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Secondary PREVENTion of schizophrenia: a randomised controlled trial

Submission date	Recruitment status	[ ] Prospectively registered
01/10/2007	No longer recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
05/12/2007	Completed	[ ] Results
Last Edited	**Condition category**	[ ] Individual participant data
19/03/2019	Mental and Behavioural Disorders	[ ] Record updated in last year

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
2007-001573-28

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
Sponsor-Number: Uni-Koeln-320; EudraCT-Number: 2007-001573-28

Study information

Scientific Title
Secondary PREVENTion of schizophrenia: a randomised controlled trial

Acronym
PREVENT

Study objectives
1. Are Clinical Management and Aripiprazole combined (CM + ARI) more effective in the treatment of persons at risk of being prodromally symptomatic of psychosis than Clinical Management and Placebo combined (CM + PL)?
2. Is Cognitive Behavioural Therapy (CBT) more effective in the treatment of persons at risk being prodromally symptomatic of psychosis than CM and placebo combined (CM + PL)?
3. Is CBT not less effective in the treatment of persons at risk being prodromally symptomatic of psychosis than CM + ARI?

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics approval received from the Ethics Board of the Medical Faculty of the University of Cologne on the 28th September 2007 (ref: 07-158).
The amendment of the trial protocol (version 3.0) from 25.02.2014, was also approved by the Ethics Board of the Medical Faculty of the University of Cologne on 07.05.2014.

Study design
Multicentre randomised, double-blind, placebo-controlled trial with regard to the CM + ARI intervention and a randomised controlled trial with regard to the CBT intervention

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Not specified

Study type(s)
Treatment

Participant information sheet

Health condition(s) or problem(s) studied
Prodromal schizophrenia

Interventions

Experimental intervention I - Clinical Management and Aripiprazole combined (CM + ARI):
ARI will be provided by the treating physician in a blister of 28 tablets and are supposed to be taken orally by the participant autonomously. In addition to ARI, 21 CM sessions will be offered in the treatment phase of 52 weeks; weekly in the first 4 weeks, biweekly in the next 20 weeks and every fourth week over the following 28 weeks. The initial session will be 45 to 60 minutes, with other sessions 20 to 30 minutes long. These sessions will include:
1. Psychoeducation about at-risk mental state syndrome
2. Pharmacotherapy
3. Side effects of pharmacotherapy
4. Monitoring target symptoms and possible side effects
5. Giving advice

Specific CBT strategies and homework tasks are not allowed.

Experimental intervention II - Cognitive Behaviour Therapy (CBT):
Individual CBT will be offered in the treatment phase of 52 weeks; weekly for the first 16 weeks, biweekly over the next 20 weeks and every fourth week over the next 16 weeks. The sessions will be 50 minutes long. The CBT will be separated into assessment/engagement, treatment and termination phases. During these phases a combination of psychoeducation, symptom- (Basic Symptoms [BS], APS, BLIPS, depression, anxiety, negative symptoms), stress- and crisis-management modules will be adapted to the specific needs of each client. The sessions will follow a detailed protocol containing the aims of the session, examples of interventions and model responses for the therapist.

Control intervention - Clinical Management and Placebo combined (CM + PL):
All procedures will be identical to CM + ARI. PL will be identical to ARI regarding package, appearance, colour and taste.

All treatments will be offered for 12 months.

Participants randomised in CM + ARI/PL will take one tablet daily. Aripiprazole and Placebo tablets will be provided in dosages of 2, 5, 10 and 15 mg. Initial doses will be 2 mg/day. After one week the dose will be increased to 5 mg a day, after two weeks to 10 mg and after 3 weeks to 15 mg/day, unless adverse effects dictate slower titration schedule. The maximum dosage is 15 mg /day. Dosage titration will be modified as regards presence of symptoms and adverse effects:

BLIPS: As long as BLIPS are present, dosage will gradually increased until the maximum of 15 mg /daily.

BS and APS: As long as BS and APS are stable or worse dosage will be increased to the next step biweekly (maximum 15 mg/daily). If symptoms are still present but improve dosage will be maintained for at least 2 weeks. Only in case of worsening of symptoms dosage can be increased again. If symptoms do not resolve after 12 weeks with maximum dosage, dosage can be gradually reduced to the dose in which residual symptoms were first observed.

In case of adverse effects dose should be reduced to the next lower dose step and maintained for at least a week.

Intervention Type
Drug

Phase

Not Specified

Drug/device/biological/vaccine name(s)
Aripiprazole

Primary outcome measure
Current primary outcome measure as of 19/03/2019:
The primary endpoint is given by the dichotomous outcome
measure “progression to psychosis”, which is summarized through estimation of a time-dependent cumulative event rate.
Progression to psychosis is defined by the transition to psychosis or progression from an early to a late initial prodromal state given the following order:
1. genetic Risk and/or schizotypal disorder and functional decline (GRFD)
2. Cognitive disturbances (COGDIS)
3. Attenuated positive symptoms (APS)
4. Brief limited intermittent psychotic symptoms (BLIPS)

Previous primary outcome measure:
The primary endpoint is given by the dichotomous outcome measure "transition to psychosis", which is summarised through an event rate within a time interval. The event "transition to psychosis" will be operationalised by one or more of 5 Scale Of Prodromal Symptomatology (SOPS) positive items rated with score = 6 longer than 7 days, to be further specified as DSM IV codes 292.11-12, 295.1-4, 295.7, 295.9, 296.04, 296.24, 296.34, 297.1, 298.8.

Secondary outcome measures
Current secondary outcome measures as of 19/03/2019:
1. Dichotomous outcome measure "transition to psychosis", which is summarised through an event rate within a time interval. The event "transition to psychosis" will be operationalised by one or more of 5 Scale Of Prodromal Symptomatology (SOPS) positive items rated with score = 6 longer than 7 days, to be further specified as DSM IV codes 292.11-12, 295.1-4, 295.7, 295.9, 296.04, 296.24, 296.34, 297.1, 298.8.
2. Psychopathological symptoms:
2.1. Prodromal symptoms (Ultra High Risk [UHR]): Severity of prodromal symptoms as described by the UHR criteria will be interview-measured by the SOPS. The SOPS is a 19-item scale designed to measure changes in symptomatology over time. It contains positive, negative, disorganisation and general symptoms sub-scores
2.2. Basic Symptoms (BS): The severity of BS will be assessed by a short version and the complete interviewer-administered Schizophrenia Prediction Instrument, Adult version (SPI-A). The SPI-A is a 34-items scale with 6 subscales designed to quantify basic symptoms and to complement SOPS
2.3. Schizophrenia symptoms will be interviewer-measured by the Positive and Negative Syndrome Scale (PANSS), which gives a total score as well as positive, negative and general psychopathology sub-scores
2.4. Depression: Symptoms of depression will be self-rated by the Beck Depression Inventory (BDI) and interviewer rated by the Montgomery Asperg Depression Rating Scale (MADRS), which contain one total score each
2.5. Anxiety: Anxiety will be self-rated by the State Trait Anxiety Inventory (STAI) which gives a state and a trait anxiety scale
2.6. Psychiatric diagnosis: Structured clinical interview for DSM-IV, Structured Clinical Interview for DSM-IV (SCID) I and II, for the structured investigation of actual and past mental illnesses according to DSM IV

3. Social functioning:
3.1. Social adjustment: The Social and Occupational Functioning Assessment Scale (SOFAS) total score will be used for interviewer-rated social functioning (one total score). In addition the SAS II, which gives 4 subscales and one general adjustment global score, will be assessed
3.2. Neuropsychological functioning: The neuropsychological battery comprises Rey Auditory Verbal Learning Test, Digit symbol substitution, Trail Making Test, Oseretzki Test, Digit Span, Letter Number Span, Verbal Fluency, MehrfachwahlWortschatz-Test-B (MWT-B). A single global measure, derived by averaged z-transformed test scores will be used
4. Subjective quality of life, examined using the core module, covering 7 areas of Quality of Life (QoL), of the self-rating measure "Modular System for Quality of Life" (MSLQ)

Previous secondary outcome measures:
1. Time to transition, summarised by a time-dependent cumulative event rate of transition to psychosis
2. Psychopathological symptoms:
2.1. Prodromal symptoms (Ultra High Risk [UHR]): Severity of prodromal symptoms as described by the UHR criteria will be interview-measured by the SOPS. The SOPS is a 19-item scale designed to measure changes in symptomatology over time. It contains positive, negative, disorganisation and general symptoms sub-scores
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4. Subjective quality of life, examined using the core module, covering 7 areas of Quality of Life (QoL), of the self-rating measure "Modular System for Quality of Life" (MSLQ)

Overall study start date
01/12/2007

Completion date
31/10/2014

Eligibility

Key inclusion criteria
Current participant inclusion criteria as of 19/03/2019:
1. Aged between 18 - 49 years
2. Belong to one of the following groups:
2.1. Attenuated Positive Symptoms (APS)
2.2. Brief Limited Intermittent Psychotic Symptoms (BLIPS)
2.3. Predictive basic symptoms
2.4. Family risk plus reduced functioning
3. Verbal Intelligence Quotient (IQ) greater than 70
4. Written informed consent

Previous participant inclusion criteria:
1. Aged between 18 - 40 years
2. Belong to one of the following groups:
2.1. Attenuated Positive Symptoms (APS)
2.2. Brief Limited Intermittent Psychotic Symptoms (BLIPS)
2.3. Predictive basic symptoms
2.4. Family risk plus reduced functioning
3. Verbal Intelligence Quotient (IQ) greater than 70
4. Written informed consent

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
49 Years

Sex
Both

Target number of participants
N = 300 (136 CBT, 102 CM+ARI, 62 CM+PL).

Key exclusion criteria
1. Present or past diagnosis of a schizophrenic, schizophreniform, schizoaffective, delusional or bipolar disorder according to Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM IV)
2. Present or past diagnosis of a brief psychotic disorder according to DSM IV with a duration equal to or of more than one week or within the last 4 weeks regardless of its duration
3. Diagnosis of delirium, dementia, amnestic or other cognitive disorder, mental retardation, autism spectrum disorders, psychiatric disorders due to a somatic factor or related to psychotropic substances according to DSM IV

4. Alcohol or drug dependence according to DSM IV
5. Diseases of the central nervous system (inflammatory, traumatic, epilepsy etc.)
6. Magnetic Resonance Imaging (MRI) or Electroencephalogram (EEG) abnormalities
7. Current or past antipsychotic treatment for longer than 1 week
8. Current or past antipsychotic treatment shorter than 1 week without a washout phase of at least 4 weeks
9. Current pregnancy, lactation or missing reliable method of contraception
10. Current suicidality or dangerous behaviour
11. Contraindication according to Summary of Product Characteristics (SmPC): known intolerance of the active pharmaceutical ingredient or another ingredient of verum or placebo
12. Use of drugs with anticipated interactions (in accordance to SmPC)
13. Participance in other clinical trials, which could intervene with the present trial
14. Persons who are depending on the investigator or the sponsor
15. Hospitalisation due to legal or regulatory devices

Date of first enrolment
01/12/2007

Date of final enrolment
01/11/2014

Locations

Countries of recruitment
Germany

Study participating centre
Department of psychiatry and psychotherapy
University of Cologne
Cologne
Germany
50937

Study participating centre
Department of psychiatry and psychotherapy
University of Aachen
Aachen
Germany
-

Study participating centre
Department of psychiatry and psychotherapy
University of Berlin

Berlin
Germany
-

Study participating centre
Department of psychiatry and psychotherapy
University of Bochum
Bochum
Germany
-

Study participating centre
Department of psychiatry and psychotherapy
University of Bonn
Bonn
Germany
-

Study participating centre
Department of psychiatry and psychotherapy
University of Dresden
Dresden
Germany
-

Study participating centre
Department of psychiatry and psychotherapy
University of Düsseldorf
Düsseldorf
Germany
-

Study participating centre
Department of psychiatry and psychotherapy
University of Göttingen
Göttingen
Germany
-

Study participating centre
Department of psychiatry and psychotherapy
University of Hamburg
Hamburg
Germany
-

Study participating centre
Department of psychiatry and psychotherapy
University of Mannheim
Mannheim
Germany
-

Study participating centre
Department of psychiatry and psychotherapy
University of Munich
Munich
Germany
-

Sponsor information

Organisation
University of Cologne (Germany)

Sponsor details
Albertus-Magnus-Platz
Cologne
Germany
50923

Sponsor type
University/education

Website
http://www.uni-koeln.de/index.e.html

ROR
https://ror.org/00rcxh774

Funder(s)

Funder type
Government

Funder Name
German Research Council (Deutsche Forschungsgemeinschaft [DFG]) (Germany) (ref: KL 970/7-1)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration