A 3-year, multi-center study to evaluate optical coherencetomography as an outcome measure in patients with multiple sclerosis

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Primary objective: To evaluate change in RNFL thickness in RRMS patients followed for up to 36 monthscompared to a group of reference subjects (without neurologic or ophthalmic disease) todetermine whether the technology is sufficiently sensitive to...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Ocular sensory symptoms NEC
Study type	Observational invasive

Summary

ID

NL-OMON37946

Source
ToetsingOnline

Brief title
CFTY720D2319

Condition

- Ocular sensory symptoms NEC
- Central nervous system infections and inflammations

Synonym
chronic impairment of the central nervous system, multiple sclerosis

Research involving
Human

Sponsors and support

Primary sponsor: Novartis
Source(s) of monetary or material Support: Pharmaceutical Industry

Intervention

Keyword: Magnetic resonance imaging (MRI), Multiple sclerosis (MS), Optic neuritis, Optimal coherence tomography (OCT)

Outcome measures

Primary outcome

The primary variable is the change from baseline in the RNFL thickness at Month

36. The analyses of the primary variable will be based on the Full Analysis

Set.

Secondary outcome

Please refer to section 9.5 of the protocol dated 25-03-2011:

The following (para) clinical variabilities will be evaluated:

- RNFL thickness (intra patient variability)

- relation between change in RNFL thickness and the percentage change in brain

volume, and the change in disability

- disability progression

- visual function

Study description

Background summary

This study will provide data of importance in the field of MS to determine if the latest OCT technology (HD) can provide a reliable and convenient tool by which to monitor disease progression, estimate the rate of neurodegeneration and assess anti-neurodegenerative treatment effect of MS therapies.

Correlations of OCT findings with MRI and clinical findings may enhance our understanding of the relationship
between CNS inflammation, tissue injury, regeneration and neurological deficit.

Study objective

Primary objective: To evaluate change in RNFL thickness in RRMS patients followed for up to 36 months
compared to a group of reference subjects (without neurologic or ophthalmic disease) to
determine whether the technology is sufficiently sensitive to disease and to change over time
to be useful as a monitoring tool.
Secondary objectives
- To evaluate the correlation of change in RNFL thickness and macular volume with change in
brain volume as measured by MRI in RRMS patients followed for up to 36 months.
- To evaluate the correlation of change in RNFL thickness and macular volume with change in
disability (as assessed by the EDSS and visual function) in RRMS patients followed for up to
36 months.
- To evaluate short-team reproducibility of the RNFL thickness measure at study start by
test/re-test estimation after a 4*week interval in a subset of RRMS patients and reference
subjects (without neurologic or ophthalmic disease).
- To evaluate short-term reproducibility (4-week interval) in macular volume measure (as
above).
- To evaluate change in macular volume over 36 months in RRMS patients compared to a
group of reference subjects (without neurologic or ophthalmic disease).

Study design

This is a 3-year, pharmacologically non-interventional study to evaluate OCT as an outcome measure in patients with RRMS.
A total of approximately 350 RRMS patients, either untreated or treated with an approved MS disease-modifying therapy and approximately 70 reference subjects without ophthalmologic or neurologic disease will be enrolled in this study. Of the treated patients, it is expected that approximately 50% will be treated with interferon beta (interferon beta 1a or 1b), approximately 25-30% with glatiramer acetate, approximately 10-15% with fingolimod, and approximately 10% with natalizumab. No study medications will be provided. The study consists of Screening (up to 1month), Baseline, and a 36-month longitudinal data collection

phase. Eligibility will be confirmed during Screening.

Study burden and risks

You will have assessments of your eyes and this may include the eye doctor dilating your pupils using eye drops which might lead to blurred vision. It is therefore recommended that you should have another person driving you home after each eye examination visit.
You need to be aware that gadolinium is used as the contrast dye during the MRI procedure. Current radiology practices and recommendations discourage the use of gadolinium-based contrast agents during pregnancy because their safety for the foetus has not yet been proven. In line, however, with the European Society of Radiology guidelines and based on the available evidence, gadolinium-based contrast agents appear to be safe in pregnancy.
Gadolinium will be injected into your vein before the last set of images in order to see lesions more clearly. A few side effects, such as mild headache, nausea and local burning can occur with gadolinium. Very rarely (less than one in a thousand), patients are allergic to gadolinium.

See protocol dd 30 August 2011 table 6-1 for an overview of the procedures and assessments per visit of the subjects.
- 4x physical examination
- 4x vital signs
- 4x opthalmologic examination (additional unscheduled opthalmologic examination may be required)
- 8x OCT (additional unscheduled OCT may be required)
- 4x MRI
The following procedures are only applicable to MS patients:
- 7x EDSS
- 9x MS relapse
- 5x SDMT

Contacts

Public
Novartis

Lichtstrasse 35
Basel CH-4056
CH
Scientific
Novartis

Lichtstrasse 35

Basel CH-4056
CH

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Inclusion criteria for patients with MS:
1. Male and female patients aged 18-55 years inclusive
2. A diagnosis of MS as defined by the 2005 revision to the McDonald criteria with a relapsing-remitting course
3. MS disease duration of more than one year (from diagnosis of MS) before study entry (Screening);Inclusion criteria for participants in the reference group:
1. Male and female subjects aged 18-55 years inclusive.
2. Matched to MS patients in terms of age (±3 years),
ethnicity, gender and visual refraction (±2 diopters) with the MS patients recruited.

Exclusion criteria

Exclusion criteria for patients with MS and reference group:
1. HIV or any other known immunodeficiency syndrome (disease or drug-induced)
2. Any ophthalmologic reason for RNFL pathology other than MS, such as optic neuropathy, active advanced glaucoma, injury of the optic nerve or history or presence of severe myopia based on the ophthalmologist*s clinical judgment or * history or presence of severe myopia: a. in patients who have not had refractive surgery, a refractive error of greater than 6.00 diopters b. pathologic fundus changes of high myopia, such as retinal pigmentary atrophy, besides peripapillary atrophy (atrophy involving the macula) or a staphyloma c. in patients that have had previous refractive surgery, an axial eye length of greater than 26 mm
3. Acute optic neuritis within the past 6 months before Baseline
4. Evidence of advanced, non-proliferative or proliferative diabetic retinopathy
5. Presence of retinal conditions associated with edema, subretinal fluid, cysts, etc.

6. History of a severe head trauma
7. Any of the following neurologic/psychiatric disorders:
* history of substance abuse (drug or alcohol) in the past five years or any other factor (i.e., serious psychiatric condition) that may interfere with the subject*s ability to cooperate and comply with the study procedures
* specific MRI findings (tumor, subdural haematoma, post-contusional changes, territorial stroke, neurodegenerative disorders, aneurysm/arteriovenous malformation, evidence of past macroscopic haemorrhage, or other relevant MRI findings that would interfere with evaluation)
* progressive neurological disorder, other than MS, which may affect participation in the study
8. Concomitant use of drugs that may directly affect retinal structure and function (e.g. chronic systemic corticosteroids [>30 consecutive days; doses higher than Cushing threshold e.g. prednisone 7.5mg/d], intraocular anti-angiogenic drugs [ranibizumab, bevacizumab], intraocular steroids etc.)
9. Any medically unstable condition, progressive disease (other than MS) or other condition that would preclude reliable participation in the study as assessed by the investigator
10. Patients unable to undergo MRI scans including gadolinium enhancement:
* reduced renal clearance (eGFR <45 ml/min)
* history of severe hypersensitivity to gadolinium-DTPA
* claustrophobia that cannot be overcome otherwise
11. Patients who have received an investigational drug or therapy within 30 days or 5 half lives, which ever is longer, of the baseline visit.;Exclusion criteria for participants in the reference group:
1. HIV or any other known immunodeficiency syndrome (disease or drug-induced)
2. Any ophthalmologic reason for RNFL pathology, such as optic neuropathy, active advanced glaucoma, injury of the optic nerve or history or presence of severe myopia based on the ophthalmologist*s clinical judgment
3. Acute optic neuritis within the past 6 months before Baseline
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5. Presence of retinal conditions associated with e.g. edema, subretinal fluid, cysts
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interfere with evaluation)
* progressive neurological disorder which may affect participation in the study
8. Any medically unstable condition, progressive disease or other condition that would preclude reliable participation in the study as assessed by the investigator
9. Concomitant use of drugs that may directly affect retinal structure and function
10. Unable to undergo MRI scans, including claustrophobia that cannot be overcome otherwise

11. Subjects who have received an investigational drug or therapy within 30 days or 5 half lives, which ever is longer, of the baseline

Study design

Design

Study phase:	3
Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-11-2012
Enrollment:	20
Type:	Actual

Ethics review

Approved WMO Date:	15-05-2012
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	27-09-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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
CCMO	NL36880.029.11