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

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Ethical review	Approved WMO
Status	Pending
Health condition type	Psychiatric and behavioural symptoms NEC
Study type	Interventional

Summary

ID

NL-OMON38186

Source
ToetsingOnline

Brief title
CONCA

Condition

- Psychiatric and behavioural symptoms NEC

Synonym
anti social behavior disorder; aggressive behavior among chilren and adolescents with externalizing behavior problems.

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Sint Radboud
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Children & Adolescents, Conduct disorder, Normal intelligence (or higher), Risperidone

Outcome measures

Primary outcome

The primary efficacy measurement for the study is the LOCF mean change from baseline to endpoint of the double-blind phase on the Nisonger Child Behavior Rating Form for Typical IQ children-ODD/CD disruptive behavior (DBD) Total Composite score (Lecavalier at al., 2004, Aman et al., 2008) using investigator-ratings based on all available information.

Secondary outcome

Secondary efficacy measures will be collected at the visits shown in the Study Schedule of Events (SOE). The measures of efficacy, functional outcome, and cognition that will be administered in this study are briefly described below:

1) ODD and CD subscores, various

- Both ODD and CD scores from Nisonger CBRF -TIQ, separately

- Modified Overt Aggression Scale (M-OAS) and subscores

2) Clinical Global Impression-Severity (CGI-S)

3) Clinical Global Impressions-Improvement (CGI-I)

4) Children*s Global Assessment (C-GAS)

5) ADHD- DSM-IV Rating Scale (ADHD-RS IV)

6) Cognition - computer tasks

7) The Child Behavior Checklist (CBCL)

8) The Child Health and Illness Profile (CHIP-CE) Parent Report Form

Physical status

Weight

Heigth

Physical examination

Cardiac examination

Blood and urine examination

Study description

Background summary

Currently, there is insufficient data available about short-term efficacy and safety/tolerability of using medication, e.g. risperidone, in children and adolescents with conduct disorder with about average IQ (85 and above). There is also insufficient data available about the maintenance of effect of risperidone in children and adolescents with conduct disorder with about average IQ. Further, there is insufficient data available about the long-term safety (treatment for up to 2 years) of using risperidone in children and adolescents with conduct disorder (or other indications).
In typically developing children with CD, a small double-blind placebo-controlled pilot study (N=20) was performed by Findling et al. (2000). Risperidone-treated patients showed greater reductions in clinician-rated symptoms and aggressive behaviour, despite a substantial attrition rate.

In Europe, risperidone has been approved for the short-term treatment of aggression in conduct disorder in children (from age 5) and adolescents with sub-average intellectual functioning or mental retardation (details in: www.medicines.org.uk/emc/medicine/12818).
Based on that, sufficient pharmacokinetic data for this age-group have apparently been established.

The current study will focus on investigating short-term (acute) efficacy and safety/tolerability of risperidone in the treatment of paediatric patients, children and adolescents, with DSM-IV-TR conduct disorder and normal intelligence (or higher), on a patient population in which this compound has not systematically been studied, but has regularly been used to a large extent in clinical routine in child and adolescent psychiatry and/or paediatrics (Kalverdijk et al., 2008, Olfson et al. 2006, Rani et al., 2008).

Study objective

The primary objective of this study is to test the hypothesis that risperidone given orally in a dose of 0.25 - 3.0 mg/d depending on body weight (eq. to approximately 0.01 - 0.04 mg/kg/d) for 12 weeks is superior to placebo in reducing disruptive behavioural symptoms associated with DSM-IV-TR defined Conduct Disorder (CD) in the treatment of in- and outpatient children and adolescents (5 - < 17 year and 9 months) not developmentally delayed/mentally retarded.

The secondary objectives of the study are as follows:
1. To test the hypothesis that risperidone is superior to placebo in reducing disruptive behaviours associated with CD over 12 weeks of double-blind treatment
2. To test the hypothesis that risperidone is superior to placebo in improving functional outcomes over 12 weeks of double-blind treatment
3. To test the effect of risperidone compared to placebo on various other behavioural domains over 12 weeks of double-blind treatment
4. To assess the effect of risperidone compared to placebo on comorbid ADHD symptoms over 12 weeks of double-blind treatment
5.To assess the effect of risperidone compared to placebo on (impairment of) cognition/cognitive functioning (e.g. due to possible sedative effects) over 12 weeks of double-blind treatment
6. To compare safety and tolerability results for risperidone and placebo in children and adolescents with CD over 12 weeks of double-blind treatment

Study design

This study is a multicenter, randomized, double-blind, parallel, placebo-controlled trial with three study periods:
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, and
Study Period III will be a double-blind 1 week down-titration period.

264 patients (e.g., 50% children 5-11 y., 50% adolescents 12- <17 years and 9 months) will be randomized into study period II.
All patients who complete Study Period II will participate in Study Period III.

Intervention

This study involves a comparison of risperidone (eq.. to approx. 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.
Dosing may then be increased (or decreased).
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).
Patients who cannot tolerate the minimum daily dose specified will be discontinued from the study. Dose changes (up or down) will only be permitted at study visits (or, due to adverse events, at unscheduled visits, for down-titration) Study medication will be given once daily in the evening.

Study burden and risks

The burden and risk for participation to this study have been kept to a minimum. The experimental conditions are similar to clinical conditions. All efforts are according to international consensus and best clinical practise. In the extent of burden for participants of the study is not significantly other than in clinical practise except a few more questionnaires. The treatment endures 12 weeks, including open label titration, maintenance period, fixed dose, dose reduction, maintenance dose and down titration. Previous studies indicated that risperidone treated patients (without mental retardation) showed improvement on interpersonal behaviour and rule compliance and reductions in clinician-rated symptoms and agressive behaviour.

Most questionnaires are completed by the legal representatives (parents/caregivers), to avoid the participation being to burdened with this.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)

Inclusion criteria

Patients are eligible to be included in the study only if they meet all of the inclusion criteria below. ;- Male or female patients aged 5.0 - <17 years and 9 months at Visit 1.;- Patients must have an IQ of > 85
- Patients must meet DSM-IV-TR diagnostic criteria for DSM-IV-TR Conduct Disorder(s) as confirmed by the Kiddie-SADS, Conduct Disorder Module: 312.8x. (Kaufman et al., 1996)
- Patients must score >= 27 on the Nisonger CBR Form, ODD/CD Disruptive Behavior Composite (D-Total)
- Patients must score >=4 (*moderately ill* (or >5, *markedly ill*) on the CGI-S rating scale
- 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.
- Patients must have a body weight of at least 25 kg at study entry.
- Patients must be able to swallow study drug.
- Patients must have venous access sufficient to allow blood sampling and are compliant with blood draws as per protocol
- Patients meeting criteria for comorbid ADHD (as to the clinical judgment of the investigator) will not be excluded from study participation.

Exclusion criteria

A patient will be excluded from the study if he or she meets any exclusion criteria described below, according to the assessment of the investigator.;- 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.
- Has participated in any investigational drug trial within six months prior to baseline (visit 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.
- 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, pervasive developmental disorder (autistic disorder or Asperger disorder).
- In the clinical judgment of the investigator, meets criteria for a primary psychiatric disorder, e.g., Anxiety Disorder, Depressive Disorder, Tic Disorder or Tourette*s Syndrome
- 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) at/beyond Visit 2. (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.)
- 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.
- Has a known or suspected seizure disorder.
- Has a history of neuroleptic malignant syndrome (NMS) or of tardive dyskinesia.
- Has a history of hypersensitivity to neuroleptics, of tardive dyskinesia, or neuroleptic malignant syndrome.
- Is pregnant or nursing.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL
Recruitment status: Pending

Start date (anticipated):	01-04-2012
Enrollment:	38
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Risperidone
Generic name:	Risperidone
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	23-04-2012
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	31-01-2013
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

ID: 21876
Source: NTR
Title:

In other registers

Register	ID
EudraCT	EUCTR2011-000567-26-NL
CCMO	NL35625.091.12
OMON	NL-OMON21876