Effects of fingolimod on functional brain adaptation and clinical measures in multiple sclerosis

Published: 17-12-2014
Last updated: 22-04-2024

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Demyelinating disorders
Study type	Interventional

Summary

ID

NL-OMON44409

Source
ToetsingOnline

Brief title
Effect of fingolimod on brain and cognition

Condition

- Demyelinating disorders

Synonym
MS, Multiple Sclerose

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: Novartis,VUmc

Intervention

Keyword: cognition, fingolimod, functional reorganization, multiple sclerosis

Outcome measures

Primary outcome

1) Changes in brain activity and brain networks

2) Changes in cognition

3) Progression of physical disability

Secondary outcome

not applicable

Study description

Background summary

Physical problems as well as cognitive impairment are frequently seen in patients with multiple sclerosis (MS). Currently, no effective treatment is available to alleviate these disabling symptoms. Important new insights into the pathophysiology of MS cognitive impairment have been gained, which are consistent with a *functional reorganization model*. This model implies that cognitive impairment is preceded by reorganization of brain function (as measured with functional magnetic resonance imaging (MRI)) and is regarded as a crucial compensatory mechanism that counterbalances on-going brain damage and delays the onset of MS cognitive decline. Recently, the first oral immunomodulating treatment, fingolimod (gilenya), has been introduced in the field of MS and has shown to be effective in terms of disease activity in relapsing remitting (RR) MS patients. Additionally, animal studies show that fingolimod might have a neuroprotective effect. To date, it is not yet known whether fingolimod has a positive effect on cognitive functioning and functional reorganization of RRMS patients.

Study objective

The main objective of the proposed study is to investigate whether the disproportionally strong clinical effects of fingolimod in RRMS can be explained by enhanced functional brain adaptation and whether enhanced functional adaptation is sustained over time. Functional brain adaptation will

be measured with task-related brain activation (during information processing) and resting-state functional connectivity. We will investigate the effects of enhanced functional adaptation on cognition, disability and progression.

Study design

The proposed study is a prospective, single-center, interventional, longitudinal patient-control study assessing the effect of fingolimod on cognition and functional brain adaptation in RRMS patients.

Subjects will visit the outpatient clinic 3 times in a period of 18 months for various measurements: neurological examination (patients only), extensive neuropsychological testing, structural and functional MRI and blood sampling.

Intervention

MRI, neuropsychological testing and blood sampling.

Study burden and risks

All patients need three visits at the outpatient clinic of VU University medical center for neurological examination (patients only; approximately 30 min.), neuropsychological testing (approximately 60 min.), MRI scanning (approximately 60 min.) and blood sampling. Prior to the visit, subjects are asked to fill out 4 questionnaires (approximately 30 min.). The baseline measurement for patients is prior to the start with medication. Follow-up measurements will be 6 and 18 months after the baseline measurement.

The treatment of patients will not be changes by this study (i.e. standard of care). Additionally, the decision to start with first line therapy or fingolimod is made by the patient and treating neurologist, and is not influenced by this study. Therefore, the intervention only consists of neurological examination, neuropsychological examination, MRI scanning and blood sampling. These measurements are risk-free: MRI is a safe technique, and subjects will be screened for safety criteria to undergo MRI scanning (and earplugs will be provided to reduce scanner noise). Side effects due to medication are not directly related to the present study.

Contacts

Public
Vrije Universiteit Medisch Centrum

Van der Boechorststraat 7

Amsterdam 1081BT
NL
Scientific
Vrije Universiteit Medisch Centrum

Van der Boechorststraat 7
Amsterdam 1081BT
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Subjects should be between 18 and 65 years of age
- Subjects should meet the safety criteria to undergo MRI examination
- Patients should be diagnosed with RRMS
- The first measurement of patients on fingolimod should be within four weeks after the start of fingolimod treatment

Exclusion criteria

- Presence or history of psychiatric or neurological disease (for patients: neurological disease other than MS) that is expected to affect outcome measures (will be discussed with the principal investigator and neurologist)
- Presence or history of drug abuse
- For patients: relapse or steroid treatment less than four weeks prior to examination
- Insufficient visual acuity and motor skills to perform the fMRI task

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	25-02-2015
Enrollment:	70
Type:	Actual

Ethics review

Approved WMO Date:	17-12-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-07-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-09-2016
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
Other	Nederlands Trial Register TC 4657
CCMO	NL50253.029.14