety and tolerability of individual participants. Orthostatic assessments of blood pressure and heart rate were made after the participant was supine for at least 5 minutes and again after the participant was sitting

for approximately 2 minutes. Last visit was defined as the last assessment visit in the treatment phase (scheduled or unscheduled visit).

End point type	Secondary
End point timeframe:	
Baseline to last visit	

End point values	Aripiprazole IM Depot 400/300 mg			
Subject group type	Reporting group			
Number of subjects analysed	74			
Units: mmHg				
arithmetic mean (standard deviation)				
Week 4 (N= 69)	-0.1 (± 13)			
Week 8 (N= 61)	-0.3 (± 11.3)			
Week 12 (N= 58)	-0.7 (± 11.3)			
Week 16 (N= 53)	1.6 (± 12.1)			
Week 20 (N= 44)	1 (± 11.5)			
Week 24 (N= 45)	-0.4 (± 12.5)			
Last visit (N= 72)	-0.7 (± 13.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change in sitting diastolic BP from Baseline in all participants.

End point title	Mean change in sitting diastolic BP from Baseline in all participants.
End point description:	
The diastolic sitting BP, which is a vital sign parameter was one of the parameters to measure the safety and tolerability of individual participants. Orthostatic assessments of blood pressure and heart rate were made after the participant was supine for at least 5 minutes and again after the participant was sitting for approximately 2 minutes. Last visit was defined as the last assessment visit in the treatment phase (scheduled or unscheduled visit).	
End point type	Secondary
End point timeframe:	
Baseline to last visit	

End point values	Aripiprazole IM Depot 400/300 mg			
Subject group type	Reporting group			
Number of subjects analysed	74			
Units: mmHg				
arithmetic mean (standard deviation)				
Week 4 (N= 69)	-0.9 (± 9.7)			

Week 8 (N= 61)	-1.7 (± 9.4)			
Week 12 (N= 58)	-0.2 (± 7.9)			
Week 16 (N= 53)	0.8 (± 7.8)			
Week 20 (N= 44)	-0.2 (± 10)			
Week 24 (N= 45)	0.4 (± 9.8)			
Last visit (N= 72)	1.4 (± 10)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change in ventricular rate from Baseline in all participants.

End point title	Mean change in ventricular rate from Baseline in all participants.
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End point description:

The measurement ventricular rate is an ECG parameter which was one of the parameters to measure the safety and tolerability of individual participants. Last visit was defined as the last assessment visit in the treatment phase (scheduled or unscheduled visit).

End point type	Secondary
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End point timeframe:

Baseline to last visit

End point values	Aripiprazole IM Depot 400/300 mg			
Subject group type	Reporting group			
Number of subjects analysed	74			
Units: beats per minute				
arithmetic mean (standard deviation)				
Week 12 (N= 56)	-1.5 (± 12)			
Week 24 (N= 43)	-1.1 (± 12.3)			
Last visit (N= 70)	-0.1 (± 13.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change in PR interval from Baseline in all participants.

End point title	Mean change in PR interval from Baseline in all participants.
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End point description:

The measurement PR interval is an ECG parameter was one of the parameters to measure the safety and tolerability of individual participants. Last visit was defined as the last assessment visit in the treatment phase (scheduled or unscheduled visit).

End point type	Secondary
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End point timeframe:

Baseline to last visit

End point values	Aripiprazole IM Depot 400/300 mg			
Subject group type	Reporting group			
Number of subjects analysed	74			
Units: msec				
arithmetic mean (standard deviation)				
Week 12 (N= 56)	3.5 (± 11.1)			
Week 24 (N= 43)	0.5 (± 12.5)			
Last visit (N= 70)	0.9 (± 11.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change in RR interval from Baseline in all participants.

End point title	Mean change in RR interval from Baseline in all participants.
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End point description:

The measurement RR interval is an ECG parameter which was one of the primary parameters to measure the safety and tolerability of individual participants. Last visit was defined as the last assessment visit in the treatment phase (scheduled or unscheduled visit).

End point type	Secondary
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End point timeframe:

Baseline to last visit

End point values	Aripiprazole IM Depot 400/300 mg			
Subject group type	Reporting group			
Number of subjects analysed	74			
Units: msec				
arithmetic mean (standard deviation)				
Week 12 (N= 56)	23.7 (± 140.9)			
Week 24 (N= 43)	23.3 (± 152.2)			
Last visit (N= 70)	8 (± 158.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change in QRS interval from Baseline in all participants.

End point title	Mean change in QRS interval from Baseline in all participants.
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End point description:

The measurement QRS interval is an ECG parameter were one of the primary parameters to measure the safety and tolerability of individual participants. Incidence of TEAEs of potential clinical relevance include abnormal changes in heart rate and ECG intervals of PR, QRS, QT, QTcB, QTcN and QTcF that were identified based on pre-defined criteria. Last visit was defined as the last assessment visit in the treatment phase (scheduled or unscheduled visit).

End point type	Secondary
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End point timeframe:

Baseline to last visit

End point values	Aripiprazole IM Depot 400/300 mg			
Subject group type	Reporting group			
Number of subjects analysed	74			
Units: Units on a scale				
arithmetic mean (standard deviation)				
Week 12 (N= 56)	-0.1 (± 5)			
Week 24 (N= 43)	0.4 (± 5.3)			
Last visit (N= 70)	0 (± 5.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change in QT interval from Baseline in all participants.

End point title	Mean change in QT interval from Baseline in all participants.
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End point description:

The measurement QT interval is an ECG parameter which was one of the parameters to measure the safety and tolerability of individual participants. Last visit was defined as the last assessment visit in the treatment phase (scheduled or unscheduled visit).

End point type	Secondary
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End point timeframe:

Baseline to last visit

End point values	Aripiprazole IM Depot 400/300 mg			
Subject group type	Reporting group			
Number of subjects analysed	74			
Units: msec				
arithmetic mean (standard deviation)				
Week 12 (N= 56)	3.1 (± 21.5)			
Week 24 (N= 43)	1.5 (± 24.9)			
Last visit (N= 70)	1 (± 25.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change in QTcB interval from Baseline in all participants.

End point title	Mean change in QTcB interval from Baseline in all participants.
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End point description:

The measurement QTcB interval is an ECG parameter which was one of the parameters to measure the safety and tolerability of individual participants. Last visit was defined as the last assessment visit in the treatment phase (scheduled or unscheduled visit).

End point type	Secondary
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End point timeframe:

Baseline to last visit

End point values	Aripiprazole IM Depot 400/300 mg			
Subject group type	Reporting group			
Number of subjects analysed	74			
Units: msec				
arithmetic mean (standard deviation)				
Week 12 (N= 56)	-1.6 (± 20.2)			
Week 24 (N= 43)	-2.4 (± 19.4)			
Last visit (N= 70)	0.3 (± 19)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change in QTcF interval from Baseline in all participants.

End point title	Mean change in QTcF interval from Baseline in all participants.
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End point description:

The measurement QTcF interval is an ECG parameter which was one of the parameters to measure the safety and tolerability of individual participants. Last visit was defined as the last assessment visit in the treatment phase (scheduled or unscheduled visit).

End point type	Secondary
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End point timeframe:

Baseline to last visit

End point values	Aripiprazole IM Depot 400/300 mg			
Subject group type	Reporting group			
Number of subjects analysed	74			
Units: msec				
arithmetic mean (standard deviation)				
Week 12 (N= 56)	-0.2 (± 13.9)			
Week 24 (N= 43)	-1.3 (± 14)			
Last visit (N= 70)	0.3 (± 12.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change in QTcN interval from Baseline in all participants.

End point title	Mean change in QTcN interval from Baseline in all participants.
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End point description:

The measurement QTcN interval is an ECG parameter which was one of the parameters to measure the safety and tolerability of individual participants. Last visit was defined as the last assessment visit in the treatment phase (scheduled or unscheduled visit).

End point type	Secondary
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End point timeframe:

Baseline to last visit

End point values	Aripiprazole IM Depot 400/300 mg			
Subject group type	Reporting group			
Number of subjects analysed	74			
Units: msec				
arithmetic mean (standard deviation)				
Week 12 (N= 56)	-0.5 (± 14.7)			
Week 24 (N= 43)	-1.7 (± 14.3)			
Last visit (N= 70)	0.3 (± 13.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change in clinically relevant body weight changes from Baseline in all participants.

End point title	Mean change in clinically relevant body weight changes from Baseline in all participants.
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End point description:

Clinically relevant body weight changes was one of the primary parameters to measure the safety and

tolerability of individual participants. Each participant's body mass index (BMI) kilogram per square meter (kg/m²) were calculated from the screening. Body weight, BMI, and waist circumference changes were evaluated by calculating mean change from Baseline and by tabulating the incidence of $\geq 7\%$ weight gain or loss. Last visit was defined as the last assessment visit in the treatment phase (scheduled or unscheduled visit).

End point type	Secondary
End point timeframe:	
Baseline to last visit	

End point values	Aripiprazole IM Depot 400/300 mg			
Subject group type	Reporting group			
Number of subjects analysed	74			
Units: kilogram(s)				
arithmetic mean (standard deviation)				
Week 12 (N= 57)	-0.1 (\pm 4.5)			
Week 24 (N= 44)	1.3 (\pm 6)			
Last visit (N= 71)	0.5 (\pm 5.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change in clinically relevant body mass index from Baseline in all participants.

End point title	Mean change in clinically relevant body mass index from Baseline in all participants.
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End point description:

Clinically relevant body mass index was one of the primary parameters to measure the safety and tolerability of individual participants. Each participant's body mass index (BMI) kilogram per square meter (kg/m²) were calculated from the screening. Body weight, BMI, and waist circumference changes were evaluated by calculating mean change from Baseline and by tabulating the incidence of $\geq 7\%$ weight gain or loss. Last visit was defined as the last assessment visit in the treatment phase (scheduled or unscheduled visit).

End point type	Secondary
End point timeframe:	
Baseline to last visit	

End point values	Aripiprazole IM Depot 400/300 mg			
Subject group type	Reporting group			
Number of subjects analysed	74			
Units: Kg/m ²				
arithmetic mean (standard deviation)				
Week 12 (N= 57)	0 (\pm 1.5)			
Week 24 (N= 44)	0.5 (\pm 2)			

Last visit (N= 71)	0.2 (\pm 1.9)			
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Statistical analyses

No statistical analyses for this end point

Secondary: Mean change in clinically relevant waist circumference from Baseline in all participants.

End point title	Mean change in clinically relevant waist circumference from Baseline in all participants.
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End point description:

Clinically relevant waist circumference was one of the primary parameters to measure the safety and tolerability of individual participants. Each participant's body mass index (BMI) kilogram per square meter (kg/m²) were calculated from the screening. Body weight, BMI, and waist circumference changes were evaluated by calculating mean change from Baseline and by tabulating the incidence of $\geq 7\%$ weight gain or loss. Last visit was defined as the last assessment visit in the treatment phase (scheduled or unscheduled visit). Only Week 24 and last visit data was included. Last visit was defined as the last assessment visit in the treatment phase (scheduled or unscheduled visit).

End point type	Secondary
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End point timeframe:

Baseline to last visit

End point values	Aripiprazole IM Depot 400/300 mg			
Subject group type	Reporting group			
Number of subjects analysed	74			
Units: centimetre				
arithmetic mean (standard deviation)				
Week 24 (N= 44)	1.6 (\pm 6.6)			
Last visit (N= 64)	1.3 (\pm 6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with clinically relevant laboratory values.

End point title	Number of participants with clinically relevant laboratory values.
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End point description:

The laboratory values were one of the parameters to measure the safety and tolerability of individual participants. Incidence of TEAEs of potential clinical relevance include abnormal values in serum chemistry, hematology, urinalyses and prolactin tests that were identified based on pre-defined criteria. Last visit was defined as the last assessment visit in the treatment phase (scheduled or unscheduled visit). There were no clinically relevant findings with regard to laboratory values reported in this study.

End point type	Secondary
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End point timeframe:

Baseline to last visit

End point values	Aripiprazole IM Depot 400/300 mg			
Subject group type	Reporting group			
Number of subjects analysed	74			
Units: participants				
number (not applicable)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with clinically relevant physical examination.

End point title	Number of participants with clinically relevant physical examination.
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End point description:

The physical examination evaluation was one of the parameters to measure the safety and tolerability of individual participants. Incidence of TEAEs of potential clinical relevance include abnormal changes in the following body systems: head, ears, eyes, nose, and throat; thorax; abdomen; urogenital; extremities; neurological; and skin and mucosae. Last visit was defined as the last assessment visit in the treatment phase (scheduled or unscheduled visit). None of the abnormalities or findings were noted during physical examination were considered clinically relevant.

End point type	Secondary
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End point timeframe:

Baseline to last visit

End point values	Aripiprazole IM Depot 400/300 mg			
Subject group type	Reporting group			
Number of subjects analysed	74			
Units: participants				
number (not applicable)	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs were recorded from the time the ICF was signed until follow-up for safety 14 (± 2) days after the last trial visit.

Adverse event reporting additional description:

A SAE was any untoward medical occurrence that results in death or was life-threatening or required inpatient hospitalization or prolonged hospitalization. An AE was an exacerbation of an existing problem or any new problem, experienced by a participant when enrolled in a trial, whether or not it was considered drug related by the study physician.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	16.0
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Reporting groups

Reporting group title	Aripiprazole IM depot 400/300 mg
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Reporting group description:

All participants in this trial received aripiprazole IM depot 400/300 mg every 4 weeks for over 24 weeks.

Serious adverse events	Aripiprazole IM depot 400/300 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 74 (6.76%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	1 / 74 (1.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Depression			
subjects affected / exposed	2 / 74 (2.70%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Schizophrenia			
subjects affected / exposed	2 / 74 (2.70%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Suicidal ideation			

subjects affected / exposed	1 / 74 (1.35%)		
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	Aripiprazole IM depot 400/300 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	40 / 74 (54.05%)		
Investigations			
Weight decreased			
subjects affected / exposed	6 / 74 (8.11%)		
occurrences (all)	6		
Weight increased			
subjects affected / exposed	22 / 74 (29.73%)		
occurrences (all)	23		
Nervous system disorders			
Akathisia			
subjects affected / exposed	9 / 74 (12.16%)		
occurrences (all)	10		
Headache			
subjects affected / exposed	6 / 74 (8.11%)		
occurrences (all)	6		
Metabolism and nutrition disorders			
Hyperlipidaemia			
subjects affected / exposed	4 / 74 (5.41%)		
occurrences (all)	5		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 September 2012	The changes in this amendment were made to reflect the updates to Protocol 31-12-291 (Trial 2012-003805-86) which eliminated an Interim Analysis. This change required trial 2012-003806-28 remove references to participants who were discontinued from Trial 2012-003805-86 due to a positive interim analysis. General revisions to the protocol were; added Lundbeck Protocol Number Lu AF41155 to cover page and synopsis and made minor formatting corrections.
12 October 2012	The change in this amendment was made to reflect the correction to needle gauge based on Body Mass Index (BMI). General revisions were made to this protocol such as; Deleted all reference to needle: 21 gauge, 1.5 inch for BMI ≤ 28 kg/m ² participants in the active treatment phase of Trial 2012-003805-86 who were discontinued from that trial due to a positive interim analysis (IA), changed text to needle: 22 gauge, 1.5 inch for BMI ≤ 28 and minor formatting corrections.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported