A Multicenter, Open-Label Study to Evaluate Fatigue in Subjects With Relapsing-Remitting Multiple Sclerosis During Treatment With Tecfidera® (Dimethyl Fumarate) Gastro-Resistant Hard Capsules (TECNERGY)

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Primary:The primary objective of this study is to determine whether DMF taken over 12 months is effective in reducing MS-related fatigue, as measured by mean changes in the Fatigue Scale for Motor and Cognitive Functions (FSMC), in subjects with...

Ethical review	Not approved
Status	Will not start
Health condition type	Demyelinating disorders
Study type	Interventional

Summary

ID

NL-OMON41702

Source
ToetsingOnline

Brief title
Biogen 109MS405 TECNERGY

Condition

- Demyelinating disorders

Synonym
Relapsing Remitting Multiple Sclerosis, RRMS

Research involving

Human

Sponsors and support

Primary sponsor: Biogen Idec Research Limited
Source(s) of monetary or material Support: Pharmaceutical Industry

Intervention

Keyword: Dimethyl Fumarate, Fatigue, Relapsing Remitting Multiple Sclerosis, Tecfidera

Outcome measures

Primary outcome

Primary:

- Mean change from Baseline in MS-related fatigue (FSMC) at 12 months in

subjects receiving DMF

Secondary outcome

Secondary:

- Mean change from Baseline in fatigue (FSMC and FSS) at 1, 3, 6, 9, and 12

months in subjects receiving DMF

- Mean change from Baseline in work productivity, quality of life, depression,

and sleepiness at 6 and 12 months in subjects receiving DMF

- Change in MS-related fatigue (FSMC) status (improved [> 4.5 increase], stable

[within ±4.5], and worsened [> 4.5 decrease])

- Correlation of fatigue with baseline demographics and disease characteristics

- Proportion of subjects with reduced dose or discontinuation of

fatigue-related medications at 6 and 12 months

Exploratory:

- Relationship of serum biomarker values to fatigue (change in biomarker value)

Study description

Background summary

Fatigue is a common symptom of multiple sclerosis (MS), impacting 75% to 95% of patients and directly contributing to cognitive and physical difficulties. More than half of patients diagnosed with MS report fatigue as one of their most disabling symptoms. Commonly used medications for MS have shown limited improvement in fatigue; hence, a treatment that would alleviate fatigue could improve the quality of life for individuals with MS. Increased oxidative stress has been observed in disorders in which fatigue is a prominent symptom, including chronic fatigue. Nonclinical and initial clinical studies of Tecfidera (dimethyl fumarate) gastro-resistant hard capsules (hereinafter referred to as DMF), a novel, oral, disease-modifying therapy developed for RRMS, suggest that the medication reduces both inflammation and oxidative stress. Given that such reductions are likely to decrease fatigue, this study will evaluate the effect of DMF on MS-related fatigue.
This study will investigate in a subset of subjects the impact of DMF treatment on serum biomarkers associated with endothelial inflammation, nitric oxide production, and chronic fatigue. Samples may also be used to identify or verify deoxyribonucleic acid (DNA), ribonucleic acid (RNA), and other biomarkers associated with disease and response to DMF. The relationship of serum biomarker levels with MS-related fatigue will also be assessed.

Study objective

Primary:
The primary objective of this study is to determine whether DMF taken over 12 months is effective in reducing MS-related fatigue, as measured by mean changes in the Fatigue Scale for Motor and Cognitive Functions (FSMC), in subjects with RRMS.

Secondary:
- To investigate changes from Baseline in FSMC and fatigue severity (Fatigue Severity Scale [FSS]) at 1, 3, 6, 9, and 12 months in subjects receiving DMF
- To assess the impact of DMF on patient-reported outcomes (PROs), including work productivity (Work Productivity and Activity Impairment-Multiple Sclerosis questionnaire [WPAI-MS]), health-related quality of life (Short Form Health Survey [SF-12] or the 15-dimensional health-related quality of life [15D HRQoL] questionnaire), depression (Beck Depression Inventory-Fast Screen [BDI-FS]), and sleepiness (Epworth Sleepiness Scale [ESS]) at 6 and 12 months in subjects receiving DMF

- To examine whether an association exists between fatigue and baseline demographics (e.g., age and sex) and disease characteristics (e.g., disease duration, baseline disease activity, treatment history, expanded disability status scale [EDSS] score, and PROs)
- To assess any changes in fatigue-related medication use

Exploratory:
- To assess the association between fatigue and serum biomarkers in a subset of subjects in Denmark and Finland

Study design

This multicenter study will evaluate MS-related fatigue in up to 320 subjects with RRMS receiving DMF at approximately 30 study sites across Europe. Subjects will have up to 6 scheduled clinic visits over a 12-month period.
Completed PRO questionnaires will be collected at various timepoints during the study. Any changes in fatigue-related medication use will be recorded with associated doses.

Intervention

The selected dose of DMF for this study is 120 mg twice daily (BID) for the first 7 days and 240 mg BID thereafter, which is consistent with the European Union Summary of Product Characteristics (SmPC).

Study burden and risks

The following assessments/evaluations will be used for all subjects:
- Demographics
- Height and weight
- Medical history, including duration of MS, relapse history in the previous 6 months, relapse status during the study, EDSS score, and any previous treatments for MS
- Alcohol consumption
- Tobacco use
- Concomitant medications and therapies
- All adverse events (AEs) and serious adverse events (SAEs)
- Changes in any fatigue-related medication use
- PRO questionnaires: FSMC, FSS, WPAI-MS, SF-12, 15D HRQoL (in Finland only), BDI-FS, and ESS

Risks and discomforts:

Serious effects of Tecfidera:
* allergic reactions * these are uncommon and may affect up to 1 in 100 people.
* reddening of the face or body (flushing) * this is a very common (may affect

more than 1 in 10 people) side effect.

Very common side effects of Tecfidera:
These may affect more than 1 in 10 people:
* reddening of the face or body, feeling warm, hot, burning, or itchy (flushing)
* loose stools (diarrhea)
* feeling sick (nausea)
* stomach pain or stomach cramps

Less common risks and side effects are described in the SmPC and ICF.

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

1. Have the ability to understand the purpose and risks of the study and provide signed and dated informed consent and authorization to use protected health information in accordance with national and local subject privacy regulations
2. Have a confirmed diagnosis of RRMS and satisfy the therapeutic indication as described in the local label.
3. Have a stable EDSS (as assessed by the Investigator) and have been on the same (type and dosage) standard of care first line treatment for at least 6 months.
4. If taking antidepressants, amphetamine, modafinil, or fampridine (Fampyra), subject must be assessed as having been clinically stable for at least 3 months prior to the Baseline Visit.
5. Age *18 years at the time of informed consent
6. FSMC total score *43 (mild fatigue) at Baseline.
7. As perceived by the Investigator, have the ability to comply with all requirements of the study protocol.
8. Female subjects of childbearing potential who are not surgically sterile must practice effective contraception during their participation in the study and be willing and able to continue contraception for 12 weeks after their last dose of study treatment.

Exclusion criteria

1. Diagnosis of major depression, as identified by the Investigator.
2. Diagnosis of primary progressive, secondary progressive, or progressive relapsing MS.
3. History of malignancy (except for basal cell carcinoma that had been completely excised prior to study entry), severe allergic or anaphylactic reactions or known drug hypersensitivity, abnormal laboratory results indicative of any significant disease, and/or a major disease that would preclude participation in a clinical trial.
4. History of a relapse within 90 days prior to study enrollment or showing transient symptoms derived from a previous relapse, irrespective of time of symptom onset.
5. Treatment of MS relapse within 90 days prior to study enrollment.
6. History of a positive test result for human immunodeficiency virus, hepatitis C virus antibody, or hepatitis B virus (defined as positive for hepatitis B surface antigen or hepatitis B core antibody.
7. Female subjects who are pregnant or planning to become pregnant during the study period, or who are currently breastfeeding.
8. Impaired hepatic or renal function, as perceived by the Investigator.
9. Any prior treatment with DMF (or other fumarate derivative), total lymphoid irradiation, cladribine, fingolimod, T cell or T-cell receptor vaccination, or any therapeutic monoclonal antibody.
10. Treatment within 1 year prior to study enrollment with mitoxantrone or cyclophosphamide.
11. Treatment within 6 months prior to study enrollment with cyclosporine, azathioprine, methotrexate, mycophenolate mofetil, intravenous immunoglobulin, plasmapheresis, cytapheresis, or another investigational drug or approved therapy for investigational use.

12. Current enrollment in any other clinical studies.
13. Known to suffer from narcolepsy or another significant sleep disorder.
14. Comorbidity that may have an impact on fatigue.
15. Other unspecified reasons that, in the opinion of the Investigator or Biogen Idec, make the subject unsuitable for enrollment.

Study design

Design

Study phase:	4
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	42
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Tecfidera
Generic name:	Dimethyl Fumarate
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	27-02-2014
Application type:	First submission
Review commission:	METC Z: Zuyderland-Zuyd (Heerlen)

Not approved

Date:	04-02-2015
Application type:	First submission
Review commission:	METC Z: Zuyderland-Zuyd (Heerlen)

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	EUCTR2013-001025-53-NL
CCMO	NL47368.096.14