Emulation of a phase 3 study comparing Rituximab with Dimethyl Fumarate in early Relapsing-Remitting Multiple Sclerosis

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Study Ongoing

Administrative details

EU PAS number

EUPAS1000000450

Study ID

1000000450

DARWIN EU® study

No

Study countries

Sweden

Study description

The objective is to emulate the comparative effectiveness of rituximab (RTX) versus dimethyl fumarate (DMF) given the results of a previously published randomized controlled trial. We aim to use observational data from the Swedish Multiple Sclerosis registry (SMSreg) to evaluate the comparative effectiveness of rituximab versus dimethyl fumarate on a variety of outcomes including relapses, MRI activity and disease progression. By comparing a strict scenario, where the inclusion/exclusion criteria mirror as closely as possible those of the published registry-based randomized clinical trial, RIFUND-MS, to a pragmatic scenario, which widens the inclusion/exclusion criteria to include subpopulations that are rarely included in traditional clinical trials (e.g. elderly, secondary-progressive MS), we seek to to evaluate the effect of these therapies on patients that are routinely treated in clinical practice. Moreover, outcomes that are difficult to evaluate in a traditional clinical trial either due to underpower or due to the limited follow-up of a trial, will be evaluated using observational data (e.g. disease progression). This study will investigate the usefulness of observational data to support, confirm and extend the reported superiority of rituximab over dimethyl fumarate on disease activity and progression in a wider range of patients and real-world settings.

Study status

Ongoing

Research institutions and networks

Institutions

Karolinska Institutet

Sweden

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Institution | Educational Institution

Contact details

Study institution contact

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Study timelines

Date when funding contract was signed

Planned: 22/11/2022

Actual: 22/11/2022

Study start date

Planned: 08/01/2025

Actual: 08/01/2025

Data analysis start date
Planned: 08/01/2025

Actual: 08/01/2025

Date of final study report
Planned: 31/12/2025

Sources of funding

- EU institutional research programme

Study protocol

HARPER_protocol_Study1and2_MS_V2_18Dec2024_Final.pdf (506.87 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 type list

Study topic:

Human medicinal product

Study type:

Non-interventional study

Scope of the study:

Effectiveness study (incl. comparative)

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:

The objective is to emulate the comparative effectiveness of rituximab versus dimethyl fumarate in a real-world setting using strict inclusion/exclusion criteria and relaxed inclusion/exclusion criteria based on the results of a randomized, registry based phase 3 study (RIFUND-MS) to evaluate the effect in populations typically excluded from clinical trials but routinely treated in clinical practice.
The secondary objective is to emulate the comparative effectiveness of rituximab and dimethyl fumarate on disease progression in a real-world setting using strict inclusion/exclusion criteria.

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

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

DIMETHYL FUMARATE

RITUXIMAB

Anatomical Therapeutic Chemical (ATC) code

(L01FA01) rituximab

rituximab

(L04AX07) dimethyl fumarate

dimethyl fumarate

Population studied

Short description of the study population

Swedish multiple sclerosis patients registered in the Swedish Multiple Sclerosis registry

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Age groups

- **Adult and elderly population (≥18 years)**

Special population of interest

Other

Special population of interest, other

Swedish multiple sclerosis patients

Estimated number of subjects

750

Study design details

Setting

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

Comparators

Dimethyl fumarate (active comparator)

Outcomes

Primary: Proportion of patients with relapse during the 24-month observational period.

Secondary: Time to first relapse, Proportion of patients free from all MRI activity during the 24-month observation period, EDSS-based 24 week Confirmed Disability Worsening (CDW), Change in EDSS from baseline to month 24, Drug persistence, No evidence of disease activity NEDA-2/-3, time to EDSS 4 and 6, time to SPMS.

Data analysis plan

The proportion of patients with relapse during a 24 month observation period, the proportion of patients free from all MRI activity and the proportion of patients with confirmed EDSS score worsening will be analysed by log-binomial regression model similar to the RIFUND-MS trial. Time to 1st relapse, drug persistence, time to NEDA-2/-3 and time to confirmed sustained EDSS 4 and 6 and SPMS will be analysed by Cox Proportional Hazards regression. Inverse probability of treatment weighting (IPtW) will be applied to all analysis to mitigate confounding.

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

Yes

CDM Mappings

Data quality specifications

Check conformance

Unknown

Check completeness

Unknown

Check stability

Unknown

Check logical consistency

Unknown

Data characterisation

Data characterisation conducted

No