An open-label study of two single oral doses of galantamine, examining the pharmacokinetics, safety, and tolerability in children with Down syndrome

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The primary objective is to determine the pharmacokinetic characteristics of galantamine after 2 single oral doses in children with Down syndrome. Secondary objectives are to evaluate safety and tolerability.

Ethical review	Approved WMO
Status	Will not start
Health condition type	Chromosomal abnormalities, gene alterations and gene variants
Study type	Interventional

Summary

ID

NL-OMON30535

Source
ToetsingOnline

Brief title
GAL-PED-1001

Condition

- Chromosomal abnormalities, gene alterations and gene variants

Synonym
Down syndrome, meiotic non-disjunction, trisomy 21

Research involving
Human

Sponsors and support

Primary sponsor: Janssen-Cilag
Source(s) of monetary or material Support: door de sponsor

Intervention

Keyword: Down syndrome, galantamine, pharmacokinetics, safety

Outcome measures

Primary outcome

Plasma concentrations of galantamine will be determined from samples taken at

baseline, then after 0.5h, 1h, 2h, 4h, 8h, 24h, and 28h following dosing on the

2 profile days.

Secondary outcome

Safety will be evaluated on the basis of adverse event reports, laboratory

values and ECG findings.

Study description

Background summary

Galantamine has been approved in almost all major markets for the treatment of mild to moderate dementia of the Alzheimer*s type. Galantamine has also been investigated for the treatment of other diseases and in healthy volunteers and was shown to be generally safe and well tolerated. Neuropsychological en neurochemical similarities between Down syndrome and Alzheimer*s disease (AD) are well established. There is a reduced cholinergic input to cortical and limbic brain regions in both Down Syndrome and AD, which supports a rationale for the study of cholinergic drugs in Down syndrome.
Down syndrome is the most common genetic disorder recognized at birth with associated adaptive and cognitive impairments. The rate of cognitive development tends to slow down as these children grow older. A study in children rather than in adults avoids possible confusion of treatment effects in Alzheimer*s disease(AD), since AD is widely prevalent in adults with Down syndrome.
Drugs which specifically activate cholinergic receptors provide amelioration of

Down syndrome symptoms in studies in children and adults. Galantamine*s unique profile of cholinergic action may offer exceptional potential for its use as a novel treatment for Downs syndrome. It is possible that subjects with Down syndrome show different pharmacokinetics to healthy subjects. In order to prepare for larger controlled clinical studies in this indication, pharmacokinetic data of galantamine in this particular population are required.

Study objective

The primary objective is to determine the pharmacokinetic characteristics of galantamine after 2 single oral doses in children with Down syndrome. Secondary objectives are to evaluate safety and tolerability.

Study design

Open-label pharmacokinetic study in a multi center with two profile days. After screening, eligible subjects will receive a single oral dose of galantamine on each of the two profile days, the lower dose first. Time is allowed after the first dose, in a sub-group of subjects, to analyze galantamine pharmacokinetics and assess safety data before proceeding to the remaining subjects or moving to the second dose.

Intervention

Galantamine will be provided as solution. The dose will be determined per kg body weight (mg/kg). Study medication will be administered in the morning of the two profile days. A dose of 0.04 mg/kg will be administered in the morning on the first profile day, and the dose will be 0.08 mg/kg on the second profile day. The two profile days will be separated by at least 7 days and by not more than 48 days.

Study burden and risks

The children will have to return to the clinic 5 times; for 2 hours at visit 1, for 9 hours at visit 2, for 4 hours at visit 3 (visit 2 and 3 together cover Profile day A), for 9 hours at visit 4 and for 4 hours at visit 5 (visit 4 and 5 together cover Profile day B). The children will be watched carefully (and will be entertained) during the Profile days. Data of the first dose will be analyzed from 6 subjects before the higher dose will be administered.
At visit 1, 10 ml blood will be collected, maximally 1 week later, visit 2 will be scheduled and 6 times 2 = 12 ml blood will be collected (0, 0.5, 1, 2, 4, and 8 hours after dosing), the subsequent day is visit 3, and 2 times 2 = 4 ml blood will be collected (24 and 28 hours after dosing), visit 4 is scheduled 7 to 48 days later and 6 times 2 = 12 ml blood will be collected and the subsequent day (visit 5) 2 times 2 = 4 ml blood will be collected, togather with once more 10 ml blood.

The study has to be performed in children with Down syndrome because (a) development of cognition decreases with age and finding an effects will be possible only in children, (b) adults with Down syndrome have an increased risk for Alzheimer's disease and this will omplicate the interpretation of results and (c) it is possible that pharmocinetics differ from others in subjects with Down syndrome.

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

Children with Down syndrome, genetically cariotyped with trysomy 21, meiotic non-disjunction, aged between 9 - 16 years, naive to any cholinerg drug, if subject is of childbearing potential she must have a negative serum beta-hcg pregnancy test and must

use a reliable contraceptives, and subjects (if > 11 years of age) and parents should have provided informed consent

Exclusion criteria

Known hypersensitivity to galantamine hydrobromide or any excipients used in the formulation, history of severe drug allergy or hypersensitivity, weight/height below the 5th percentile for age on the standardized curve for subjects with Down syndrome Trisomy 21, mosaic (mitotic non-disjunction) Trisomy 21, translocation, subject having received prohibited medication, history or presence of one of the specified conditions possibly resulting in cognitive impairment, current clinically significant cardiovascular disease, gastrointestinal disease, psychiatric disease, uncorrected hearing or visual disturbances, hepatic, renal or pulmonary disturbances, urinary outflow obstructions, history of epilepsy, malignancy

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Start date (anticipated):	01-02-2007
Enrollment:	16
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Reminyl 4 mg/ml, oral solution
Generic name:	galantamine 4 mg/ml, oral solution
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	06-06-2007
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	07-08-2007
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	07-09-2007
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

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

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2006-003359-19-NL
Other	Het wordt nog geregistreerd
CCMO	NL14063.000.06