EU Clinical Trials Register

Clinical trial results:
Aripiprazol Addon – Treatment to improve cognitive function in bipolar disorder (Cognitive impairment in bipolar disorder treated with aripiprazole)

Summary

EudraCT number	2009-017581-22
Trial protocol	DE
Global end of trial date	31 December 2013

Results information

Result version number	v1 (current)
This version publication date	18 December 2021
First version publication date	18 December 2021

Trial information

Trial identification

Sponsor protocol code	20091003

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Charité - Universitätsmedizin Berlin
Sponsor organisation address	Charitéplatz 1, Berlin , Germany, 10117
Public contact	PD Dr. med. Mazda Adli, Charité - Universitätsmedizin Berlin, +49 30 450 517146, mazda.adli@charite.de
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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	31 December 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 December 2013
Global end of trial reached?	Yes
Global end of trial date	31 December 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To improve baseline cognitive functioning regarding verbal memory by 12 weeks aripiprazole add-on therapy in bipolar, euthymic patients.

Protection of trial subjects:

No SAE and no SUSAR occurred. An impairment of the safety of the subjects in the sense of a risk-benefit analysis cannot be assumed.

Background therapy: -	
Evidence for comparator: -	
Actual start date of recruitment	27 January 2011
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	Germany: 62
Worldwide total number of subjects	62
EEA total number of subjects	62

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)	6
Adults (18-64 years)	56
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at study centers Charité-UnversitätsmedizinKlinik für Psychiatrie und Psychotherapie in Germany, between 27/01/2011 and 28/02/2013.

Pre-assignment

Screening details:

A total of 44 subjects entered the screening period according the inclusion criteria for Bipolar disorder (Bipolar I+II patients , Euthymic interval for at least 6 months,HAMD-21 < 10 and YMRS < 12, subjectively reported neurocognitive impairment, assessed by FEDA. N= 3 sreening failures
N= 21 healthy control group match to the patient group

Period 1

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

Blinding implementation details:

N/A

Arms

Are arms mutually exclusive?	Yes
Arm title	Aripiprazol Group

Arm description:

Subjects received up to 15 mg of Aripiprazol

Arm type	Experimental
Investigational medicinal product name	Aripiprazol
Investigational medicinal product code	N 05 AX 12
Other name	Abilify
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

daily, duration 12 weeks, three dosage units are available for this study (5mg, 10mg, 15mg) depending on weight

Arm title	Control group

Arm description:

21 healthy control subjects were included in the study. The control group was matched to the patient group in age and sex in parallel .

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 1	Aripiprazol Group	Control group
Started	41	21
Completed	21	21
Not completed	20	0
Consent withdrawn by subject	9	-
Adverse event, non-fatal	9	-

Protocol deviation	2	-

Baseline characteristics

Reporting groups

Reporting group title	Aripiprazol Group
Reporting group description:	
Subjects received up to 15 mg of Aripiprazol	
Reporting group title	Control group
Reporting group description:	
21 healthy control subjects were included in the study. The control group was matched to the patient group in age and sex in parallel .	

Reporting group values	Aripiprazol Group	Control group	Total
Number of subjects	41	21	62
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)	6	0	6
Adults (18-64 years)	35	21	56
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	26.2	26.2	
full range (min-max)	12 to 52	18 to 60	-
Gender categorical			
Units: Subjects			
Female	22	11	33
Male	19	10	29
Status			
Sociodemographic Data			
Units: Subjects			
single	13	6	19
married living together	13	13	26
married living separated	2	0	2
living together in partnership	2	1	3
divorced	3	1	4
n/a	8	0	8
High school degree			
Units: Subjects			
Highschool	2	0	2
O-Level	7	4	11
A-Level	25	17	42
n/a	7	0	7
Highest professional qualification			

Units: Subjects			
Apprenticeship	12	3	15
Technical school	3	2	5
College / University	17	12	29
Not yet finished	1	0	1
No qualification	1	4	5
n/a	7	0	7

Current professional situation
Units: Subjects

employed, fulltime	10	13	23
employed, part-time	5	3	8
Housewife /-man, not employed	3	0	3
Protected employment	1	0	1
unemployed	3	1	4
Occupational/disability pension, Pension procedure	7	0	7
Retirement pension/ pension	1	0	1
Pupil / student	2	3	5
Training/ Apprenticeship	1	1	2
n/a	8	0	8

Netto income / month in Euro
Units: Subjects

less than 500	7	2	9
500-1000	6	3	9
1000-2000	11	5	16
2000-3000	5	7	12
3000-5000	2	4	6
more than 5000	1	0	1
n/a	9	0	9

Number of episodes: total
Units: Scale

arithmetic mean	12.4	0	
standard deviation	± 8.56	± 0	-

Number of episodes: depressive
Units: Scale

arithmetic mean	7.0	0	
standard deviation	± 5.29	± 0	-

Number of episodes: manic
Units: Scale

arithmetic mean	2.9	0	
standard deviation	± 2.33	± 0	-

Number of episodes: mixed
Units: Scale

arithmetic mean	1.2	0	
standard deviation	± 2.04	± 0	-

Number of episodes: sub depressive
Units: Scale

arithmetic mean	0.1	0	
standard deviation	± 0.49	± 0	-

Number of episodes: hypomanic
Units: Scale

arithmetic mean	3.5	0	

standard deviation	± 4.23	± 0	-
HAMD			
Hamilton rating scale for depression			
Units: Score			
arithmetic mean	3.7	0	
standard deviation	± 3.42	± 0	-
YMRS			
Young Mania Rating Scale			
Units: Score			
arithmetic mean	0.9	0	
standard deviation	± 1.72	± 0	-
FAST total score			
Functional Arm Scale for Throwers			
Units: Score			
arithmetic mean	22.30	0	
standard deviation	± 12.32	± 0	-
CSS total score			
calibrated severity scores			
Units: Score			
arithmetic mean	20.00	0	
standard deviation	± 16.38	± 0	-

End points

End points reporting groups

Reporting group title	Aripiprazol Group
Reporting group description:	
Subjects received up to 15 mg of Aripiprazol	
Reporting group title	Control group
Reporting group description:	
21 healthy control subjects were included in the study. The control group was matched to the patient group in age and sex in parallel .	

Primary: Change in verbal memory function measured with California Verbal Learning Test

End point title	Change in verbal memory function measured with California Verbal Learning Test
End point description:	
Regarding to the primary hypothesis, there were no significant differences between patient and control group in declarative verbal memory on the scales Absolute recall performance after temporal delay, loss after interference as well as loss after time delay (See attachment table 14 and figure 4 for more details). Even after 12 weeks of treatment with aripiprazole, no improvement was observed with regard to verbal memory.	
End point type	Primary
End point timeframe:	
12 Weeks	

End point values	Aripiprazol Group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	21		
Units: Score				
number (not applicable)				
Total score	52.9	54.7		
Absolute recall performance after temporal delay	12.3	10.7		
Loss after interference	1.9	4.8		
Loss after time delay	1.7	2.5		

Attachments (see zip file)	Table 14 and Figure 4/Tables and Figures from the report.pdf

Statistical analyses

Statistical analysis title	Comparison of the Auditory Verbal Learning Test
Statistical analysis description:	
The collected data were analyzed according to the intention-to-treat principle. The statistical analyses were calculated by SPSS. Group differences were calculated by using T-tests for independent samples and analyses of variance.	

Comparison groups	Aripiprazol Group v Control group
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	> 0.2
Method	t-test, 2-sided

Secondary: the psychosocial functioning level: FAST

End point title	the psychosocial functioning level: FAST

End point description:

The psychosocial functioning level of the patient group differs significantly from the healthy control group on all scales (cognitive and professional functioning, independence, financial affairs, interpersonal relationships, spare time). For further detailed results see attachment, table 8 and figur 1.

End point type	Secondary

End point timeframe:

12 weeks

End point values	Aripiprazol Group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	21		
Units: Score				
number (not applicable)				
Total score	22.3	5.7		
Scale_cognitive function	5.6	2.2		
Scale_professionial function	6.4	0.7		
Scale_independence	2.1	0.6		
Scale_financial affairs	1.2	0.3		
Scale_interpersonal relationships	5.7	1.3		
Scale_spare time	2.6	0.5		

Attachments (see zip file)	Tables and Figures/Tables and Figures from the report.pdf

Statistical analyses

No statistical analyses for this end point

Secondary: the neuropsychological examination: FEDA

End point title	the neuropsychological examination: FEDA

End point description:

The subjective perception of attention and memory performance measured by FEDA shows a difference between the patient and control groups. The group difference is significant on all three scales (cognition, fatigue, motivation)

End point type	Secondary

End point values	Aripiprazol Group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	21		
Units: Score				
number (not applicable)				
Total score	96.6	122.6		
Scale cognition	45.9	57.3		
Scale fatigue	28.4	36.9		
Scale motivation	20.1	27.8		

Attachments (see zip file)	Table 9 and Figure 2/Tables and Figures from the report.pdf

Statistical analyses

Statistical analysis title	Comparison of mean values of the scales of the FED

Statistical analysis description:

The collected data were analyzed according to the intention-to-treat principle. The statistical analyses were calculated by SPSS. Group differences were calculated by using T-tests for independent samples and analyses of variance.

Comparison groups	Aripiprazol Group v Control group
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.01
Method	t-test, 2-sided

Secondary: Alsterdorfer Face Test

End point title	Alsterdorfer Face Test

End point description:

There was no significant difference between patient and control groups for direct retrieval, delayed retrieval after direct retrieval, or no direct retrieval in face recognition (see Table 10, Figure 3 for more informations).

End point type	Secondary

End point timeframe:

12 Weeks

End point values	Aripiprazol Group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	21		
Units: Score				
number (not applicable)				
Direct recall	67.9	67.6		
Delayed recall after direct recall	56.8	59.3		
Delayed recall without direct recall	48.9	47.4		

Attachments (see zip file)	Table and Figure/Tables and Figures from the report.pdf

Statistical analyses

No statistical analyses for this end point

Secondary: Regensburger Word Fluency Test

End point title	Regensburger Word Fluency Test

End point description:

Mean comparisons in terms of word fluency, assessed with the Regensburg Word Fluency Test, also show no group difference (see Table 12 for more informations)

End point type	Secondary

End point timeframe:

12 weeks

End point values	Aripiprazol Group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	21		
Units: Score				
number (not applicable)				
Subtest 1	18.8	20.7		
Subtest 2	19.3	20.3		

Attachments (see zip file)	Table 12.pdf

Statistical analyses

No statistical analyses for this end point

Secondary: Wechsler Adult Intelligence Scale

End point title	Wechsler Adult Intelligence Scale

End point description:

Mean analyses of the Wechsler Intelligence Test show that the patient and control groups differ

significantly. The patient group is superior to the comparison population in the subscales Number Reasoning and Number Symbol Test (for more informations see Table 13).

End point type	Secondary
End point timeframe:	
12 weeks	

End point values	Aripiprazol Group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	21		
Units: Score				
number (not applicable)				
Matrix reasoning	10.9	12.1		
Digit span	10.8	9.3		
Letter-Number Sequencing	9.1	11.7		

Attachments (see zip file)	Table 13.pdf

Statistical analyses

No statistical analyses for this end point

Secondary: Tests for Attentional Performance (TAP)

End point title	Tests for Attentional Performance (TAP)
End point description:	

TAP shows no significant difference between patient and control group (for more informations see Table 15)

End point type	Secondary
End point timeframe:	
12 weeks	

End point values	Aripiprazol Group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	21		
Units: Score				
number (not applicable)				
Working memory	619.9	527.7		
Alertness without warning signal	274.1	271.1		
Alertness with warning signal	271.1	261.3		
Flexibility total	791.6	791.1		

Attachments (see zip file)	Table 15.pdf

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:	
12 Weeks	
Adverse event reporting additional description:	
Patients discontinued the study due to ADR (1x drowsiness, 2x sleep disturbance/early awakening, 1x inner restlessness, 1x manic relapse, 1x depressive relapse, 2x visual disturbances, 1x headache and dizziness).	
Assessment type	Non-systematic

Dictionary used

Dictionary name	own
Dictionary version	1

Reporting groups

Reporting group title	Aripiprazol Group

Reporting group description: -

Serious adverse events	Aripiprazol Group		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 41 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Aripiprazol Group		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 41 (21.95%)		
Psychiatric disorders			
ADR	Additional description: Adverse Drug Reaction		
subjects affected / exposed	9 / 41 (21.95%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol?   No

Interruptions (globally)

Were there any global interruptions to the trial?   No

Limitations and caveats

 None reported