An extension of the 24-month, double-blind, randomized, multicenter, placebo-controlled, parallel-group study comparing efficacy and safety of FTY720 1.25 mg and 0.5 mg administered orally once daily versus placebo in patients with relapsing-remitting multiple sclerosis

Published: 26-03-2008
Last updated: 11-05-2024

Study CFTY720D2301E1 is designed to assess the following properties of FTY720 inpatients with relapsing MS:* To evaluate long-term safety and tolerability* To evaluate long-term efficacy

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

Summary

ID

NL-OMON37171

Source
ToetsingOnline

Brief title
FreedoMS extension

Condition

- Demyelinating disorders

Synonym
Relapsing-Remitting Multiple Sclerose

Research involving
Human

Sponsors and support

Primary sponsor: Novartis
Source(s) of monetary or material Support: Farmaceutische industrie

Intervention

Keyword: FTY720, multiple sclerose, RRMS.

Outcome measures

Primary outcome

- Safety:

The safety data from both core and extension studies will be included in the analysis on the safety population. The assessment of safety will be based mainly on the frequency of adverse events and on the incidence of clinically notable laboratory abnormalities. Other safety assessments will include laboratory data summaries, vital signs, bradycardia events, pulmonary function tests, chest x-ray or HRCT, ophthalmic, and ECG data.

- Tolerability:

Tolerability will be assessed by summarizing AEs or abnormal laboratory values by treatment group. No special questionnaires will be offered for assessment of acceptability/tolerability of the study medication.

- Efficacy:

No primary efficacy variables are defined in this extension study.

The efficacy variables are annualized relapse rate, time to confirmed

disability progression, EDSS score, MSFC score, number of Gd-enhanced

T1-weighted lesion, and number of new or newly-enlarged T2 lesions.

Secondary outcome

Not applicable

Study description

Background summary

This is an extension to the double-blind, randomized, placebo-controlled parallel-group,
multicenter study comparing efficacy and safety of FTY720 1.25 mg and 0.5 mg administered
orally versus placebo in patients with relapsing-remitting multiple sclerosis (MS). The
primary objective of the core study was to evaluate the effect of FTY720 on relapse rate
during 24 months. For full details, please refer to the core protocol CFTY720D2301 (core
study).
The extension study offers to eligible patients who complete the 24 month core study FTY720
treatment until FTY720 becomes available on the market or until development is terminated.
The extension study is designed to evaluate long-term safety, tolerability and efficacy of
FTY720 in MS patients.

Study objective

Study CFTY720D2301E1 is designed to assess the following properties of FTY720 in patients with relapsing MS:
* To evaluate long-term safety and tolerability
* To evaluate long-term efficacy

Study design

This is a long-term extension study of a 24-month double-blind, randomized, multicenter,
placebo-controlled, parallel-group study in approximately 1250 patients with RRMS (study
CFTY720D2301).
The extension study has two phases:
1. Dose-blinded extension phase: from the time the first patient enters the extension
study until the last patient completes the core study and core study results become
available;
2. Open-label extension phase: from the end of the dose-blinded phase until FTY720
becomes available in the participating country or development is terminated.

Patients entering the extension study will be grouped as follows:
* Patients who were receiving either 1.25 mg/day or 0.5 mg/day of FTY720 in the core
study will continue on the same dose of study medication.
* Patients who were randomized to placebo in the core study will be re-randomized (1:1
ratio) to either 1.25 mg/day or 0.5 mg/day of FTY720.
At the end of the dose-blinded extension phase all patients will be offered open-label FTY720
treatment. Unless clinically contraindicated patients will remain on the dose they had been
previously randomized to.
Eligibility of patients who elect to participate in the extension study will be assessed based on
the inclusion/ exclusion criteria. Patients who participated in the core study but prematurely
discontinued the study will not be eligible to enter the extension study.

Intervention

Patients entering the extension study will be grouped as follows:
* Patients who were receiving either 1.25 mg/day or 0.5 mg/day of FTY720 in the core
study will continue on the same dose of study medication.
* Patients who were randomized to placebo in the core study will be re-randomized (1:1
ratio) to either 1.25 mg/day or 0.5 mg/day of FTY720.
At the end of the dose-blinded extension phase all patients will be offered open-label FTY720
treatment. Unless clinically contraindicated patients will remain on the dose they had been

previously randomized to.

Study burden and risks

Occurence of Brachycardia after first administration, first dose intake will be monitored.
Complications related to blood sample collection, i.e. bruces
Side effects. Few side effects have been reported in related trials with FTY 720.

Contacts

Public
Novartis

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Scientific
Novartis

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Patients should complete the 24 month core study
2. Written informed consent provided prior to participation in extension study
3. Female patients at risk of becoming pregnant must have a negative pregnancy test and use simultaneously two forms of effective contraception

Exclusion criteria

1. Premature discontinuation of the study drug during the core study FTY720D2301 due to:
a. An adverse event or serious adverse event or laboratory abnormality, except pregnancy
b. Conditions leading to permanent study drug discontinuation such as macular edema, elevated liver enzymes five times ULN (upper limit of normal), pulmonary function tests below 60% of baseline values. The full description of these exclusion criteria and monitoring guidelines is outlined in Appendix 4: Guidance on Safety Monitoring
2. Chronic disease of the immune system other than MS which may require immunosuppressive treatment
3. History or presence of malignancy
4. Known diagnosis of diabetes mellitus or a blood glucose obtained suspicious for diabetes (* 126 mg/dl or * 7 mmol/L if fasting; * 200 mg/dl or * 11.1 mmol/L if random)
5. Macular edema during the core study
6. Active systemic bacterial, viral or fungal infections, or known to have AIDS, Hepatitis B, Hepatitis C infection or have positive HIV antibody, Hepatitis B surface antigen or Hepatitis C antibody tests
7. Previous treatment with cladribine, cyclophosphamide or mitoxantrone
8. Treatment with immunoglobulins and/or monoclonal antibodies (including Natalizumab) in the past 3 months
9. Any medically unstable condition, that may interfere with the patient*s ability to cooperate and comply with the study procedures, as assessed by the treating physician
10. Any of the following cardiovascular conditions:
a. myocardial infarction within the past 6 months prior to entry in the extension study or with current unstable ischemic heart disease;
b. cardiac failure (Class III, according to New York Heart Association Classification) or any severe cardiac disease as determined by the investigator;
c. arrhythmia requiring current treatment with Class III antiarrhythmic drugs (e.g., amiodarone, bretylium, sotalol, ibulitide, azimilide, dofelitide)
d. history or presence of a third degree AV block
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Approved for report publication by Zhang Zheng in East Hanover at Fri, 09 Nov 2007 08:58:46 AM EST

e. proven history of sick sinus syndrome or sino-atrial heart block
f. known history of angina pectoris due to coronary spasm or Raynaud*s phenomenon
11. Any of the following pulmonary conditions:
a. Severe respiratory disease or pulmonary fibrosis diagnosed [during the core study]
b. History of tuberculosis
c. Abnormal chest x-ray or high resolution computer tomography (HRCT) [at selected sites] suggestive of active pulmonary disease in the core study
12. Known history of alcohol abuse, chronic liver disease
13. Current participation in any clinical research study evaluating another investigational drug or therapy
14. Female patients that are nursing (lactating)

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	09-04-2008
Enrollment:	89
Type:	Actual

Ethics review

Approved WMO

Application type:	First submission
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	EUCTR2007-004122-24-NL
ClinicalTrials.gov	NCT00355134
CCMO	NL21638.029.08