A multi-center double-blind parallel-group placebo-controlled study of the efficacy and safety of teriflunomide in patients with relapsing multiple sclerosis who are treated with interferon-beta.

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To assess the effect of teriflunomide in comparison to placebo, on frequency of multiple sclerosis (MS) relapses in patients with relapsing forms of MS who are treated with interferon beta (IFN-β)

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

Summary

ID

NL-OMON38164

Source
ToetsingOnline

Brief title
TERACLES

Condition

- Demyelinating disorders

Synonym
MS, multiple sclerosis

Research involving
Human

Sponsors and support

Primary sponsor: Sanofi-aventis
Source(s) of monetary or material Support: sponsor

Intervention

Keyword: efficacy, multiple sclerosis, safety, teriflunomide

Outcome measures

Primary outcome

Annualized relapse rate, defined as number of relapses per patientyear.

Secondary outcome

Key secondary endpoints:

• Brain MRI measure of number of gadolinium enhancing (Gdenhancing)

T1-weighted hypointense lesions (T1)-lesions.

• Time to disability progression.

Study description

Background summary

Multiple sclerosis (MS) is an inflammatory condition that damages the myelin of the central nervous system resulting in neurological impairment and, frequently, severe disability. It is the most frequent cause of disability in young adults, after car accidents. The disease affects approximately 2.5 million people worldwide at an incidence of 7 in 100 000/year. The following disease-modifying drugs are approved for the treatment of MS: Avonex (interferon beta-1a), Betaseron or Extavia (interferon beta-1b), Copaxone (glatiramer acetate), Rebif (interferon beta-1a), Novantrone (mitoxantrone), and Tysabri®. Interferon beta (IFN-β) has been used as first line disease-modifying drug in the treatment of RMS for more than a decade. However it is only partially effective, as most patients continue to have clinical relapses even while under treatment. Some patients remain on IFN-β since they perceive the treatment to be somewhat beneficial, even though it does not completely control disease activity. In these cases, the patients could benefit from having a tighter control on their

disease, and one option is to use an adjunct therapy to improve efficacy. Therefore, the purpose of this study is to assess the efficacy and safety of 7 mg and 14 mg of teriflunomide in comparison to the placebo in patients with relapsing MS who are treated with IFN-β.

Study objective

To assess the effect of teriflunomide in comparison to placebo, on frequency of multiple sclerosis (MS) relapses in patients with relapsing forms of MS who are treated with interferon beta (IFN-β)

Study design

Approximately 1455 patienten will be randomized in 3 parallel groups of terflunomide 7 mg, teriflunomide 14 mg and placebo on top IFN-β based on a 1:1:1 randomization ration . Teriflunomide and placebo are double-blind. The treatment duration is
approximately 48 weeks for the last patient recruited.

Intervention

Patients treated with IFN-β will be randomized in the placebo-, teriflunomide 7 mg or teriflunomide 14 mg arm. Patients will use the teriflunomide or placebo till the end of the trial or untill treatment discontinuation.

Study burden and risks

The common side effects reported in patients taking teriflunomide during clinical studies are nasopharyngitis (upper respiratory infection), flu symptoms, hair thinning/loss, nausea, elevated liver function test, paresthesia and hypoesthesia (abnormal skin sensations like numbness and tingling), pain (limb, joint or back), diarrhea, constipation, rash, and abdominal pain. An increase in blood pressure (usually mild) may occur. Blood tests have shown a mild decrease in the number of white blood cells but are not common. Teriflunomide may reduce your immune defense, which may increase susceptibility to infections.

Side effects reported for cholestyramine commonly include: constipation, stomach pain, nausea, diarrhea, heartburn or indigestion, abdominal gas, vomiting, belching, dizziness, and headache; and rarely include: bleeding tendencies, and weight loss. Side effects for activated charcoal include black stools, nausea and constipation.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Patient with relapsing forms of multiple sclerosis (MS) treated with Interferon beta (IFN-β) defined by:
- Stable dose of IFN-β for at least 6 months prior to randomization,and
- Disease activity in the 12 months prior to randomization and after first 3 months of IFN-β treatment (at least one relapse supported by Expanded Disability status Scale (EDSS) or equivalent neurological examination, or, at least one brain or spinal cord Magnetic Resonance Imaging (MRI) with at least one T1 gadolinium enhancing lesion).

Exclusion criteria

< 18 years of age or >= 56 years of age.

McDonald*s criteria for MS diagnosis not met at time of screening visit.
EDSS score > 5.5 at randomization visit.
A relapse within 30 days prior randomization.
Human Immunodeficiency Virus (HIV) positive patient.
Prior use within 6 months preceding randomization or concomitant use of nataluzimab and any other immunosuppressant agents such as azathioprine, cyclophosphamide, cyclosporin, methotrexate, mycophenolate or fingolimod.
Prior use in the 3 months preceding randomization of cytokine therapy (except baseline IFN-β), glatiramer acetate or intravenous immunoglobulins, or concomitant use of these treatments.
Prior use within 2 years preceding randomization or concomitant use of cladribine and mitoxantrone.
Pregnant or breast-feeding women or those who plan to become pregnant during the study.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	06-06-2011
Enrollment:	20
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	NA
Generic name:	teriflunomide

Ethics review

Approved WMO Date:	25-11-2010
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	15-02-2011
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	07-03-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	31-03-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	15-02-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	16-02-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	22-05-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO	

Date:	03-07-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	12-07-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	26-11-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	11-12-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	12-12-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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	EUCTR2010-023172-12-NL
CCMO	NL34295.060.10
Other	Zie sectie J.