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The effect of simvastatin on the cognitive deficits of children with neurofibromatosis I (NF1): a randomised, double-blind placebo-controlled study

Submission date
14/02/2006

Recruitment status
No longer recruiting

Registration date
14/02/2006

Overall study status
Completed

Last Edited
25/07/2008

Condition category
Nervous System Diseases

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
NTR542

Study information

Scientific Title

Acronym
NF1 simvastatin trial

Study objectives
Statin-treatment has been shown to normalise the learning and attention deficits in NF1 +/- mice by decreasing Ras activity. The fact that statins are effective in NF1 mice, combined with their very good safety profile, makes them an ideal candidate drug to treat cognitive impairments associated with NF1 in human patients.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics approval received from the local medical ethics committee.

Study design
Randomised, double-blind placebo-controlled study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Neurofibromatosis type 1 (NF1)

Interventions
Simvastatin (10 mg/day for month 1, 20 mg/day month 2, 20 mg/day month 3 for children 8-12 years old or 40 mg/day month 3 for children 12-16 years old) or placebo once a day.

Intervention Type
Drug

Phase
Not Specified

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

Primary outcome(s)
1. Performance on neuropsychological tests on visuospatial memory and attention after 1 and 3 months (Rey Complex Figure test [recall], Bourdon Vos Test)
2. Performance on neurophysiological tests on adaptation of eye movements after 1 and 3 months (saccade-adaptation test, adaptation of eye-hand coordination)

3. Measurement of the size, number, localization and spectra of unidentified bright objects (UBOs), hyperintensities on T2 weighed magnetic resonance imaging (MRI) and 3D CSI 1H magnetic resonance spectroscopy (MRS) after 3 months

Key secondary outcome(s))
1. Score on the following neuropsychological tests after 1 and 3 months (after 1 month = under METC review as of 02 May 2006):
1.1. Judgement of line orientation test
1.2. Rey Complex Figure Test (copy)
1.3. Beery VMI Test
2. Score on the following neuropsychological tests after 3 months:
2.1. IQ-test: WISC-RN
2.2. Verbal Fluency Test
2.3. Trailmaking Test A&B
2.4. Wisconsin Card Sorting Test
2.5. Peabody Picture Vocabulary Test
2.6. Boston Naming Test
2.7. 15 Word-Test
2.8. Stroop Color Word Test
3. Identification of facial emotions (ANT). Outcome of the following questionnaires after 3 months:
3.1. Child Behavior Check List (CBCL parents)
3.2. Teacher Report form (TRF)
3.3. Child Behavior Check List (CBCL child)
3.4. Quality of Life Questionnaire CHQ-CF87 Dutch edition (child) (under METC review as of 02 May 2006)
3.5. Quality of Life Questionnaire CHQ-PF50 Dutch edition (parents) (under METC review as of 02 May 2006)
4. Performance on the following neurophysiological tests after 1 and 3 months:
4.1. Basic saccade performance
4.2. Smooth pursuit

Completion date
01/03/2007

Eligibility

Key inclusion criteria
1. Children aged between 8 and 16 years
2. NF1 diagnosis according to the criteria of the National Institutes of Health
3. Visiting the multidisciplinary NF1-outpatient clinic at the Erasmus MC-Sophia Children's Hospital
4. Informed consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group

Child

Lower age limit
8 years

Upper age limit
16 years

Sex
All

Key exclusion criteria
1. Pathology of the central nervous system (CNS) (hydrocephalus, epilepsy, radiotherapy, neurosurgery etc.)
2. Deafness and/or severely impaired vision
3. Use of anti-epileptics and/or neuroleptics

Additional exclusion criteria (under METC review as of 2nd May 2006):
4. Insufficient cognitive abilities to obtain a reliable score on a verbal IQ test (WISC-RN)
5. Contra-indications for simvastatin-treatment
6. Planned hospitalisation within three months after planned date of inclusion

Date of first enrolment
20/01/2006

Date of final enrolment
01/03/2007

Locations

Countries of recruitment
Netherlands

Study participating centre
Erasmus Medical Center
Rotterdam
Netherlands
3000 DR

Sponsor information

Organisation
Erasmus Medical Center (The Netherlands)

ROR

https://ror.org/018906e22

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Sophia Children's Hospital Fund (The Netherlands)

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?
Results article	Results	16/07/2008		Yes	No