A Multicenter, Global, Observational Study to Collect Information on Safety and to Document the Drug Utilization of Tecfidera™ (Dimethyl Fumarate) When Used in Routine Medical Practice in the Treatment of Multiple Sclerosis (ESTEEM)

First published: 19/12/2014

Last updated: 02/07/2024

Study | Finalised

Administrative details

EU PAS number

EUPAS6782

Study ID

46164

DARWIN EU® study

No

Study countries

Argentina
Australia
Austria
Canada
Denmark
France
Germany
Hungary
Ireland
Italy
Netherlands
New Zealand
Norway
Poland
Portugal
Puerto Rico
Slovakia
Spain
Switzerland
United Kingdom
United States

Study description

The primary objective of the study is to determine the incidence, type, and pattern of serious adverse events (SAEs), including but not limited to infections (including opportunistic infections), hepatic events, malignancies, and renal events, and of adverse events (AEs) leading to treatment discontinuation in patients with MS treated with dimethyl fumarate (DMF). Secondary objectives of this study in this population are as follows: To determine dimethyl fumarate (DMF) prescription and utilization patterns in routine clinical practice in patients

with multiple sclerosis (MS), To assess the effectiveness of dimethyl fumarate (DMF) on multiple sclerosis (MS) disease activity and disability progression in routine clinical practice as determined by the Expanded Disability Status Scale (EDSS) score and multiple sclerosis (MS) relapse information, and To assess the effect of dimethyl fumarate (DMF) on health-related quality of life, healthcare resource consumption, and work productivity.

Study status

Finalised

Research institutions and networks

Institutions

Biogen

First published: 01/02/2024

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Institution

Multiple centres: 468 centres are involved in the study

Contact details

Study institution contact

Study Director Biogen ctrr@biogen.com

Study contact

ctrr@biogen.com

Primary lead investigator

Study Director Biogen

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 31/12/2013

Actual: 04/06/2013

Study start date

Planned: 31/12/2013

Actual: 19/11/2013

Date of final study report

Planned: 30/11/2024

Actual: 21/08/2023

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Biogen

Study protocol

109MS401 Protocol V3 (EU) Final 15Aug14_Redacted.pdf (1.98 MB)

Regulatory

Was the study required by a regulatory body?

Yes

Is the study required by a Risk Management Plan (RMP)?

EU RMP category 3 (required)

Other study registration identification numbers and links

109MS401

https://clinicaltrials.gov/ct2/show/NCT02047097?term=109ms401&rank=1

Methodological aspects

Study type

Study type list

Study topic:

Disease /health condition

Human medicinal product

Study type:

Non-interventional study

Scope of the study:

Assessment of risk minimisation measure implementation or effectiveness

Data collection methods:

Primary data collection

Main study objective:

The primary objective of the study is to determine the incidence, type, and pattern of serious adverse events (SAEs), including but not limited to infections (including opportunistic infections), hepatic events, malignancies, and renal events, and of adverse events (AEs) leading to treatment discontinuation in patients with Multiple Sclerosis (MS) treated with dimethyl fumarate (DMF).

Study Design

Non-interventional study design

Cohort

Other

Non-interventional study design, other

Prospective, global, observational study

Study drug and medical condition

Study drug International non-proprietary name (INN) or common name

Medical condition to be studied

Multiple sclerosis

Population studied

Short description of the study population

The study population included patients aged 18 years or older diagnosed with multiple sclerosis (MS) newly prescribed with treatment of dimethyl fumarate (DMF) under routine clinical practice.

Inclusion criteria:

- Patients must be naïve to DMF, Fumaderm®, and compounded fumarates at the time of enrollment, but need not be naïve to other MS treatments, and must not be currently enrolled in any other clinical trial or study except for the DMF Pregnancy Registry or other studies that, according to the study Medical Director, do not conflict with this observational study (e.g., health economic studies).

Exclusion criteria:

- Patients with previous exposure to DMF, Fumaderm®, and compounded fumarates are excluded so as not to introduce bias; these patients may be more or less likely to experience AEs and may fail to report AEs that occurred before study enrollment.
- Patients participating in other clinical studies are excluded so as not to unduly confound causality assessments when a concomitant experimental agent’s safety profile has yet to be established and/or the physician is blinded to the patient’s treatment assignment.

Age groups

- Adults (18 to < 46 years)
- Adults (46 to < 65 years)
- Adults (65 to < 75 years)
- Adults (75 to < 85 years)
- Adults (85 years and over)

Special population of interest

Other

Special population of interest, other

Patients with multiple sclerosis

Estimated number of subjects

5496

Study design details

Outcomes

The number of participants that experience Adverse Events (AEs) that lead to discontinuation of dimethyl fumarate (DMF) and the number of participants that experience Serious Adverse Events (SAEs). DMF prescription and utilization patterns, Effectiveness of DMF on MS disease activity and disability progression, Changes in health-related quality of life measures will be evaluated over time.

Data analysis plan

Statistical analyses will be based on all patients who enroll in the study and take at least 1 dose of DMF. Statistical analyses will generally be descriptive and exploratory in nature. No formal statistical hypothesis testing is planned. Ninety-five percent CIs for incidence and incidence rate point estimates will be

calculated using the binomial distribution and the Poisson distribution, respectively. Analyses of clinical laboratory parameters may include summaries of actual values over time, change from baseline over time, percent change from baseline over time, shift tables, and/or summaries of worst post-baseline values. Annualized relapse rate will be analyzed using a negative binomial model, adjusted for appropriate prognostic factors, and time-to-event endpoints will be analyzed using Kaplan-Meier estimates. Summary statistics will be presented for health-related quality of life, healthcare resource consumption, and work productivity outcomes over time.

Documents

Study results

109MS401_CSR Synopsis 21Aug2023_Redacted.pdf (293.54 KB)

Data management

ENCePP Seal

The use of the ENCePP Seal has been discontinued since February 2025. The ENCePP Seal fields are retained in the display mode for transparency but are no longer maintained.

Data sources

Data sources (types)

Other

Data sources (types), other

Prospective patient-based data collection

Use of a Common Data Model (CDM)

CDM mapping

No

Data quality specifications

Check conformance

Unknown

Check completeness

Unknown

Check stability

Unknown

Check logical consistency

Unknown

Data characterisation

Data characterisation conducted

No