



## Clinical trial results: The Bergen Psychosis Project 2 Summary

EudraCT number	2010-022307-22
Trial protocol	NO AT
Global end of trial date	20 December 2017

### Results information

Result version number	v1 (current)
This version publication date	21 December 2021
First version publication date	21 December 2021

### Trial information

#### Trial identification

Sponsor protocol code	BergenPsychosisProject2
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#### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01446328
WHO universal trial number (UTN)	-

Notes:

#### Sponsors

Sponsor organisation name	Haukeland University Hospital
Sponsor organisation address	Jonas Liesvei 65, Bergen, Norway,
Public contact	Department of Research, Sandviken, Haukeland University Hospital, Division of Psychiatry, Department of Research, +47 55958400, erij@helse-bergen.no
Scientific contact	Department of Research, Sandviken, Haukeland University Hospital, Division of Psychiatry, Department of Research, +47 55958400, erij@helse-bergen.no

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	20 December 2017
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	20 December 2017
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

Compare the clinical effectiveness of amisulpride, aripiprazole, and olanzapine, in patients with schizophrenia and related psychotic disorders, in a head-to-head pragmatic, randomized trial funded independently of the pharmaceutical industry; and , through a translational approach, to link drug-induced changes in symptoms, neurocognitive functioning and side effects, to changes in biological substrates on neurochemical, functional and structural levels. .

Protection of trial subjects:

None

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 June 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	Norway: 24
Country: Number of subjects enrolled	Austria: 120
Worldwide total number of subjects	144
EEA total number of subjects	144

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)	142
From 65 to 84 years	2
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

Recruitment from mental health hospital wards and outpatient clinics between October 20, 2011 and December 30, 2016. Recruitment in Bergen, Stavanger and Trondheim in Norway, and Innsbruck in Austria.

### Pre-assignment

Screening details:

Eligible patients were adults (18 years or more of age), with schizophrenia-spectrum disorder (ICD-10 F20-29), and ongoing psychosis.

A total of 359 patients assessed for eligibility. 215 patients were excluded (107 did not meet inclusion criteria, 82 declined to participate, and 26 other reasons).

### Pre-assignment period milestones

Number of subjects started	144
Number of subjects completed	144

### Period 1

Period 1 title	Baseline
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Assessor <sup>[1]</sup>

Blinding implementation details:

According to the pragmatic design aiming to mimick usual clinical practice, only assessors were blinded to treatment.

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Amisulpride
Arm description: -	
Arm type	Active comparator
Investigational medicinal product name	Amisulpride
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

50-1200 mg per day

<b>Arm title</b>	Aripiprazole
Arm description: -	
Arm type	Active comparator
Investigational medicinal product name	Aripiprazole
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

5-30 mg per day

<b>Arm title</b>	Olanzapine
Arm description: -	
Arm type	Active comparator
Investigational medicinal product name	Olanzapine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
2.5-20 mg per day	

Notes:

[1] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: According to the pragmatic design aiming to mimick usual clinical practice, only assessors were binded to treatment.

<b>Number of subjects in period 1</b>	Amisulpride	Aripiprazole	Olanzapine
Started	44	48	52
Completed	44	48	52

## Period 2

Period 2 title	Overall trial
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Assessor <sup>[2]</sup>

Blinding implementation details:

According to the pragmatic design aiming to mimick usual clinical practice, only assessors were binded to treatment.

## Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Amisulpride
Arm description: -	
Arm type	Active comparator
Investigational medicinal product name	Amisulpride
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
50-1200 mg per day	
<b>Arm title</b>	Aripiprazole
Arm description: -	
Arm type	Active comparator

Investigational medicinal product name	Aripiprazole
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
5-30 mg per day	
<b>Arm title</b>	Olanzapine
Arm description: -	
Arm type	Active comparator
Investigational medicinal product name	Olanzapine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
2.5-20 mg per day	
Investigational medicinal product name	Olanzapine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
2.5-20 mg per day	

Notes:

[2] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: According to the pragmatic design aiming to mimick usual clinical practice, only assessors were binded to treatment.

Number of subjects in period 2	Amisulpride	Aripiprazole	Olanzapine
Started	44	48	52
Completed	21	13	25
Not completed	23	35	27
Lost to follow-up	23	35	27

## Baseline characteristics

### Reporting groups

Reporting group title	Baseline
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Reporting group description: -

Reporting group values	Baseline	Total	
Number of subjects	144	144	
Age categorical			
Units: Subjects			
Adults (18-64 years)	142	142	
From 65-84 years	2	2	
Age continuous			
Units: years			
arithmetic mean	31.7		
standard deviation	± 12.7	-	
Gender categorical			
Units: Subjects			
Female	51	51	
Male	93	93	

### Subject analysis sets

Subject analysis set title	Amisulpride
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Subject analysis set type	Intention-to-treat
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Subject analysis set description:

Participants allocated to amisulpride

Subject analysis set title	Aripiprazole
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Subject analysis set type	Intention-to-treat
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Subject analysis set description:

Participants allocated to aripiprazole

Subject analysis set title	Olanzapine
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Subject analysis set type	Intention-to-treat
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Subject analysis set description:

Participants allocated to olanzapine

Reporting group values	Amisulpride	Aripiprazole	Olanzapine
Number of subjects	44	48	52
Age categorical			
Units: Subjects			
Adults (18-64 years)	43	47	52
From 65-84 years	1	1	0
Age continuous			
Units: years			
arithmetic mean	30.6	32.1	32.2
standard deviation	± 11.7	± 13.1	± 13.3

Gender categorical			
Units: Subjects			
Female	16	16	19
Male	28	32	33

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## End points

### End points reporting groups

Reporting group title	Amisulpride
Reporting group description: -	
Reporting group title	Aripiprazole
Reporting group description: -	
Reporting group title	Olanzapine
Reporting group description: -	
Reporting group title	Amisulpride
Reporting group description: -	
Reporting group title	Aripiprazole
Reporting group description: -	
Reporting group title	Olanzapine
Reporting group description: -	
Subject analysis set title	Amisulpride
Subject analysis set type	Intention-to-treat
Subject analysis set description: Participants allocated to amisulpride	
Subject analysis set title	Aripiprazole
Subject analysis set type	Intention-to-treat
Subject analysis set description: Participants allocated to aripiprazole	
Subject analysis set title	Olanzapine
Subject analysis set type	Intention-to-treat
Subject analysis set description: Participants allocated to olanzapine	

### Primary: PANSS total score

End point title	PANSS total score
End point description:	
End point type	Primary
End point timeframe: 12 months	

End point values	Amisulpride	Aripiprazole	Olanzapine	Amisulpride
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	44	48	52	44
Units: PANSS				
arithmetic mean (standard deviation)	-32.7 (± 3.1)	-21.9 (± 3.9)	-23.3 (± 2.9)	-32.7 (± 3.1)

End point values	Aripiprazole	Olanzapine	Amisulpride	Aripiprazole
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Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	48	52	44	48
Units: PANSS				
arithmetic mean (standard deviation)	-21.9 (± 3.9)	-23.3 (± 2.9)	-32.7 (± 3.1)	-21.9 (± 3.9)

<b>End point values</b>	Olanzapine			
Subject group type	Subject analysis set			
Number of subjects analysed	52			
Units: PANSS				
arithmetic mean (standard deviation)	-23.3 (± 2.9)			

### Statistical analyses

<b>Statistical analysis title</b>	Primary outcome
Comparison groups	Amisulpride v Aripiprazole v Olanzapine
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Confidence interval	
level	95 %
sides	2-sided
Variability estimate	Standard deviation

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

0-12 months

Adverse event reporting additional description:

Information about adverse events were systematically collected by use of the UKU-Side Effect Rating Scale, patient-rated version at each assessment point.

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	10
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### Reporting groups

Reporting group title	Amisulpride
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Reporting group description:

Participants allocated amisulpride

Reporting group title	Aripiprazole
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Reporting group description:

Participants allocated aripiprazole

Reporting group title	Olanzapine
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Reporting group description:

Participants allocated olanzapine

Serious adverse events	Amisulpride	Aripiprazole	Olanzapine
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 44 (9.09%)	10 / 48 (20.83%)	6 / 52 (11.54%)
number of deaths (all causes)	0	1	1
number of deaths resulting from adverse events	0	0	0
General disorders and administration site conditions			
Death			
subjects affected / exposed	0 / 44 (0.00%)	1 / 48 (2.08%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Accident			
subjects affected / exposed	0 / 44 (0.00%)	1 / 48 (2.08%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Somatic admission			

subjects affected / exposed	0 / 44 (0.00%)	1 / 48 (2.08%)	2 / 52 (3.85%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Pregnancy			
subjects affected / exposed	1 / 44 (2.27%)	0 / 48 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Psychosis exacerbation			
subjects affected / exposed	1 / 44 (2.27%)	0 / 48 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Readmission			
subjects affected / exposed	2 / 44 (4.55%)	7 / 48 (14.58%)	6 / 52 (11.54%)
occurrences causally related to treatment / all	0 / 2	0 / 7	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prolonged hospitalization			
subjects affected / exposed	0 / 44 (0.00%)	1 / 48 (2.08%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

<b>Non-serious adverse events</b>	Amisulpride	Aripiprazole	Olanzapine
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 44 (38.64%)	9 / 48 (18.75%)	13 / 52 (25.00%)
Nervous system disorders			
Extrapyramidal disorder			
subjects affected / exposed	5 / 44 (11.36%)	5 / 48 (10.42%)	6 / 52 (11.54%)
occurrences (all)	5	5	6
Reproductive system and breast disorders			
Sexual dysfunction			

subjects affected / exposed occurrences (all)	4 / 44 (9.09%) 4	4 / 48 (8.33%) 4	2 / 52 (3.85%) 2
Endocrine disorders Hyperprolactinaemia subjects affected / exposed occurrences (all)	14 / 44 (31.82%) 14	3 / 48 (6.25%) 3	10 / 52 (19.23%) 10

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported