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Risperidone in children and adolescents with aggressive behaviour

Submission date	Recruitment status	[ ] Prospectively registered
26/01/2012	No longer recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
16/04/2012	Completed	[ ] Results
Last Edited	**Condition category**	[ ] Individual participant data
24/07/2020	Mental and Behavioural Disorders	[ ] 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 examine the effectiveness and safety of risperidone in children and adolescents with CD and normal IQ.

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

What does the study involve?
Patients are randomly allocated to be treated with either risperidone or placebo (dummy medication) for 12 weeks.

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?
April 2012 to April 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

Clinical Trials Information System (CTIS)
2011-000567-26

Protocol serial number
PERS2 - NTR3218

Study information

Scientific Title
A randomized double blind, placebo controlled study of risperidone in the treatment of DSM-IV-TR conduct disorder in children and adolescents

Study objectives
Risperidone given orally in a dose of 0.25 mg/d 3.0 mg/d depending on body weight (equivalent to approximately 0.01 0.04 mg/kg/d) for 12 weeks is superior to placebo in reducing disruptive behavioural symptoms associated with Diagnostic and Statistical Manual of Mental Disorders, 4th Edition, Text Revision (DSM-IV-TR) defined Conduct Disorder (CD) in the treatment of inpatient and outpatient children and adolescents (aged 5 years to 17 years and 9 Months), who are not developmentally delayed/mentally retarded.

Ethics approval required
Old ethics approval format

Ethics approval(s)
CMO Region, Arnhem-Nijmegen, The Netherlands, 09/02/2012

Study design
Multicenter randomized double-blind parallel placebo-controlled trial

Primary study design

Interventional

Study type(s)
Treatment

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

Interventions
Study Period I will be a 2 week screening (and washout) period
Study Period II will be a 12-week double-blind, randomized, placebo-controlled period
Study Period III will be a double-blind 1 week down-titration period.

This study involves a comparison of risperidone in the range of 0.25 mg/d 3.0 mg/d (equivalent to approximately up to 0.04 mg/kg/d) with placebo.

During Study Period II, dosing of risperidone will be initiated and modified according to the weight group of the patient at Baseline (Visit 3). Dosing may then be increased (or decreased) by 0.25 mg/d (or 0.5mg/kg/d increments, respectively, at specified visits/dates according to the weight of the subject, with minimum daily doses of 0.25 mg/day for patients under 50 kg body weight and 0.5 mg/day for patients who weigh 50 kg or more. Stepwise up-titration is recommended to the target dose or the highest tolerable dose by week 8. Dosing should remain stable during the last 4 weeks of Study Period II, unless a dose reduction is necessary for safety or tolerability reasons. In case of dose-adjustments due to adverse events unscheduled visits can be performed (for stepwise down-titration).

There are three study periods. Study Period I is a 2 week screening and washout period; during this period patients will be screened for study eligibility. Study Period II is a 12-week, randomized, double-blind, and placebo-controlled acute treatment period. Patients will be randomly assigned to risperidone or placebo in a 1:1 ratio. For patients in the risperidone treatment group, dosing will begin in either 0.25 or 0.5 mg/d, given in the evening depending on the patients weight, and will be up-titrated by 0.25 mg/d or 0.5 mg/d increments each week to maximum doses that vary by patient weight. Study Period III is a 1 week double-blind down-titration period from study medication, risperidone, or placebo. Any patient who completes Study Period II will continue into Study Period III. In order to keep the blind, all patients will receive the respective amounts of study drug (risperidone or placebo).

Intervention Type
Drug

Phase
Not Applicable

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

Primary outcome(s)
1. Nisonger Child Behavior Rating Form (CBRF)
2. Typical IQ Version-ODD/CD disruptive behavior (DBD)
3. Composite Total score (Aman et al., 2008) using investigator-ratings based on all available information

Key secondary outcome(s))
The secondary outcome measures focus on assessment of changes with active treatment vs. placebo:
1. Clinical Global Impressions-Improvement (CGI-I) and Clinical Global Impressions-Severity (CGI-S) (Guy 1976; NIMH 1985)
2. Children's Global Assessment Scale (C-GAS) (Shaffer et al., 1983)
3. ADHD-DSM IV_RS (DuPaul et al., 1998)
4. OAS (Yudofsky et al., 1986)
5. Child Health & Illness Profile - Child Edition (CHIP-CE) (Riley et al., 2004)
6. Child Behavior Checklist (CBCL), parent-reported (Achenbach, 1991a)
7. PAERS (March et al., 2007) (The PAERS will be used to evaluate AEs in a standardized approach (March et al., 2007)
8. ANT subtests (de Sonneville, 1999)
9. Columbia Suicide Severity Rating (SSR) (Posner et al., 2007b)
10. Additional outcomes related to Informed Consent procedures, treatment compliance, etc., potential mediators and moderators for efficacy and tolerability/safety parameters.

Previous placebo-controlled studies in children and adolescents with CD with risperidone have shown that patients treated with risperidone manifested increases in body weight compared with placebo (Reyes et al. 2006a, Shea et al. 2004). Therefore it is appropriate to monitor patients' weight and BMI throughout the study.

In addition, it is also appropriate for patients taking second-generation antipsychotics such as risperidone to have, e.g., their fasting lipid profile, fasting glucose, blood pressure, and prolactin monitored.

Completion date
01/04/2015

Eligibility

Key inclusion criteria
1. This study will include male and female inpatients or outpatients
2. Aged between 5 years and 17 years and 9 months
3. Patients must meet DSM-IV-TR diagnostic criteria for DSM-IV-TR Conduct Disorder(s)
4. Patients must have an IQ of > 85
5. If a female of child-bearing potential, patients must test negative for pregnancy at the time of enrollment based on a serum pregnancy test and agree to use a reliable method of birth control
6. Patients must have a body weight of at least 20 kg at study entry
7. Patients must be able to swallow study drug
8. Patients must have venous access sufficient to allow blood sampling and are compliant with blood draws

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 been treated with a drug within 14 days before Visit 1 that has not received regulatory approval for any indication at the time of study entry
2. Has participated in any investigational drug trial within six months prior to baseline
3. Has previously completed or withdrawn from this study or any other study investigating risperidone or has previously been identified as being a nonresponder or intolerant of risperidone
4. Has a current (within 6 months of the start of the study) or lifetime DSM-IV-TR diagnosis of schizophrenia-related disorders, schizophrenia, bipolar disorder, major depressive disorder, or 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).
5. 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
6. Starts any psychotropic medication, including health-food supplements that the investigator feels could have central nervous system activity
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. Has a history of neuroleptic malignant syndrome (NMS) or of tardive dyskinesia
10. Has a history of hypersensitivity to neuroleptics
11. Is pregnant or nursing

Date of first enrolment
01/04/2012

Date of final enrolment
01/04/2015

Locations

Countries of recruitment
United Kingdom

Belgium

France

Germany

Italy

Netherlands

Spain

Study participating centre
Radboud University Nijmegen Medical Centre
Nijmegen
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6525 CG

Sponsor information

Organisation
Radboud University Nijmegen Medical Centre (Netherlands)

ROR
https://ror.org/05wg1m734

Funder(s)

Funder type
Government

Funder Name
Seventh Framework Programme

Alternative Name(s)
EC Seventh Framework Programme, European Commission Seventh Framework Programme, EU Seventh Framework Programme, European Union Seventh Framework Programme, 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

Not provided at time of registration

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