

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

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		<input type="checkbox"/> Protocol
<b>Registration date</b> 16/04/2012	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan
		<input type="checkbox"/> Results
<b>Last Edited</b> 10/08/2020	<b>Condition category</b> Mental and Behavioural Disorders	<input type="checkbox"/> Individual participant data
		<input type="checkbox"/> 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?

Prof. Dr JK Buitelaar

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### **Study website**

<http://www.pers-project.com>

## **Contact information**

### **Type(s)**

Scientific

### **Contact name**

Prof Jan Buitelaar

### **Contact details**

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## **Additional identifiers**

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

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

**Secondary study design**

Randomised controlled trial

**Study setting(s)**

Hospital

**Study type(s)**

Treatment

**Participant information sheet**

Patient information material can be found at <http://www.pers-project.com/index.php/why-should-i-or-my-kid-participate-in-the-pers-studies/>

**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 measure**

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.

## **Secondary outcome measures**

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

## **Overall study start date**

01/06/2012

## **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

**Age group**

Child

**Lower age limit**

5 Years

**Upper age limit**

17 Years

**Sex**

Both

**Target number of participants**

200

**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 exclusionary), 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 one 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**

Belgium

France

Germany

Italy

Netherlands

Spain

United Kingdom

**Study participating centre**

**Radboud University Medical Centre Nijmegen**

Nijmegen

Netherlands

6525 EZ

# Sponsor information

## Organisation

Radboud University Nijmegen Medical Centre (Netherlands)

## Sponsor details

c/o Prof. Dr. J.K. Buitelaar  
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## Sponsor type

Hospital/treatment centre

## 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)

EC Seventh Framework Programm, European Commission Seventh Framework Programme, EU Seventh Framework Programme, European Union Seventh Framework Programme, EU 7th Framework Programme, European Union 7th Framework Programme, Siebten Rahmenprogramm, Séptimo Programa Marco, Septième programme-cadre, Settimo programma quadro, 7th Framework Programme, Seventh EU Framework Programme, FP7

## Funding Body Type

Government organisation

## Funding Body Subtype

National government

## Location

# 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