Malignancies in Multiple Sclerosis: Multi-country cohort database studies – French Study (MALBEC)

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Study Finalised

Administrative details

PURI

https://redirect.ema.europa.eu/resource/48836

EU PAS number

EUPAS26535

Study ID

48836

DARWIN EU® study

No

Study countries

☐ France

Study description

Disease Modifying Drugs (DMD) are used in the therapeutic management of Multiple Sclerosis (MS) to reduce the frequency of relapses and delay the progression of the disease. In the oral cladribine development program, efficacy data showed a significant effect of cladribine with a decrease in the frequency of relapses, associated lesions, and progression of MS. However, the safety results of the CLARITY Phase III pivotal study, evaluating cladribine versus placebo treatment in MS patients, revealed 4 cases of cancer in cladribine treated patients and no case in the placebo group. Taking into account safety and efficacy data, the European Medicines Agency Committee for Medicinal Products for Human Use issued a favourable marketing authorization opinion in June 2017 for cladribine in MS indication and conditioned by the achievement of a risk management plan defining cancer as a significant potential risk. In this context, the MALBEC study purpose is to supplement existing data by providing estimates of cancer incidence in the general population and in MS patients, whether or not treated with DMD, before the launch of cladribine (main objective). This study based on French nationwide healthcare insurance system database (SNDS) with data from the general scheme is part of a study program performed in three other countries (Denmark, the Netherlands, and the United States). The cohort will include all patients with a MS diagnosis, identified between 2007 and 2015 (inclusion date) by using hospitalization for MS, long term disease status or disability allowance with a diagnosis code of MS, or dispensing of DMD specific to MS, with a follow-up until the first date of death, occurrence of malignancy, or end of study period (31 Dec. 2015), and 1-year history prior inclusion date in the database. The crude annual incidence rates (exact Poisson) and standardized incidence rates will be calculated and stratified by age, gender, history of malignancy.

Study status

Finalised

Research institutions and networks

Institutions

Bordeaux PharmacoEpi, University of Bordeaux

France

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

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: 01/06/2018

Study start date
Planned: 01/05/2019

Actual: 18/07/2019

Data analysis start date
Planned: 01/05/2019

Actual: 18/07/2019

Date of final study report
Planned: 30/09/2020

Actual: 05/02/2021

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Merck KGaA

Study protocol

MALBEC SNDS Protocol-v3.0-20190124.pdf(6.66 MB)

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

Disease epidemiology

Drug utilisation

Data collection methods:

Secondary use of data

Main study objective:

To estimate the incidence of any malignancies (including or excluding non-melanoma skin cancer) and by individual malignancy type, overall and stratified by age, gender and history of malignancy in:-MS patients in comparison to a sample of non-MS patients from the general population -Untreated patients of

the MS cohort -Patients of the MS cohort newly treated with DMD, according to the DMD group

Study Design

Non-interventional study design

Cohort

Other

Non-interventional study design, other

Case-control study nested in the cohort

Study drug and medical condition

Anatomical Therapeutic Chemical (ATC) code

(L03AB07) interferon beta-1a

interferon beta-1a

(L03AX13) glatiramer acetate

glatiramer acetate

(L03AB08) interferon beta-1b

interferon beta-1b

(L03AB13) peginterferon beta-1a

peginterferon beta-1a

(L04AA31) teriflunomide

teriflunomide

(L04AA27) fingolimod

fingolimod

(L04AX07) dimethyl fumarate

dimethyl fumarate

(L04AA34) alemtuzumab

alemtuzumab

(L04AA23) natalizumab

natalizumab

Medical condition to be studied

Multiple sclerosis

Neoplasm malignant

Population studied

Short description of the study population

The study focused on patients with multiple sclerosis (MS), aged 18 or older, affiliated to the general scheme, diagnosed between January 2007 and December 2014, and with at least 12 months of history identified from the SNDS database.

The untreated MS sub-cohort includes patients without any disease modifying drugs (DMD) treatment or hospitalization for MS treatment administration.

The newly treated MS sub-cohort includes patients who receive their first DMD treatment or hospitalization for MS treatment.

Non-MS patients are those from the general population of the EGB database, aged 18 or older at January 2007 and without any MS diagnosis between January 2007 and December 2015.

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

100000

Study design details

Outcomes

The primary outcome is defined as the first occurrence of malignancy (excluding metastasis) identified during the study period. As defined by the algorithm of the French National Health Insurance, malignancy will be identified by any hospitalization or LTD with ICD-10 codes of cancer or by any specific anti-cancer treatment dispensing, excluding cancer recurrences and secondary tumours.

Data analysis plan

-Description of MS patients, untreated and newly treated MS patients, cases and controls: demographic characteristics, MS variables at inclusion or index date as applicable, relapse, medical history, medication, healthcare consumption during the pre-inclusion or pre-initiaion period as applicable, relapse, medication, number of visits with any healthcare provider during the follow-up -Estimation of crude annual incidence rates (exact Poisson) and standardized incidence rates for all malignancies and by individual malignancy

type in each cohort or sub-cohort, stratified by age, gender, history of malignancy, and according to type of IS if enough cases among the newly treated MS patients -Estimation of association between DMD exposure and risk of malignancy in the sub-cohort of newly treated MS patients (intention-to-treat, Cox proprotional hazard model after adjusting for propensity score), and among cases and controls nested in this sub-cohort (conditional logistic regression model)

Documents

Study publications

Bosco-Lévy P, Foch C, Grelaud A, Sabidó M, Lacueille C, Jové J, Boutmy E, Blin ...

Data management

ENCePP Seal

Conflicts of interest of investigators

MALBEC-ENCePP-DOI PBl-20190122.pdf(197.3 KB)

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