The safety and cost-effectiveness of discontinuing disease-modifying therapies in relapsing-onset multiple sclerosis (DOT-MS): a randomized rater-blinded multicenter trial.

No registrations found.

Ethical review	Not applicable
Status	Pending
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON21462

Source
NTR

Brief title
DOT-MS

Health condition

Multiple Sclerosis

Sponsors and support

Primary sponsor: Amsterdam UMC, location VUmc
Source(s) of monetary or material Support: ZonMW, Stichting MS Research

Intervention

Outcome measures

Primary outcome

The primary endpoint is number of patients with return of inflammatory disease activity after 2 years based on: a clinically confirmed relapse (defined according to the definition most often used in MS phase-III trials: the onset of new or recurrent symptoms that last > 24 hours, that are accompanied by new objective abnormalities on a neurological examination and that are not explained by non-MS processes such as fever, infection, severe stress or drug toxicity (Gold et al NEJM 2012)) , or any emerging subclinical disease activity proven to be due to active disease/new inflammation (defined as 3 or more lesions on T2—weighted images or 2 or more gadolinium enhancing lesions on T1-weighted post-contrast MRI) in the discontinuation group.

Secondary outcome

Secondary end points are:
- Changes in neurological functioning (EDSS, MSFC)
- Individual MRI-parameters (T1-post contrast lesion numbers and volumes, T2-lesion numbers and volumes, atrophy measurements)

Study description

Background summary

The aim of this study is to identify whether it is possible to safely discontinue treatment in MS patients who have shown no evidence of active inflammation in the years prior to inclusion clinically and/or radiologically. The secondary objectives address the questions whether the discontinuation of first-line treatment has an effect on disability progression and whether the discontinuation of first-line treatment improves the quality of life for the patient. Furthermore, blood collections will be included to assess whether it is possible to retrospectively predict possible return of inflammatory activity with biomarkers such as neurofilament light (NFL) or patient characteristics such as disease activity prior to disease modifying therapy (DMT). In case of emerging disease activity after the cessation of therapy we will assess if reinitiation will lead to NEDA again, and if there are long-term consequences. If possible, post-hoc analysis are performed for the different types of treatment compounds.

Study objective

Discontinuation of first-line disease modifying medication (DMT) in patients with relapsing-onset multiple sclerosis that are inflammatory stable for at least 5 years, can be safely done without the return of inflammatory activity.

Study design

Data collection at the end of the trial, interim analysis

Intervention

Discontinuation of disease-modifying treatment

Contacts

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Eligibility criteria

Inclusion criteria

1. A minimum age of 18 years
2. Ability to understand the purpose and risks of the study and provide signed and dated informed consent and authorization to use protected health information (PHI) in accordance with national and local privacy regulations.
3. Definite diagnosis of relapsing-onset MS according to the revised McDonald 2017 criteria
4. All relapsing-onset MS patients treated with one of the first-line treatments: any of the interferons, glatiramer acetate, dimethylfumarate, teriflunomide
5. Complete absence of inflammatory activity (no objectively defined and confirmed relapses, no significant number (2 or more) of new-T2 lesions and no contrast-enhancing lesions) for 5 consecutive years under first-line treatment

Exclusion criteria

1. A switch between first-line disease modifying therapy over two years prior to inclusion, in case the switch has been due to in effectivity of the first DMT. In case the switch has been due to side-effects or by a personal preference of the patient (such as the wish to switch to oral therapies), this is not considered as an exclusion criterium.
2. Women who want to discontinue medication because of a pregnancy wish and women who are pregnant or expect to become pregnant during the study period

3. Patients that have previously used interferon-beta and have been tested positive for neutralizing antibodies (NAbs). This is determined by measuring MxA-bioactivity and is a test that is part of routine follow-up in patients that use interferon-beta. The reason for this is that development of NAbs has been shown to affect interferon-beta treatment efficacy.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Active

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-01-2020
Enrollment:	130
Type:	Anticipated

IPD sharing statement

Plan to share IPD: Undecided

Ethics review

Not applicable

Application type:	Not applicable

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
NTR-new	NL8188
Other	METC VUmc : METc VUmc 2019.662

Study results