A target trial emulation with an extension to subgroups: an example for relapsing-remitting multiple sclerosis

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Study Ongoing

Administrative details

EU PAS number

EUPAS1000000135

Study ID

1000000135

DARWIN EU® study

No

Study countries

Netherlands

Sweden

Study description

The objective is to emulate the comparative effectiveness of oral dimethyl fumarate versus glatiramer acetate in the Swedish multiple sclerosis registry (SMSreg) given the results of a previously published randomized controlled trial. The target trial emulation (TTE) framework will be used in a strict and pragmatic setting. The research objective for both settings is the same: to study the effect of first treatment initiation with oral dimethyl fumarate on the two year annualized relapse rate, using subcutaneous glatiramer acetate as an active comparator, in Swedish relapsing-remitting multiple sclerosis patients.

This strict scenario is used to validate the target trial emulation framework by trying the reproduce the findings of the CONFIRM trial. In the pragmatic scenario, we aim to include additional patient groups by applying milder in- and exclusion criteria as opposed to the strict scenario. The milder in- and exclusion criteria in the pragmatic scenario will lead to more diverse patient characteristics and thereby to the inclusion of the previously mentioned subpopulations. Possible subpopulations that will be included in the pragmatic scenario as opposed to the strict scenario are: elderly and pediatric patients. These subpopulations have been identified through the protocol and results of the CONFIRM trial and the European public assessment reports and summaries of product characteristics of both dimethyl fumarate (Tecfidera) and glatiramer acetate (Copaxone or Copolymer-1).

Study status

Ongoing

Research institutions and networks

Institutions

University of Groningen

Netherlands

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Institution | Educational Institution

Contact details

Study institution contact

Stefan Verweij stefan.verweij@rug.nl

Study contact

stefan.verweij@rug.nl

Primary lead investigator

Stefan Verweij 0000-0001-7566-1776

Primary lead investigator

ORCID number:

0000-0001-7566-1776

Study timelines

Date when funding contract was signed

Planned: 01/02/2024

Actual: 01/02/2024

Study start date
Planned: 01/04/2024

Actual: 01/07/2024

Data analysis start date
Planned: 01/07/2024

Actual: 01/07/2024

Date of final study report
Planned: 01/10/2024

Sources of funding

- Other public funding (e.g. hospital or university)

More details on funding

No funding was received for this study.

Study protocol

HARPER_protocol_TTE_CONFIRM_V3.pdf (521.78 KB)

Regulatory

Was the study required by a regulatory body?

No

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

Not applicable

Methodological aspects

Study type

Study topic:

Human medicinal product

Study type:

Non-interventional study

Scope of the study:

Effectiveness study (incl. comparative)

Method development or testing

Data collection methods:

Secondary use of data

Study design:

Target trial emulation following a strict and pragmatic scenario (Retrospective new user active comparator cohort study).

Main study objective:

To compare the effect estimates from the strict scenario with those obtained from the pragmatic scenario to identify the effect estimates of subpopulations neglected in the strict scenario and in the CONFIRM trial.

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Medicinal product name

TECFIDERA

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

DIMETHYL FUMARATE

GLATIRAMER ACETATE

Anatomical Therapeutic Chemical (ATC) code

(L03AX13) glatiramer acetate

glatiramer acetate

(L04AX07) dimethyl fumarate

dimethyl fumarate

Medical condition to be studied

Relapsing-remitting multiple sclerosis

Secondary progressive multiple sclerosis

Population studied

Short description of the study population

Swedish multiple sclerosis patients registered in SMSreg.

Age groups

- **Adult and elderly population (≥18 years)**
  - Adults (18 to < 65 years)
    - Adults (18 to < 46 years)
    - Adults (46 to < 65 years)
  - Elderly (≥ 65 years)

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

Estimated number of subjects

500

Study design details

Setting

Swedish multiple sclerosis patients registered in SMSreg initiating either dimethyl fumarate or glatiramer acetate.

Comparators

Glatiramer acetate (active comparator).

Outcomes

Time to first confirmed relapse.

Annualized relapse rate after two years.

Summary results

Using strict eligibility criteria, 288 RRMS patients were included, whereas the pragmatic scenario comprised 1831 patients. The ARR ratio for DMF versus GA was 0.78 (95%CI 0.59–1.05) in CONFIRM, 0.75 (95%CI: 0.44–1.29) in the strict scenario, and 0.58 (95% CI: 0.36–0.94) in the pragmatic scenario. Similarly, the hazard ratio was 0.92 (95%CI 0.70–1.22), 1.05 (95%CI: 0.83–1.33) and 0.56 (95%CI: 0.46–0.67), respectively. Post-hoc analysis implied existence of calendar bias. Comparable results between CONFIRM and the strict scenario were observed, while the second step demonstrates how methodological advantages of TTEs can be extended to excluded subgroups.

Documents

Study publications

DOI:10.1007/s10654-026-01379-1

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 source(s), other

Swedish multiple sclerosis registry (SMSreg)

Data sources (types)

Disease registry

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