Malignancies in Multiple Sclerosis: multi-country cohort database studies (feasibility study) (MALBEC-f)

First published: 12/01/2018

Last updated: 02/04/2024

Study Finalised

Administrative details

EU PAS number

EUPAS21870

Study ID

46551

DARWIN EU® study

No

Study countries

- Denmark
- France
- Netherlands
- United States

Study description

The pattern of malignancies in the cladribine clinical program in multiple sclerosis (MS) (all exposed subjects) did not show an obvious difference compared to the available data on malignancies in the general population, or in MS patients. There is no obvious evidence of an increase of the risk of a particular tumor type in cladribine treated subjects compared to European reference populations. No dose-relationship could be found. The effect of age, immunomodulators (IM) and immunosuppressants (IS) treatments on the risk of malignancy in patients with MS is currently uncertain. MS patients seem to have a similar risk of malignancy than the general population but further studies using external data sources are needed to estimate the risk in MS as compared to general population. In this context, this study will provide estimates of malignancies incidence for a cohort of MS patients compared to non-MS patients of the general population, and for a cohort of MS patients newly treated with MS modifying drugs (DMDs), according to the type of medication used. This study will be done in 4 countries: France, the Netherlands, Denmark, United States. The overall results will be used with a view to a later post-marketing evaluation of cladribine.

Study status

Finalised

Research institutions and networks

Institutions

Bordeaux PharmacoEpi, University of Bordeaux

France

First published: 07/02/2023

Last updated: 08/12/2025

Institution | Educational Institution | Hospital/Clinic/Other health care facility | Not-for-profit | ENCePP partner

The PHARMO Institute for Drug Outcomes Research (PHARMO Institute)

Netherlands

First published: 07/01/2022

Last updated: 19/12/2025

Institution | Non-Pharmaceutical company | ENCePP partner

Bordeaux PharmacoEpi, University of Bordeaux

France

First published: 07/02/2023

Last updated: 08/12/2025

Institution | Educational Institution | Hospital/Clinic/Other health care facility | Not-for-profit | ENCePP partner

Aarhus University & Aarhus University Hospital DEPARTMENT OF CLINICAL EPIDEMIOLOGY

Denmark

First published: 20/07/2021

Last updated: 08/05/2026

Institution | Educational Institution

Contact details

Study institution contact

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Study contact

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Primary lead investigator

Patrick Blin

Primary lead investigator

Study timelines

Date when funding contract was signed
Actual: 08/09/2017

Study start date
Actual: 10/09/2017

Data analysis start date
Actual: 01/11/2017

Date of final study report
Planned: 31/12/2018

Actual: 10/12/2018

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Merck KGaA

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

Disease /health condition

Study type:

Non-interventional study

Scope of the study:

Assessment of risk minimisation measure implementation or effectiveness

Data collection methods:

Secondary use of data

Main study objective:

To estimate the incidence of malignancies stratified by age and gender:- in the MS cohort compared to a sample of non-MS patients from the general population,- in untreated patients of the MS cohort,- in newly treated patients with disease modifying drugs (DMD) according to the DMD group,To characterize the association between DMD treatment exposure and any occurrence of malignacies.

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

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

INTERFERON BETA-1A

INTERFERON BETA-1B

GLATIRAMER ACETATE

PEGINTERFERON BETA-1A

DACLIZUMAB

TERIFLUNOMIDE

FINGOLIMOD HYDROCHLORIDE

DIMETHYL FUMARATE

ALEMTUZUMAB

MITOXANTRONE

NATALIZUMAB

METHOTREXATE

CYCLOPHOSPHAMIDE

MYCOPHENOLIC ACID

AZATHIOPRINE

RITUXIMAB

Medical condition to be studied

Multiple sclerosis

Population studied

Short description of the study population

Multiple sclerosis patients

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

Immunocompromised

Estimated number of subjects

632

Study design details

Outcomes

Occurrence of any malignancies (including/excluding Non-melanoma skin cancer) :- Overall- Per individual malignancy type.

Data analysis plan

The statistical analysis will be performed using the SAS software (latest current version), following a detailed statistical analysis plan.Descriptive analyses will be conducted on the MS population, the untreated MS population and the MS population newly treated with a DMD. Crude and adjusted incidence rates of malignancy will also be calculated stratified on age and gender, in the MS, the untreated MS and the MS newly treated populations. The malignancy incidence estimated in the MS cohort will be then compared to the malignancy incidence estimated after age- and sex-standardization in a sample of non-MS patients from the general population. In the MS newly treated population, the association between DMD and risk of malignancy will be assessed with a time varying cox model.

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)

Administrative healthcare records (e.g., claims)

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