Clinical trial results:
Evaluation of the necessity of a pharmacological treatment with antipsychotics for the prevention of relapse in long-term stabilized schizophrenic patients: a randomized, single-blind, longitudinal trial

Summary

EudraCT number	2013-000338-37
Trial protocol	DE
Global end of trial date	22 June 2016

Results information

Result version number	v1 (current)
This version publication date	18 November 2020
First version publication date	18 November 2020
Summary attachment (see zip file)	CSR_Reduce (Reducing antipsychotic drugs in stable patients with chronic schizophrenia.pdf)

Trial information

Trial identification

Sponsor protocol code	1723/1-1

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02307396
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Technische Universität München, Fakultät für Medizin
Sponsor organisation address	Ismaninger Str. 22, Munich, Germany, 81675
Public contact	Prof. Dr. Stefan Leucht, Klinikum rechts der Isar der TU München, Klinik für Psychiatrie, Technische Universität München, Fakultät für Medizin, -49 89 4140 4249, stefan.leucht@tum.de
Scientific contact	Prof. Dr. Stefan Leucht, Klinikum rechts der Isar der TU München, Klinik für Psychiatrie, Technische Universität München, Fakultät für Medizin, -49 89 4140 4249, stefan.leucht@tum.de

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	01 June 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	22 June 2016
Global end of trial reached?	Yes
Global end of trial date	22 June 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of the Trial is to evaluate for the first time employing high-Quality methodology, how long an antipsychotic relapse-prevention should be continued and to which time a patient is protected enough, so that a withdrawal of the medication seems appropriate. Relapse is defined as primary outcome.

Protection of trial subjects:

The conduct of this clinical study met the local legal and regulatory requirements. The study was conducted in accordance the ethical principles of Good Clinical Practice (GCP).
Participating subjects signed informed consent form and could withdraw from the study at any time without any disadvantage and without having to provide a reason for this decision.
The study was regularly monitored by the Sponsor and all investigators connected to the study were GCP trained.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 February 2015
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	Germany: 20
Worldwide total number of subjects	20
EEA total number of subjects	20

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)	20

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Pre-screening processes were in place. Between 01.02.2015 and 22.06.2016 all patients were randomised.

Pre-assignment

Screening details:

Adult patients with chronic schizophrenia or schizoaffective disorder, who were treated with any antipsychotic drug except clozapine, who had not been hospitalized in the last 3 years and who were in symptomatic remission at baseline were included.

Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Assessor[1]

Blinding implementation details:

The ratings were done by clinicians who were blind to the allocation

Arms

Are arms mutually exclusive?	Yes
Arm title	Reducing medication

Arm description:

In the intervention group, antipsychotic dose was gradually reduced and stopped if possible, based on the participant's psychopathological status. As a rule the initial antipsychotic dose should be reduced by 1/6 every other week for the first three months, but this was adapted for each patient individually according to her/his needs and psychopathological status.
So antipsychotic doses were reduced as far as possible for the first three months and then patients were followed-up with stable medication for three months.

Arm type	Experimental
Investigational medicinal product name	Olanzapin
Investigational medicinal product code	N05AH03
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

5-20 milligram per day

Investigational medicinal product name	Amisulprid
Investigational medicinal product code	ATC N05AL05
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

100-1200 mg milligram(s) per day

Investigational medicinal product name	Risperidon
Investigational medicinal product code	ATC N05AX08
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

1-10 mg milligram(s) per day

Investigational medicinal product name	Haloperidol
Investigational medicinal product code	ATC N05AD01
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 1-100 mg milligram(s) per day	
Investigational medicinal product name	Quetiapin
Investigational medicinal product code	ATC N05AH04
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details: 100-800 mg milligram(s) per day	
Investigational medicinal product name	Aripiprazol
Investigational medicinal product code	ATC N05AX12
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 5-30 mg milligram(s) per day	
Investigational medicinal product name	Perphenazin
Investigational medicinal product code	ATC N05AB03
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 4-24 mg milligram(s) total	
Investigational medicinal product name	Sulpirid
Investigational medicinal product code	ATC N05AL01
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 50-1000 mg milligram(s) total	
Investigational medicinal product name	Bromperidol
Investigational medicinal product code	ATC N05AD06
Other name	
Pharmaceutical forms	Oral drops
Routes of administration	Oral use
Dosage and administration details: 1-10 mg milligram(s) per day	
Investigational medicinal product name	Zuclopenthixol
Investigational medicinal product code	ATC N05AF05
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 2-75 mg milligram(s) per day	
Investigational medicinal product name	Thioridazin
Investigational medicinal product code	ATC N05AC02
Other name	

Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 25-600 mg milligram(s) per day	
Investigational medicinal product name	Paliperidon
Investigational medicinal product code	ATC N05AX13
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 1-12 mg milligram(s) per day	
Investigational medicinal product name	Ziprasidon
Investigational medicinal product code	ATC N05AE04
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 20-160 mg milligram(s) total	
Investigational medicinal product name	Benperidol
Investigational medicinal product code	ATC N05AD07
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 2-40 mg milligram(s) per day	
Investigational medicinal product name	Fluspirilen
Investigational medicinal product code	N05AG01
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use
Dosage and administration details: 4-8 mg milligram(s) total	
Investigational medicinal product name	Pimozid
Investigational medicinal product code	ATC N05AG02
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 1-16 mg milligram(s) per day	
Investigational medicinal product name	Perazin
Investigational medicinal product code	ATC N05AB10
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 25-600 mg milligram(s) per day	
Investigational medicinal product name	Fluphenazin
Investigational medicinal product code	ATC N05AB02
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details: 2-40 mg milligram(s) per day	
Investigational medicinal product name	Flupentixol
Investigational medicinal product code	ATC N05AF01
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 1-60 mg milligram(s) per day	
Investigational medicinal product name	Levomepromazin
Investigational medicinal product code	ATC N05AA02
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 15-150 mg milligram(s) per day	
Investigational medicinal product name	Chlorprothixen
Investigational medicinal product code	ATC N05AF03
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 15-200 mg milligram(s) per day	
Investigational medicinal product name	Sertindol
Investigational medicinal product code	ATC N05AE03
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 4-20 mg milligram(s) per day	
Arm title	Control group
Arm description: Medication in the control group was maintained.	
Arm type	Active comparator
Investigational medicinal product name	Olanzapin
Investigational medicinal product code	N05AH03
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use
Dosage and administration details: 5-20 milligram per day	
Investigational medicinal product name	Amisulprid
Investigational medicinal product code	ATC N05AL05
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 100-1200 mg milligram(s) per day	
Investigational medicinal product name	Risperidon
Investigational medicinal product code	ATC N05AX08
Other name	

Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 1-10 mg milligram(s) per day	
Investigational medicinal product name	Haloperidol
Investigational medicinal product code	ATC N05AD01
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 1-100 mg milligram(s) per day	
Investigational medicinal product name	Quetiapin
Investigational medicinal product code	ATC N05AH04
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details: 100-800 mg milligram(s) per day	
Investigational medicinal product name	Aripiprazol
Investigational medicinal product code	ATC N05AX12
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 5-30 mg milligram(s) per day	
Investigational medicinal product name	Perphenazin
Investigational medicinal product code	ATC N05AB03
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 4-24 mg milligram(s) total	
Investigational medicinal product name	Sulpirid
Investigational medicinal product code	ATC N05AL01
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 50-1000 mg milligram(s) total	
Investigational medicinal product name	Bromperidol
Investigational medicinal product code	ATC N05AD06
Other name	
Pharmaceutical forms	Oral drops
Routes of administration	Oral use
Dosage and administration details: 1-10 mg milligram(s) per day	
Investigational medicinal product name	Zuclopenthixol
Investigational medicinal product code	ATC N05AF05
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details: 2-75 mg milligram(s) per day	
Investigational medicinal product name	Thioridazin
Investigational medicinal product code	ATC N05AC02
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 25-600 mg milligram(s) per day	
Investigational medicinal product name	Paliperidon
Investigational medicinal product code	ATC N05AX13
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 1-12 mg milligram(s) per day	
Investigational medicinal product name	Ziprasidon
Investigational medicinal product code	ATC N05AE04
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 20-160 mg milligram(s) total	
Investigational medicinal product name	Benperidol
Investigational medicinal product code	ATC N05AD07
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 2-40 mg milligram(s) per day	
Investigational medicinal product name	Fluspirilen
Investigational medicinal product code	N05AG01
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use
Dosage and administration details: 4-8 mg milligram(s) total	
Investigational medicinal product name	Pimozid
Investigational medicinal product code	ATC N05AG02
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 1-16 mg milligram(s) per day	
Investigational medicinal product name	Perazin
Investigational medicinal product code	ATC N05AB10
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 25-600 mg milligram(s) per day	

Investigational medicinal product name	Fluphenazin
Investigational medicinal product code	ATC N05AB02
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 2-40 mg milligram(s) per day	
Investigational medicinal product name	Flupentixol
Investigational medicinal product code	ATC N05AF01
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 1-60 mg milligram(s) per day	
Investigational medicinal product name	Levomepromazin
Investigational medicinal product code	ATC N05AA02
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 15-150 mg milligram(s) per day	
Investigational medicinal product name	Chlorprothixen
Investigational medicinal product code	ATC N05AF03
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 15-200 mg milligram(s) per day	
Investigational medicinal product name	Sertindol
Investigational medicinal product code	ATC N05AE03
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 4-20 mg milligram(s) per day	

Notes:

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

Justification: The ratings were done by clinicians who were blind to the allocation.

Number of subjects in period 1	Reducing medication	Control group
Started	11	9
Completed	11	8
Not completed	0	1
Lost to follow-up	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Reducing medication
Reporting group description:	
In the intervention group, antipsychotic dose was gradually reduced and stopped if possible, based on the participant's psychopathological status. As a rule the initial antipsychotic dose should be reduced by 1/6 every other week for the first three months, but this was adapted for each patient individually according to her/his needs and psychopathological status. So antipsychotic doses were reduced as far as possible for the first three months and then patients were followed-up with stable medication for three months.	
Reporting group title	Control group
Reporting group description:	
Medication in the control group was maintained.	

Reporting group values	Reducing medication	Control group	Total
Number of subjects	11	9	20
Age categorical Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			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)			0
From 65-84 years			0
85 years and over			0
Age continuous Units: years			
arithmetic mean	44.73	46.11	
standard deviation	± 10.33	± 12.09	-
Gender categorical Units: Subjects			
Female	5	3	8
Male	6	6	12
PANSS overall Units: PANSS Units			
arithmetic mean	50.09	47.67	
standard deviation	± 10.41	± 8.09	-

End points

End points reporting groups

Reporting group title	Reducing medication

Reporting group description:

In the intervention group, antipsychotic dose was gradually reduced and stopped if possible, based on the participant's psychopathological status. As a rule the initial antipsychotic dose should be reduced by 1/6 every other week for the first three months, but this was adapted for each patient individually according to her/his needs and psychopathological status.
So antipsychotic doses were reduced as far as possible for the first three months and then patients were followed-up with stable medication for three months.

Reporting group title	Control group

Reporting group description:

Medication in the control group was maintained.

Primary: Relapse

End point title	Relapse

End point description:

The primary outcome was relapse defined as a CGI > 3 AND at least two of the following positive PANSS items > 3: delusions, conceptual disorganisation, hallucinations, mannerisms and posturing and unusual thought content assessed at every visit.

End point type	Primary

End point timeframe:

Whole study period 26 weeks.

End point values	Reducing medication	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	9		
Units: Number of relapses	1	2		

Statistical analyses

Statistical analysis title	Relapse

Statistical analysis description:

The primary dichotomous outcome was the number of patients relapsed in the intervention group compared with that in the control group. Fisher's Exact Test was applied to compare the number of relapsed patients.

Comparison groups	Reducing medication v Control group

Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.566
Method	Fisher exact

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events:	
The reporting of AEs / SAEs begins with the patient's baseline visit and ends 7 days after termination of the study participation or or 7 days after (early) termination.	
Adverse event reporting additional description:	
Events caused by the underlying disease or by routine treatments were not recorded.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	999

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

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: The study had no serious adverse events and no adverse events. Side effects were recorded according to the UKU-scale. The results are presented in details in Table 1a+1b of the publication of the study. The PDF is attached to the trial results and avialable open access. (https://doi.org/10.1007/s00406-020-01109-y)

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

Online references

http://www.ncbi.nlm.nih.gov/pubmed/3206272