Efficacy, safety and cost-effectiveness of B cell tailored ocrelizumab versus standard ocrelizumab in relapsing remitting multiple sclerosis: a randomized controlled trial

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With this study we aim to prove that personalized B cell tailored ocrelizumab treatment is non-inferior in the suppression of MS disease activity (clinically and radiologically) compared to the standard (fixed 24 week interval) treatment.

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

Summary

ID

NL-OMON52141

Source
ToetsingOnline

Brief title
BLOOMS trial

Condition

- Demyelinating disorders

Synonym
MS

Research involving
Human

Sponsors and support

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

Intervention

Keyword: B cell tailored dosing, Multiple sclerosis, Ocrelizumab

Outcome measures

Primary outcome

Relapses and new/enlarging T2 lesions on MRI.

Secondary outcome

confirmed disability progression on the EDSS

disability scores on the MSFC

neurofilament light

quality of life

burden of treatment

wearing-off effect

IgG levels

(serious) adverse events

Study description

Background summary

Multiple sclerosis (MS) is a devastating disease of the central nervous system (CNS), most commonly affecting young adults in western society.
Over the last two decades, immunomodulating drugs for RRMS have exponentially increased. One of the most effective drugs (introduced to the market in 2018) is ocrelizumab which has shown to reduce 46-47% of relapses and 91-98% of gadolinium enhancing MS lesions on MRI compared to first-line MS therapy.
Ocrelizumab is currently one of the most frequently described drugs in active

RRMS worldwide. In March 2020, approximately 1,450 MS (and 1,120 RRMS) patients in the Netherlands and 160,000 patients worldwide received ocrelizumab.

Ocrelizumab is approved in a 600 mg dose every 24 weeks (the first infusion is divided in two 300 mg infusions 2 weeks apart). However, B cell depletion is long-lasting with a medium repopulation after 72 weeks (range 27-175) after the last 600 mg dose. In 80% of patients, there is no sign of starting repopulation after 24 weeks. These are strong indicators of an *over-treatment* in the large majority of patients.

Study objective

With this study we aim to prove that personalized B cell tailored ocrelizumab treatment is non-inferior in the suppression of MS disease activity (clinically and radiologically) compared to the standard (fixed 24 week interval) treatment.

Study design

This is a national multicenter non-inferiority randomized controlled trial in the Netherlands. Follow-up will be 96 weeks.

Intervention

In this study, patients currently treated with ocrelizumab will be randomized (1:1) to stay on the standard treatment or receive a personalized B cell tailored ocrelizumab treatment.

In patients in the personalized group, starting at 24 weeks after the last ocrelizumab infusion, blood will be drawn to test B cells. As ocrelizumab can interfere with the flow cytometry analysis of CD20 cells, CD19 cells which carry a similar expression profile, are used for establishing B-cell depletion and repopulation. When CD19 B cells start to replete, with a cut-off of 10 cells/µL, patients will be scheduled for an ocrelizumab infusion in the next two weeks

Study burden and risks

Patients in the personalized group will likely receive less ocrelizumab, therefore there is a small chance of recurrence of disease activity.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

multiple sclerosis
minimally 48 weeks of treatment with ocrelizumab

Exclusion criteria

age below 18
inability to undergo frequent MRIs

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	20-04-2022
Enrollment:	296
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Ocrevus
Generic name:	ocrelizumab
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	15-03-2022
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-03-2022
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-12-2022

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-01-2023
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-02-2024
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-02-2024
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-02-2024
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-05-2024
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	30-05-2024
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-06-2024
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
EudraCT	EUCTR2021-004791-34-NL
ClinicalTrials.gov	NCT05296161
CCMO	NL78986.029.21