Long-term extension of the multinational, double-blind, placebo controlled study EFC6049 (HMR1726D/3001) to document the safety of two doses of teriflunomide (7 and 14 mg) in patients with multiple sclerosis with relapses

Published: 14-01-2008
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To document the long-term safety and tolerability of teriflunomide in MS patients with relapses.

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

Summary

ID

NL-OMON39264

Source
ToetsingOnline

Brief title
LTS6050

Condition

- Demyelinating disorders

Synonym
multiple sclerosis (MS)

Research involving
Human

Sponsors and support

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

Intervention

Keyword: extension, multiple sclerosis with relapses, teriflunomide

Outcome measures

Primary outcome

The primary endpoint is the safety of teriflunomide. Safety parameters include adverse events, Physical examinations, vital signs, blood and urine laboratory parameters and ultra-sound image of pancreas.

Secondary outcome

The secondary endpoints are the proportion of disability free patients and annualized MS relapse rate.

MRI variables: burden of disease defined as the total volume of T2 lesions (primary MRI variable), number of enhanced T1 lesion, total volume of post -gadolinium T1 hypo intense lesion (black holes), atrophy, total volume of enhanced T1 lesions, and Z4 composite score (exploratory variable)

Study description

Background summary

A double-blind, placebo controlled efficacay study (EFC6049) of two doses of teriflunomide (7 and 14 mg) in patients with multiple sclerosis with relapses was ongoing. This study was extended with the LTS5050 study. This LTS6050 study was for the second time extended, until 292 weeks and will allow to

gather long-term safety information and additional efficacy information.

Study objective

To document the long-term safety and tolerability of teriflunomide in MS patients with relapses.

Study design

International, multi-center study:
Parallel, double-blind study of two fixed doses of teriflunomide (7 and 14 mg/day), maintaining the double-blind status of the treatment in the previous study. Patients receiving placebo in the previous EFC6049 study will be randomized to either 7 or 14mg/day. Other patients will be blindly maintained on treatment dose group 7 mg or 14 mg. After randomisation the treatment period is maximal 288 weeks.
A post-treatment phase of 4 weeks is planned for all patients discontinuing study drug, with a washout procedure.

Intervention

Patients will be randomized in two groups, one group with 7 mg teriflunomide and one group with 14 mg teriflunomide.

Study burden and risks

The common side effects reported in patients taking teriflunomide during clinical studies are: nasopharyngitis (upper respiratory infection), flu symptoms, throat pain, hair thinning/loss, nausea, elevated liver function test, headache, paresthesia (abnormal skin sensations like numbness or tingling), hypoesthesia (diminished sensation), pain (limb, joint, or back), diarrhea, constipation, rash, itching 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. Teriflunomide breaks down in the body to a compound that has been shown to cause changes in DNA (genetic material) in test tube studies. The long-term effects of these findings in humans are unknown. However, these changes have the possibility of contributing to cell diseases, including cancer.
Side effects of washout medication
Side effects reported for cholestyramine include as common: constipation, stomach pain, nausea, diarrhea, heartburn or indigestion, abdominal gas, vomiting, belching, dizziness, headache; and as rare: bleeding tendencies, weight loss. Side effects for activated charcoal include black stools, nausea and constipation. Charcoal may also reduce the effectiveness of other drugs

and should be taken at least 2 hours before or 1 hour after other drugs.

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

- Patients who have completed the last study visit of the previous study (EFC6049) and do not meet criteria for treatment withdrawal;- Female patients of childbearing potential must agree to comply with the contraception requirement described in section 7.4 of the protocol.;- Female patients have demonstrated not to be pregnant by serum pregnancy test or breast feeding at the time of study entry.;- McDonald's criteria must continue to support the diagnosis of clinically definite MS (see protocol appendix A).;- An informed consent must be obtain in writing from the patient for this extension study prior to enrollment. Patients must demonstrate a willingness and ability to participate in a long term safety and efficacy trial with the opportunity to continue treatment on either 7 mg or 14 mg/day of teriflunomide

under double-blind conditions, until availability of the results for study EFC6049 (HMR1726D/3001). Patients must actively refuse existing approved therapies. ;In addition a supplemental HIV-testing informed consent will be required for patients who have not yet signed it in the main study (EFC6049) in order to have an HIV testing at baseline and yearly.

Exclusion criteria

- Patients who do not complete the EFC6049 (HMR1726D/3001) study.;- Patients who developed clinically relevant cardiovascular, hepatic, endocrine, or other major systematic disease making implementation of the protocol or interpretation of the study results difficult or that would put the patient at risk by participing in the study.;- Any known condition or circumstance that would prevent in the investigator's opinion, compliance or completion of the study.;- Pregnancy;- Breast-feeding;- Women of child-bearing potential, except if they satisfy all conditions described in protocol section7.4.;- Patients wishing to parent children during the course of the trial, or following the trial except if they agree to follow the appropriate drug washout procedure when they stop their study participation (protocol section 10.2);- Patients requiring treatment during the study period with drugs not permitted by the study protocol (Protocol section 8.9.2);- Prior use within 4 weeks before randomization or concomitant use of cholestyramine and/or activated charcoal;- Patients with a history of recent and clinically significant drug or alcohol abuse;- Liver function impairment or persisting ALT or direct bilirubin elevations of more than 1.5-fold the upper limit of normal;- Mental conditions rendering the patient unable to understand the nature, scope and possible consequence of the study.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Masking:	Double blinded (masking used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	10-06-2008

Enrollment:	31
Type:	Actual

Medical products/devices used

Product type:	Medicine

Ethics review

Approved WMO Date:	14-01-2008
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	11-02-2008
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	12-02-2008
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	15-04-2008
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	25-06-2008
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	12-11-2008
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United

	(Nieuwegein)
Approved WMO Date:	19-11-2008
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	03-12-2008
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	22-01-2009
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	21-06-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	23-06-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	14-01-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	17-01-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	15-06-2011

Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	21-11-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	14-06-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	27-06-2012
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:	19-12-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	08-03-2013
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	07-05-2013
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	EUCTR2006-003361-14-NL
ClinicalTrials.gov	NCT00134563
CCMO	NL21148.040.07