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Relapse prevention in children and adolescents with aggressive behaviour problems treated with risperidone

Submission date
27/01/2012

Recruitment status
No longer recruiting

Registration date
16/04/2012

Overall study status
Completed

Last Edited
10/08/2020

Condition category
Mental and Behavioural Disorders

[X] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Risperidone is a drug that is widely prescribed to children and adolescents with a variety of conditions that cause aggressive behaviour, such as Conduct Disorder (CD). The effectiveness and safety of risperidone have been shown in children and adolescents with mild mental retardation but there is a lack of data regarding patients with an average IQ. The long-term safety of risperidone is also a matter of concern since children and adolescents seem particularly vulnerable to side effects such as weight gain. The aim of this study is to investigate whether the patients' response to risperidone is maintained when the risperidone treatment is stopped.

Who can participate?
Patients aged 5 to 18 with CD and an IQ of at least 85.

What does the study involve?
Patients are treated with risperidone for 11 weeks and are then randomly allocated to either continue taking risperidone or to switch to taking a placebo (dummy) drug.

What are the possible benefits and risks of participating?
Aside from the possible side effects of risperidone no other risks are involved.

Where is the study run from?
This study takes place at hospitals and psychiatrist centers in the Netherlands, UK, Germany, Belgium, France, Spain and Italy

When is the study starting and how long is it expected to run for?
June 2012 to June 2015

Who is funding the study?
European Community's Seventh Framework Programme

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
PERS3

Study information

Scientific Title
Relapse prevention in children and adolescents with Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) Conduct Disorder treated with risperidone: a randomized double-blind, placebo-controlled discontinuation study

Study objectives
The primary objective is to test the hypothesis that, after at least 15 weeks of daily administration (4 for titration, 7 of relatively stable dose, 4 at fixed doses; Study Period II), risperidone given orally in a dose of 0.25 to 3.0 mg/d depending on body weight (eq. to approximately 0.01 to 0.04 mg/kg/d) is superior to placebo in preventing relapse of symptoms of conduct disorder (CD), as assessed through an 11-week, double-blind discontinuation trial (Study Period III) of children and adolescents not developmentally delayed/mentally retarded, and measured by comparison with mean change from the double-blind baseline to endpoint on the Nisonger Child Behavior Rating Form (CBRF) - Typical IQ Version (Aman et al., 2008) using investigator-ratings based on all available information.

Ethics approval required
Old ethics approval format

Ethics approval(s)

Not provided at time of registration

Study design
Double-blind randomized placebo-controlled discontinuation study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Conduct disorder / Oppositional Defiant Disorder

Interventions
The current study will investigate the maintenance of clinical response to risperidone in children and adolescents with CD and normal IQ by performing a placebo-controlled discontinuation study in patients who had previously had a stable open-label response of at least 11 weeks duration.

Study Period I: Screening

Study Period II (open-label titration and maintenance): Patients will receive risperidone at a dosage of 0.01-0.04 mg/kg per day, with an up-titration period of approximately 4 weeks, then continued at the optimal dose (within the given range) for 11 weeks, of which at minimum in the last 4 weeks a stable dose is given

Patients unable to tolerate the minimum dose of 0.25 or 0.5 mg/day, depending on weight group will be discontinued from the study

Study Period III (double-blind discontinuation treatment phase): Patients will begin double-blind therapy (visit 10, first visit of Study Period III)

Study Period IV (down-titration): After Study Period III all patient medication will be withdrawn in two weeks.

The last visit (Visit 18) will be completed at week 28

Intervention Type
Drug

Phase
Not Applicable

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

Primary outcome(s)
The primary objective is to test the hypothesis that, after at least 15 weeks of daily administration (4 for titration, 7 of relatively stable dose, 4 at fixed doses; Study Period II), risperidone given orally in a dose of 0.25 to 3.0 mg/d depending on body weight (eq. to

approximately 0.01 to 0.04 mg/kg/d) is superior to placebo in preventing relapse of symptoms of CD, as assessed through an 11-week, double-blind discontinuation trial (Study Period III) of children and adolescents not developmentally delayed/mentally retarded, and measured by comparison with mean change from the double-blind baseline to endpoint on the Nisonger Child Behavior Rating Form (CBRF) - Typical IQ Version (Aman et al., 2008) using investigator-ratings based on all available information.

Key secondary outcome(s))

1. To establish the long-term efficacy of treatment with risperidone, measuring mean change from the double-blind baseline to endpoint on the pivotal (Nisonger) scale between risperidone and placebo.
2. To test the effect of risperidone compared to placebo on various behavioural domains following seven months of daily administration of risperidone assessed in a 11 week, double blind discontinuation trial
3. To compare changes (impairment) in neurocognitive function following risperidone, assessed in both the 15 weeks open label and the 11-week double-blind discontinuation trial
4. To assess the effect of risperidone compared to placebo on comorbid ADHD symptoms following seven months of daily administration of risperidone assessed in a 11-week, double-blind discontinuation trial
5. To compare safety and tolerability results for risperidone and placebo in children and adolescents with CD over 11 weeks of double-blind treatment

Completion date

01/06/2015

Eligibility

Key inclusion criteria

1. Patients (male or female) must be at least 5 years of age, and not more than 17 years and 5 months of age at Visit 1
2. Patients must meet DSM-IV-TR diagnostic criteria for DSM-IV CD (312.xx)
3. Patients must have an intelligence quotient (IQ) of > 85
4. Patients must score > 27 on the Nisonger Child Behavior Rating (CBR) Form, Oppositional Defiant Disorder (ODD)/Conduct Disorder (CD) Disruptive Behavior Composite (D-Total) at baseline (Visit 1 or 2)
5. Patients must have a body weight comprised between 5th and 95th percentile based on WHO Body Mass Index for age-sex specific charts, at study entry
6. Patients must be able to swallow the study drug
7. Patients must have venous access sufficient to allow blood sampling and are compliant with blood draws as per protocol
8. If the patient is a female with child-bearing potential, she must test negative for pregnancy (based on a urine pregnancy test) at the time of enrollment and agree to use a reliable method of birth control
9. Laboratory results, including serum chemistries, hematology and urinalysis, show no significant abnormalities (significant would include laboratory deviations requiring acute medical intervention or further medical evaluation) and there is no clinical information that, in the judgment of a physician, should preclude a patients participation at study entry
10. All patients must have an electrocardiogram (ECG) at Visit 1 or 2. Results must be available prior to dispensing drug at Visit 3. If an ECG shows any severe abnormality, the patient must be excluded from the study. Patients with other abnormalities may be included at the discretion of the investigator.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Child

Lower age limit
5 years

Upper age limit
17 years

Sex
All

Key exclusion criteria
1. Has previously completed or withdrawn from this study or has been previously identified as being a non-responder or intolerant of risperidone
2. Has been treated within 14 days before Visit 1 with a drug that has not received regulatory approval for any indication at the time of study entry, or has participated in any investigational drug trial within six months prior to baseline (visit 1)
3. Has a current (within 6 months of the start of the study) or lifetime DSM-IV diagnosis of schizophrenia-related disorders, schizophrenia, bipolar disorder, major depressive disorder or a current substance dependence disorder (given the nature of the study population substance misuse or abuse is not exlusionary), pervasive developmental disorder (autistic disorder or Asperger disorder)
4. In the clinical judgment of the investigator, currently meets criteria for a primary psychiatric disorder, e.g., Anxiety Disorder, Depressive Disorder, Tic Disorder or Tourettes Syndrome [comorbid Attention deficit hyperactivity disorder (ADHD) is permitted]
5. Starts any psychotropic medication, including health-food supplements that the investigator feels could have central nervous system activity (for example, St. John's Wort, melatonin), during the course of the study, or is taking any other excluded concomitant medication(s). (An ongoing long-term medication, e.g., to treat a comorbid disorder such as ADHD, is permitted as long as compound and dose are not changed throughout the course of the study)
6. Has a history of hypersensitivity to neuroleptics, of tardive dyskinesia, or neuroleptic malignant syndrome
7. Has any acute or unstable medical condition, physiological condition, clinically significant laboratory, or ECG results that, in the opinion of the investigator, would compromise participation in the study
8. Has a known or suspected seizure disorder
9. Female patients who are pregnant or breastfeeding
10. Patients with a history of severe allergies to more than oneb class of medications or multiple adverse drug reactions

Date of first enrolment
01/06/2012

Date of final enrolment
01/06/2015

Locations

Countries of recruitment
United Kingdom

Belgium

France

Germany

Italy

Netherlands

Spain

Study participating centre
Radboud University Medical Centre Nijmegen
Nijmegen
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6525 EZ

Sponsor information

Organisation
Radboud University Nijmegen Medical Centre (Netherlands)

ROR
https://ror.org/05wg1m734

Funder(s)

Funder type
Government

Funder Name
Seventh Framework Programme (FP7/2007-2013) (Belgium) (grant ref: 241959)

Alternative Name(s)
Seventh framework programme of the European Community for research and technological development and demonstration activities (2007-2013), FP7

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location

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?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Study website	Study website	11/11/2025	11/11/2025	No	Yes