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Amisulpride augmentation in clozapine-unresponsive schizophrenia

Submission date
02/03/2010

Recruitment status
No longer recruiting

Registration date
24/05/2010

Overall study status
Completed

Last Edited
10/09/2019

Condition category
Mental and Behavioural Disorders

[X] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[X] Results
[ ] Individual participant data

Plain English summary of protocol

Background and study aims
Schizophrenia is a mental health problem usually starting in the late teens or early twenties, and often lasting many years. It affects behaviour, thinking and perception, and, in more severe cases, a person's ability to socialise, work and carry out routine daily tasks. The symptoms of schizophrenia include false beliefs and hallucinations (most commonly, hearing voices). The standard medication (antipsychotics) for this problem is usually helpful, and if taken continually can keep people well, reducing the likelihood of further episodes. However, in up to one in three people with schizophrenia, the illness does not show much improvement with antipsychotic medication. For some of these 'resistant' illnesses, one particular antipsychotic, clozapine, can work well, but one disadvantage is the risk of a severe blood side effect which means that regular blood testing is necessary. If the response to clozapine treatment is disappointing, there is some evidence that adding another antipsychotic can sometimes produce more improvement. However, it seems that the added antipsychotic may need to be taken by the person for at least 10 weeks in order to work well. The evidence for this mainly comes from research studies which have only looked at the change in general symptoms when another antipsychotic is added to clozapine, and not whether particular symptoms that are particularly disturbing or disabling are reduced. Also, other aspects of schizophrenia, such as how well the person copes with day-to-day tasks and the demands of a job, have not been measured in these studies. Further, the possible side effects of combining another antipsychotic with clozapine have not been carefully and fully assessed. So we plan to test carefully the possible benefits and problems when the antipsychotic amisulpride is added to clozapine for 12 weeks in people whose schizophrenia illness has not been helped much by any antipsychotic medication on its own, and who are now taking clozapine, but again with not much improvement. We have chosen amisulpride because its effects may be complementary to those of clozapine, and also it is less likely than some other antipsychotics to increase some of the characteristic side effects of clozapine, such as sedation, weight gain and other metabolic problems.

Who can participate?
Patients aged 18-65 with schizophrenia who have been treated with clozapine for at least 12 weeks

What does the study involve?
Participants currently being treated with clozapine are randomly allocated to also receive either amisulpride or a dummy tablet (placebo)

What are the possible benefits and risks of participating?
We expect that adding amisulpride will be more likely to cause an improvement than adding placebo. Also, we should gain a greater understanding of the possible benefits of adding another antipsychotic to clozapine in relation to particular problem symptoms, and a person's ability to live and work in the community. However, we also need to learn more about the risks and side effects of combining these two medications.

Where is the study run from?
Imperial College London (UK)

When is the study starting and how long is it expected to run for?
September 2010 to August 2013

Who is funding the study?
NIHR Health Technology Assessment Programme (HTA) (UK)

Who is the main contact?
Prof. Thomas Barnes

Contact information

Type(s)
Scientific

Contact name
Prof Thomas Barnes

Contact details
Centre for Mental Health
Imperial College London
Charing Cross Campus
St Dunstan's Road
London
United Kingdom
W6 8RP

Additional identifiers

ClinicalTrials.gov (NCT)
NCT01246232

Protocol serial number
HTA 08/116/12; CRO1498

Study information

Scientific Title
Amisulpride augmentation in clozapine-unresponsive schizophrenia: a randomised, double-blind, placebo-controlled trial

Acronym
AMICUS

Study objectives
The main research question is whether, for confirmed, treatment-resistant schizophrenia that has proved to be poorly responsive to an adequate trial of clozapine, augmentation of clozapine with a second, suitable antipsychotic, amisulpride, at a clinically optimised dose for an adequate trial period, is clinically and cost effective and associated with an acceptable side effect burden.

More details can be found at: http://www.nets.nihr.ac.uk/projects/hta/0811612
Protocol can be found at: http://www.nets.nihr.ac.uk/__data/assets/pdf_file/0017/52046/PRO-08-116-12.pdf

Ethics approval required
Old ethics approval format

Ethics approval(s)
Charing Cross Research Ethics Committee, 21/10/2009

Study design
Randomised double-blind placebo-controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Schizophrenia

Interventions
Participants will receive additional treatment with either clozapine or identical placebo, randomly assigned. Treatment with clozapine will be initiated at 20mg/day for the first 4 weeks (or one placebo capsule), followed by the option to increase the dose to 40mg per day (or two placebo capsules) for the remainder of the study period, i.e. daily for up to a year. If there are problems with tolerability, the clinician can reduce the dose back to 20mg/day (or one placebo capsule). For both treatment arms, the total duration of treatment will be 12 months.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Clozapine, amisulpride

Primary outcome(s)
The proportion of patients with a criterion response threshold of a 20% reduction in total Positive and Negative Syndrome Scale (PANSS) score. All outcomes will be assessed at baseline and 3, 9 and 12 months.

Key secondary outcome(s))
1. PANSS negative symptom subscale score
2. Calgary Depression Rating Scale for Schizophrenia
3. Social and Occupational Functioning Assessment Scale
4. Service Engagement Scale
5. Antipsychotic side effect measures
6. Euroqol EQ-5D health status questionnaire
7. Resource use data questionnaire
All outcomes will be assessed at baseline and 3, 9 and 12 months.

Completion date
31/08/2013

Eligibility

Key inclusion criteria
1. A criterion level of persistent symptom severity despite an adequate trial of clozapine monotherapy in terms of dosage, duration and adherence (as used by Honer et al 2006):
1.1. Treatment for at least 12 weeks at a stable dose of 400 mg or more of clozapine a day, unless the size of the dose was limited by side effects
1.2. A total score of 80 or greater at baseline on the Positive and Negative Syndrome Scale (PANSS: Kay et al 1987, 1988); the range of possible scores is 30 to 210, with higher scores indicating more severe symptoms.
1.3. A Clinical Global Impressions (CGI: Guy 1976) score of 4 or greater (range of possible scores, 1=not mentally ill to 7=extremely ill)
1.4. A Social and Occupational Functioning Assessment Scale (SOFAS: Goldman et al 1992, DSM-IV 1994) score of 40 or less; range of possible scores, 1 to 100, with lower scores indicating impaired functioning.
2. Age 18-65 years, inclusive
3. Clinically stable for the last 3 months with a consistent clozapine regimen
4. Competent and willing to provide written, informed consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
65 years

Sex
All

Key exclusion criteria
1. Clinically-significant alcohol/substance use in the previous three months
2. Developmental disability
3. Indication for current treatment with clozapine was intolerance/movement disorder
4. A previous trial of clozapine augmentation with amisulpride
5. Existing relevant physical health problems: such as cardiovascular disease, previous problems with prolactin, and impaired liver/renal function

Date of first enrolment
01/09/2010

Date of final enrolment
31/08/2013

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Imperial College London
London
United Kingdom
W6 8RP

Sponsor information

Organisation
Imperial College London (UK)

ROR
https://ror.org/041kmwe10

Funder(s)

Funder type
Government

Funder Name
Health Technology Assessment Programme

Alternative Name(s)
NIHR Health Technology Assessment Programme, Health Technology Assessment (HTA), HTA

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/09/2017		Yes	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes