A Randomized, Double-blind, Placebo-controlled, Parallel-Group, Dose-Ranging Study to Investigate the MRI Efficacy and Safety of Six Months* administration of Ofatumumab in Subjects with Relapsing-Remitting Multiple Sclerosis (RRMS) (OMS112831)

Published: 26-09-2011
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Primary: To determine whether ofatumumab 3, 30 or 60 milligrams (mg) given subcutaneously (SQ), reduces the cumulative number of new T1 GdE brain lesions over a period of 12 weeks, as compared with placebo.Secondary: Cumulative number of new T1 GdE...

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

Summary

ID

NL-OMON39973

Source
ToetsingOnline

Brief title
OMS112831 (MIRROR)

Condition

- Demyelinating disorders

Synonym

MS, mutiple sclerosis

Research involving
Human

Sponsors and support

Primary sponsor: GlaxoSmithKline
Source(s) of monetary or material Support: GlaxoSmithKline BV

Intervention

Keyword: MRI, Multiple sclerosis, ofatumumab, relapsing remitting

Outcome measures

Primary outcome

Cumulative number of new T1 GdE brain lesions over 12 weeks.

Secondary outcome

Cumulative number of new T1 GdE brain lesions over 24 weeks, safety and tolerability, preliminary assessment of effect on relapses, extent of B-cell depletion, immunogenicity.

Study description

Background summary

Ofatumumab is a novel monoclonal antibody that specifically binds to the human CD20 antigen of which expression is restricted to B lymphocytes from the pre-B cell stage to the plasmacytoid immunoblast stage only. A recent trial with rituximab demonstrated that targeting B-cells reduces the number of gadolinium-enhancing T1 lesions and the relapse rate in Relapsing-Remitting Multiple Sclerosis (RRMS).
Ofatumumab is marketed under the trade name Arzerra for the intravenous treatment of chronic lymphocytic leukemia in patients refractory to fludarabine and alemtuzumab.
A Phase II study of ofatumumab in RRMS subjects is ongoing. The primary objective of this study was to investigate the safety of a range of doses (100mg, 300 mg, and 700 mg) of ofatumumab in RRMS subjects, using an IV formulation. The treatment period has been completed; there are currently 4

subjects ongoing in the Follow up Phase. In the Week 0 to 24 period the majority of subject who were exposed to active treatment with ofatumumab (active/placebo) had CD19+ and CD20+ levels that were suppressed to zero; recovery started for the 100 mg and 300 mg active/placebo groups, at approximately, 12 and 20 weeks after discontinuation of dosing with ofatumumab, respectively. In the 700 mg active/placebo group, all but one subject had a persistent and complete CD19+ suppression at Week 24. In the Week 24 to 48 period, when those who had previously been exposed to placebo were treated with ofatumumab (placebo/active), the majority of the subjects' CD19+ and CD20+ levels were suppressed to zero (mm3) within one week. Recovery started for the subjects in the 100 mg placebo/active group after approximately 16 weeks (from these subjects* first infusion). In the 300 mg and 700 mg placebo/active groups, all subjects except one (700 mg) had persistent and complete CD19+ suppression at Week 48.
The present study will evaluate the MRI efficacy in subjects with RRMS, as well as continue to investigate the safety, of ofatumumab using a subcutaneous formulation.

Study objective

Primary: To determine whether ofatumumab 3, 30 or 60 milligrams (mg) given subcutaneously (SQ), reduces the cumulative number of new T1 GdE brain lesions over a period of 12 weeks, as compared with placebo.
Secondary: Cumulative number of new T1 GdE brain lesions over 24 weeks, safety and tolerability, preliminary assessment of effect on relapses, extent of B-cell depletion, immunogenicity.

Study design

Multicenter randomized double blind phase II dose ranging parallel group study.
Screening 6 weeks, treatment phase 24 weeks, follow-up 24 weeks.
Randomization naar behandeling met:
* Ofatumumab 3 mg s.c. every 12 weeks
* Ofatumumab 30 mg s.c. every 12 weeks
* Ofatumumab 60 mg s.c. every 12 weeks
* Ofatumumab 60 mg s.c. every 4 weeks
* Placebo and 12 weeks thereafter ofatumumab 3 mg s.c. .

1 week prior to start of the treatment phase start dose with ofatumumab 3 mg s.c. or placebo.
Study duration 54 weeks.
Upon completion or withdrawal from the core study period, subjects whose CD19+ B-cell counts are less than the lower limit of normal or baseline will be followed in the Individualized Follow-up Phase until recovery of the count.
The Netherlands will not participate in the sub-studies.
Approx. 196 patients (245 to be screened).

Intervention

Treatment with ofatumumab or placebo.

Study burden and risks

Risk: Adverse effects of study medication.
Burden: Study duration 54 weeks, possibly plus individualized follow-up thereafter.

During the 54 weeks:
12-13 visits. Duration 2-8 h.
S.c. injections (1 mL) with study drug or placebo every 4 weeks during the treatment phase (plus 1 week after start treatment), 7x in total..
Blood draws: approx. 45 mL per occasion, every visit. Optional pharmacogenetic testing (10 mL blood).
Pregnancy test 12x.
ECG 1x.
Some short tests to assess arm, hand and leg function 10x.
MRI brain (with gadolinium) 9x.
Questionnaires (2) 14x (1 should be answered by telephone). Mental status and fatigue. Duration 5-10 min.

Individualized follow-up:
Visit every 12 weeks.
Blood draws and questionnaires every visit.

Contacts

Public
GlaxoSmithKline

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Scientific
GlaxoSmithKline

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

* Males and females 18-55 years of age.
* Definite diagnosis of MS according to the 2010 revisions of the McDonald diagnostic criteria for MS.
* No manifestation of another type of MS other than RRMS.
* Relapsing-remitting course of disease with at least one of the following prior to screening:
A. At least one confirmed relapse within the previous year or
B. At least two confirmed relapses within the previous 2 years or
C. At least one relapse in the previous 2 years, with a GdE brain lesion on an MRI scan in the past year.
* EDSS score of 0-5.5 (inclusive) at screening.
* Neurologically stable with no evidence of relapse for at least 30 days.
* Safe contraception for women of childbearing potential.

Exclusion criteria

* Unable to undergo MRI scans.
* Any clinically significant brain abnormality other than MS found on MRI.
* Neurological findings consistent with PML or confirmed PML.
* Relapse during screening.
* Prior treatment with any of the following:
A. Systemic glucocorticoids or ACTH within one month prior to screening
B. Receipt of a live vaccine within 6 weeks prior to screening
C. Glatiramer acetate or IFN-* within 3 months prior to screening
D. Any immunomodulatory therapies, excluding glatiramer acetate or IFN-*, within 6 months prior to screening
E. Any monoclonal antibodies at any time, other than natalizumab
F. Any lymphocyte-depleting therapies

G. Any immunosuppressive agents
* Chronic or ongoing active infectious disease requiring long term systemic treatment.
* Previous serious opportunistic or atypical infections.
* Positive polymerase chain reaction (PCR) screening for JC Virus.
* Positive serology for Hepatitis B.
* Prior history, or suspicion, of TB
* Known history of positive serology for HIV.

Study design

Design

Study phase:	2
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):	11-01-2012
Enrollment:	8
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	ofatumumab
Generic name:	ofatumumab
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	26-09-2011
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	23-11-2011
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO

Date:	13-12-2011
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO

Date:	30-03-2012
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO

Date:	24-04-2012
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	10-05-2012
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO

Date:	06-07-2012
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO

Date:	02-08-2012
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO

Date:	07-08-2012
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO

Date:	15-10-2012
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO

Date:	16-10-2012
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO

Date:	16-04-2013
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO Date:	08-05-2013
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	30-04-2014
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	15-05-2014
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	09-01-2015
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	13-01-2015
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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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	clinicaltrials.gov
EudraCT	EUCTR2011-002333-19-NL
CCMO	NL38224.098.11