



## Clinical trial results:

### A 28-week, randomised, open-label study evaluating the effectiveness of aripiprazole once-monthly versus paliperidone palmitate in adult patients with schizophrenia

#### Summary

EudraCT number	2012-002785-12
Trial protocol	SE IT DE ES CZ EE GB
Global end of trial date	29 September 2014

#### Results information

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

#### Trial information

##### Trial identification

Sponsor protocol code	14724A
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01795547
WHO universal trial number (UTN)	-

Notes:

##### Sponsors

Sponsor organisation name	H. Lundbeck
Sponsor organisation address	Ottliavej 9, Valby, Denmark, 2500
Public contact	LundbeckClinicalTrials@lundbeck.com, H. Lundbeck A/S, +45 36301311, , LundbeckClinicalTrials@lundbeck.com
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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	29 September 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	29 September 2014
Global end of trial reached?	Yes
Global end of trial date	29 September 2014
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

To assess the effectiveness of aripiprazole once-monthly in the maintenance treatment of patients with a diagnosis of schizophrenia as defined by the Diagnostic and Statistical Manual of Mental Disorders, 4th edition, Text Revision (DSM-IV-TR®), in a naturalistic care setting by comparing it to an existing long-acting antipsychotic, paliperidone palmitate

Protection of trial subjects:

The trial was conducted in accordance with the Declaration of Helsinki (2008) and ICH Good Clinical Practice (1996)

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	28 February 2013
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	Spain: 38
Country: Number of subjects enrolled	Sweden: 8
Country: Number of subjects enrolled	United Kingdom: 1
Country: Number of subjects enrolled	Czech Republic: 28
Country: Number of subjects enrolled	Estonia: 30
Country: Number of subjects enrolled	Germany: 31
Country: Number of subjects enrolled	Italy: 32
Country: Number of subjects enrolled	United States: 100
Country: Number of subjects enrolled	Canada: 12
Country: Number of subjects enrolled	France: 15
Worldwide total number of subjects	295
EEA total number of subjects	183

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)	295
From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Subjects who met each of the inclusion and none of the exclusion criteria were eligible to participate in the study

### Period 1

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

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Aripiprazol

Arm description:

Aripiprazole and aripiprazole once-monthly: Oral aripiprazole tablets according to Summary of Product Characteristics (SmPC)/United States Prescription Information (USPI) daily for 4 weeks followed by the 1st aripiprazole intramuscular (IM) injection. Oral tablets was taken for 2 more weeks after the 1st injection. Additional injections every 4 weeks until Week 24

Arm type	Experimental
Investigational medicinal product name	Aripiprazole (tablet)
Investigational medicinal product code	
Other name	Abilify
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

5 to 30 mg/day during three week Oral Conversion. Followed by one week 10-30 mg/day. Then 400 mg injection followed by two weeks with 10-20 mg/day (5, 10, and 15 mg tablets, orally. )

Investigational medicinal product name	Aripiprazole (injection)
Investigational medicinal product code	
Other name	Abilify
Pharmaceutical forms	Powder and solvent for prolonged-release suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

400 and 300 mg every 4 weeks (once-monthly). Total 6 times total during week 5 to 28

<b>Arm title</b>	Paliperidone
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Arm description:

Paliperidone and paliperidone palmitate: Oral paliperidone tablets according to SmPC/USPI daily for 3 weeks followed by paliperidone palmitate IM injections every 4 weeks with last dose at Week 24 according to SmPC/USPI

Arm type	Experimental
Investigational medicinal product name	Paliperidone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

3 to 12 mg/day during three week Oral Conversion. (3, 6, and 9 mg tablets, orally. )

Investigational medicinal product name	Paliperidone (injection)
Investigational medicinal product code	
Other name	Xeplion®, Invega®, Sustenna®
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

150 mg and 300 mg every 4 weeks (once-monthly). Total 6 times total during week 5 to 28

<b>Number of subjects in period 1</b>	Aripiprazol	Paliperidone
Started	148	147
Treated	144	137
Completed	100	83
Not completed	48	64
non-compliance with IMP	1	1
Consent withdrawn by subject	7	12
not treated	4	10
Others	4	1
Adverse event, non-fatal	16	27
Lost to follow-up	2	5
Not stated	-	1
Lack of efficacy	8	3
Protocol deviation	6	4

## Baseline characteristics

### Reporting groups

Reporting group title	Aripiprazol
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Reporting group description:

Aripiprazole and aripiprazole once-monthly: Oral aripiprazole tablets according to Summary of Product Characteristics (SmPC)/United States Prescription Information (USPI) daily for 4 weeks followed by the 1st aripiprazole intramuscular (IM) injection. Oral tablets was taken for 2 more weeks after the 1st injection. Additional injections every 4 weeks until Week 24

Reporting group title	Paliperidone
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Reporting group description:

Paliperidone and paliperidone palmitate: Oral paliperidone tablets according to SmPC/USPI daily for 3 weeks followed by paliperidone palmitate IM injections every 4 weeks with last dose at Week 24 according to SmPC/USPI

Reporting group values	Aripiprazol	Paliperidone	Total
Number of subjects	148	147	295
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)	148	147	295
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	42.6	41	
standard deviation	± 10.83	± 10.87	-
Gender categorical			
Units: Subjects			
Female	59	59	118
Male	89	88	177
Race			
Units: Subjects			
Asian	1	3	4
White	102	102	204
American Indian or Alaska Native	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	44	38	82
More than one race	0	0	0
Unknown or Not Reported	1	4	5

## End points

### End points reporting groups

Reporting group title	Aripiprazol
Reporting group description: Aripiprazole and aripiprazole once-monthly: Oral aripiprazole tablets according to Summary of Product Characteristics (SmPC)/United States Prescription Information (USPI) daily for 4 weeks followed by the 1st aripiprazole intramuscular (IM) injection. Oral tablets was taken for 2 more weeks after the 1st injection. Additional injections every 4 weeks until Week 24	
Reporting group title	Paliperidone
Reporting group description: Paliperidone and paliperidone palmitate: Oral paliperidone tablets according to SmPC/USPI daily for 3 weeks followed by paliperidone palmitate IM injections every 4 weeks with last dose at Week 24 according to SmPC/USPI	

### Primary: Change From Baseline to Week 28 in Quality of Life Scale (QLS) Total Score

End point title	Change From Baseline to Week 28 in Quality of Life Scale (QLS) Total Score
End point description: The QLS is a clinician-rated scale designed to assess deficit symptoms of schizophrenia and functioning during the preceding 4 weeks. The QLS consists of 21 items in 4 domains: Interpersonal Relations (eight items), Instrumental Role (four items), Intrapsychic Foundations (seven items), and Common Objects and Activities (two items). Each item was rated on a 7-point scale, from 0 (severe impairment) to 6 (normal or unimpaired functioning). Definitions were provided for 4 anchor points of the 7 points. Each item had a brief description of the judgement to be made and a set of suggested probes for the clinician. The total score was calculated as the sum of all 21 items giving a range of 0 to 126, where the higher score indicated normal or unimpaired functioning.	
End point type	Primary
End point timeframe: Baseline to Week 28	

End point values	Aripiprazol	Paliperidone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	136	132		
Units: units on a scale				
least squares mean (standard error)	7.47 ( $\pm$ 1.53)	2.8 ( $\pm$ 1.62)		

### Statistical analyses

Statistical analysis title	Aripiprazol vs Paliperidone
Comparison groups	Aripiprazol v Paliperidone

Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	other <sup>[1]</sup>
P-value	= 0.036
Method	Mixed models analysis
Parameter estimate	Least Squares Mean Difference
Point estimate	4.666
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.316
upper limit	9.015

Notes:

[1] - Non-inferiority of the primary endpoint was considered confirmed if the lower bound of the 2-sided 95% CI at Week 28 was > -5 or equivalently if the p-value for the 1-sided test of H0: D ≤ -5 against H1: D > -5 was ≤ 2.5%, where D was the mean treatment difference (aripiprazole minus paliperidone). Superiority was then tested as pre-specified with the FAS and demonstrated for aripiprazole over paliperidone, since the lower bound of the 95% CI was >0

### Secondary: Investigator's Assessment Questionnaire (IAQ) Total Score at Week 28

End point title	Investigator's Assessment Questionnaire (IAQ) Total Score at Week 28
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End point description:

The IAQ is a clinician-rated scale designed to assess the relative effectiveness (efficacy, safety and tolerability) of antipsychotic medications in patients with schizophrenia or schizoaffective disorder. The IAQ consists of 12 items: positive symptoms, negative symptoms, other efficacy symptoms, cognition, energy, mood, somnolence, weight gain, signs and symptoms of prolactin elevation, akathisia, EPS (other than akathisia) and other safety or tolerability issues. For each item, the current medication was compared with previous antipsychotic medication on a five-point scale from 1 (Much better) to 5 (Much worse), or that item is Not applicable. The sum of the 12 items ranged from 12 (the current medication was much better than previous antipsychotic medication) to 60 (the current medication was much worse than previous antipsychotic medication).

End point type	Secondary
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End point timeframe:

Week 28

End point values	Aripiprazol	Paliperidone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	133	131		
Units: units on a scale				
least squares mean (standard error)	32.32 (± 0.52)	33.81 (± 0.55)		

### Statistical analyses

Statistical analysis title	Aripiprazol vs Paliperidone
Comparison groups	Aripiprazol v Paliperidone

Number of subjects included in analysis	264
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.043
Method	Mixed models analysis
Parameter estimate	Least Squares Mean Difference
Point estimate	-1.492
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.935
upper limit	-0.049

### Secondary: Change From Baseline to Week 28 in CGI-S Score

End point title	Change From Baseline to Week 28 in CGI-S Score
End point description:	
Clinical Global Impression - Severity of Illness (CGI-S) score provides the clinician's impression of the patient's current state of mental illness. The clinician uses his or her clinical experience of this patient population to rate the severity of the patient's current mental illness on a 7-point scale ranging from 1 (normal - not at all ill) to 7 (among the most extremely ill patients).	
End point type	Secondary
End point timeframe:	
Baseline, Week 28	

End point values	Aripiprazol	Paliperidone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	136	132		
Units: units on a scale				
least squares mean (standard error)	-0.75 (± 0.07)	-0.46 (± 0.07)		

### Statistical analyses

<b>Statistical analysis title</b>	Aripiprazol vs Paliperidone
Comparison groups	Aripiprazol v Paliperidone
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.004
Method	Mixed models analysis
Parameter estimate	Least Squares Mean Difference
Point estimate	-0.283

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.477
upper limit	-0.09

### Secondary: Change From Baseline to Week 28 in the 'Common Objects and Activities' QLS Domain Score

End point title	Change From Baseline to Week 28 in the 'Common Objects and Activities' QLS Domain Score
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End point description:

The QLS is a clinician-rated scale designed to assess deficit symptoms of schizophrenia and functioning during the preceding 4 weeks. The QLS consists of 21 items in 4 domains: Interpersonal Relations (eight items), Instrumental Role (four items), Intrapsychic Foundations (seven items), and Common Objects and Activities (two items). Each item was rated on a 7-point scale, from 0 (severe impairment) to 6 (normal or unimpaired functioning). The Common Objects and Activities domain score was calculated as the sum of 2 items (numbers 18 and 19) giving a range of 0 to 12, where the higher score indicated less unimpaired functioning

End point type	Secondary
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End point timeframe:

Baseline, Week 28

End point values	Aripiprazol	Paliperidone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	136	132		
Units: units on a scale				
least squares mean (standard error)	0.52 ( $\pm$ 0.16)	0.18 ( $\pm$ 0.17)		

### Statistical analyses

<b>Statistical analysis title</b>	Aripiprazol vs Paliperidone
Comparison groups	Aripiprazol v Paliperidone
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.149
Method	Mixed models analysis
Parameter estimate	Least Squares Mean Difference
Point estimate	0.331
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.12
upper limit	0.782

## Secondary: Change From Baseline to Week 28 in the 'Intrapsychic Foundations' QLS Domain Score

End point title	Change From Baseline to Week 28 in the 'Intrapsychic Foundations' QLS Domain Score
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### End point description:

The QLS is a clinician-rated scale designed to assess deficit symptoms of schizophrenia and functioning during the preceding 4 weeks. The QLS consists of 21 items in 4 domains: Interpersonal Relations (eight items), Instrumental Role (four items), Intrapsychic Foundations (seven items), and Common Objects and Activities (two items). Each item was rated on a 7-point scale, from 0 (severe impairment) to 6 (normal or unimpaired functioning). The Intrapsychic Foundations domain score was calculated as the sum of 7 items (numbers 13 to 17 and 20 and 21) giving a range of 0 to 42, where the higher score indicated less unimpaired functioning.

End point type	Secondary
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### End point timeframe:

Baseline, Week 28

End point values	Aripiprazol	Paliperidone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	136	132		
Units: units on a scale				
least squares mean (standard error)	2.25 ( $\pm$ 0.59)	0.5 ( $\pm$ 0.63)		

## Statistical analyses

<b>Statistical analysis title</b>	Aripiprazol vs Paliperidone
Comparison groups	Aripiprazol v Paliperidone
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.039
Method	Mixed models analysis
Parameter estimate	Least Squares Mean Difference
Point estimate	1.753
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.093
upper limit	3.412

## Secondary: Change From Baseline to Week 28 in the 'Interpersonal Relations' QLS Domain Score

End point title	Change From Baseline to Week 28 in the 'Interpersonal
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## End point description:

The QLS is a clinician-rated scale designed to assess deficit symptoms of schizophrenia and functioning during the preceding 4 weeks. The QLS consists of 21 items in 4 domains: Interpersonal Relations (eight items), Instrumental Role (four items), Intrapsychic Foundations (seven items), and Common Objects and Activities (two items). Each item was rated on a 7-point scale, from 0 (severe impairment) to 6 (normal or unimpaired functioning). The Interpersonal Relations domain score was calculated as the sum of 8 items (numbers 1 to 8) giving a range of 0 to 48, where the higher score indicated less unimpaired functioning

End point type	Secondary
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End point timeframe:

Baseline, Week 28

End point values	Aripiprazol	Paliperidone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	136	132		
Units: units on a scale				
least squares mean (standard error)	3.24 ( $\pm$ 0.68)	1.47 ( $\pm$ 0.72)		

**Statistical analyses**

Statistical analysis title	Aripiprazol vs Paliperidone
Comparison groups	Aripiprazol v Paliperidone
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.07
Method	Mixed models analysis
Parameter estimate	Least Squares Mean Difference
Point estimate	1.764
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.143
upper limit	3.672

**Secondary: Change From Baseline to Week 28 in the 'Instrumental Role' QLS Domain Score**

End point title	Change From Baseline to Week 28 in the 'Instrumental Role' QLS Domain Score
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## End point description:

The QLS is a clinician-rated scale designed to assess deficit symptoms of schizophrenia and functioning during the preceding 4 weeks. The QLS consists of 21 items in 4 domains: Interpersonal Relations (eight items), Instrumental Role (four items), Intrapsychic Foundations (seven items), and Common Objects and Activities (two items). Each item was rated on a 7-point scale, from 0 (severe impairment) to 6 (normal or unimpaired functioning). The Instrumental Role domain score was calculated as the sum of 4 items (numbers 9 to 12) giving a range of 0 to 24, where the higher score indicated less unimpaired

functioning.

End point type	Secondary
End point timeframe:	
Baseline, Week 28	

<b>End point values</b>	Aripiprazol	Paliperidone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	136	132		
Units: units on a scale				
least squares mean (standard error)	1.76 ( $\pm$ 0.42)	0.83 ( $\pm$ 0.45)		

### Statistical analyses

<b>Statistical analysis title</b>	Aripiprazol vs Paliperidone
Comparison groups	Aripiprazol v Paliperidone
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.13
Method	Mixed models analysis
Parameter estimate	Least Squares Mean Difference
Point estimate	0.922
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.275
upper limit	2.119

### Secondary: Change From Baseline to Week 28 in SWN-S Total Score

End point title	Change From Baseline to Week 28 in SWN-S Total Score
End point description:	
	The SWN-S is a patient-rated scale designed to measure subjective effects of neuroleptic drugs to psychopathology, quality of life, and compliance over the past 7 days. The 20 items (10 positive and 10 negative statements) are grouped in 5 subscales (mental functioning, self-control, physical functioning, emotional regulation and social integration). Each subscale contains 4 items. Each item was rated on a six-point Likert scale, from not at all to very much. A score was calculated for each subscale, and the total score ranged from 20 to 120, where the higher score indicated better well-being.
End point type	Secondary
End point timeframe:	
Baseline, Week 28	

<b>End point values</b>	Aripiprazol	Paliperidone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	136	132		
Units: units on a scale				
least squares mean (standard error)	4.82 ( $\pm$ 1.24)	3.81 ( $\pm$ 1.31)		

### Statistical analyses

<b>Statistical analysis title</b>	Aripiprazol vs Paliperidone
Comparison groups	Aripiprazol v Paliperidone
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.561
Method	Mixed models analysis
Parameter estimate	Least Squares Mean Difference
Point estimate	1.007
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.402
upper limit	4.417

### Secondary: Change From Baseline to Week 28 in the Tool Total Score

End point title	Change From Baseline to Week 28 in the Tool Total Score
End point description:	Tolerability and Quality of Life (Tool) is a patient-rated scale developed to measure the impact of side-effects on the quality of life in patients treated with antipsychotic medication. The Tool consists of 8 domains: mood (worry-upset), function capabilities, fatigue-weakness, weight gain, stiffness-tremor, physical restlessness, sexual dysfunction, and dizziness-nausea. Each domain was rated on a four-point scale from 1 (no impact) to 4 (maximum impact). Total scores ranged from 8 (no impact) to 32 (maximum impact).
End point type	Secondary
End point timeframe:	Baseline, Week 28

<b>End point values</b>	Aripiprazol	Paliperidone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	136	132		
Units: units on a scale				
least squares mean (standard error)	-1.75 ( $\pm$ 0.3)	-1.05 ( $\pm$ 0.32)		

## Statistical analyses

<b>Statistical analysis title</b>	Aripiprazol vs Paliperidone
Comparison groups	Aripiprazol v Paliperidone
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.095
Method	Mixed models analysis
Parameter estimate	Least Squares Mean Difference
Point estimate	-0.695
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.511
upper limit	0.121

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

First dose to follow-up

Assessment type	Non-systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	16.1
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### Reporting groups

Reporting group title	PALIPERIDONE
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Reporting group description:

PALIPERIDONE

Reporting group title	ARIPIPRAZOLE
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Reporting group description:

ARIPIPRAZOLE

<b>Serious adverse events</b>	PALIPERIDONE	ARIPIPRAZOLE	
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 137 (7.30%)	12 / 144 (8.33%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Nasopharyngeal cancer			
subjects affected / exposed	1 / 137 (0.73%)	0 / 144 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Head injury			
subjects affected / exposed	1 / 137 (0.73%)	0 / 144 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intentional overdose			
subjects affected / exposed	0 / 137 (0.00%)	1 / 144 (0.69%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			

Cirrhosis alcoholic subjects affected / exposed	1 / 137 (0.73%)	0 / 144 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 137 (0.73%)	0 / 144 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Psychotic disorder			
subjects affected / exposed	4 / 137 (2.92%)	5 / 144 (3.47%)	
occurrences causally related to treatment / all	3 / 4	2 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Schizophrenia			
subjects affected / exposed	1 / 137 (0.73%)	5 / 144 (3.47%)	
occurrences causally related to treatment / all	1 / 1	3 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicidal ideation			
subjects affected / exposed	0 / 137 (0.00%)	1 / 144 (0.69%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Gastroenteritis viral			
subjects affected / exposed	1 / 137 (0.73%)	0 / 144 (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 %

<b>Non-serious adverse events</b>	<b>PALIPERIDONE</b>	<b>ARIPIPRAZOLE</b>	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	74 / 137 (54.01%)	65 / 144 (45.14%)	
Investigations			

Weight increased subjects affected / exposed occurrences (all)	19 / 137 (13.87%) 21	13 / 144 (9.03%) 13	
Injury, poisoning and procedural complications Accidental overdose subjects affected / exposed occurrences (all)	13 / 137 (9.49%) 15	30 / 144 (20.83%) 37	
Nervous system disorders Dizziness subjects affected / exposed occurrences (all)  Akathisia subjects affected / exposed occurrences (all)  Headache subjects affected / exposed occurrences (all)  Somnolence subjects affected / exposed occurrences (all)	12 / 137 (8.76%) 12  6 / 137 (4.38%) 8  11 / 137 (8.03%) 12  8 / 137 (5.84%) 8	5 / 144 (3.47%) 5  8 / 144 (5.56%) 10  3 / 144 (2.08%) 3  9 / 144 (6.25%) 10	
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all)  Injection site pain subjects affected / exposed occurrences (all)	7 / 137 (5.11%) 8  11 / 137 (8.03%) 14	4 / 144 (2.78%) 5  4 / 144 (2.78%) 4	
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all)	8 / 137 (5.84%) 9	3 / 144 (2.08%) 3	
Psychiatric disorders Anxiety subjects affected / exposed occurrences (all)  Insomnia	12 / 137 (8.76%) 13	8 / 144 (5.56%) 9	

subjects affected / exposed occurrences (all)	17 / 137 (12.41%) 19	17 / 144 (11.81%) 21	
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	8 / 137 (5.84%) 9	6 / 144 (4.17%) 6	

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 September 2013	Adjustment of the study design (including the addition of up to 2 further cohorts and therefore a change in the number of subjects planned) to explore and better define the safety window of Lu AF34134  Timing of Change: Prior to Cohort 5

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported