Long-term effectiveness of cladribine in patients previously treated with oral cladribine: a Real-World Evidence analysis using data from the Italian Registry of Multiple Sclerosis (CLARINET-MS)

First published: 04/10/2018

Last updated: 23/03/2026

Study | Finalised

Administrative details

EU PAS number

EUPAS25783

Study ID

25784

DARWIN EU® study

No

Study countries

Italy

Study status

Finalised

Research institutions and networks

Institutions

Merck Healthcare KGaA

Germany

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Institution **Pharmaceutical company**

Contact details

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Primary lead investigator

Communication Center Merck KGaA

Primary lead investigator

Study timelines

Date when funding contract was signed
Actual: 01/08/2018

Study start date
Actual: 04/10/2018

Date of final study report
Actual: 24/07/2019

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Merck KGaA

Study protocol

20181004_MS700568_0027_EnCepP_CTP_Redacted version for review_Redacted.pdf (3.88 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 topic:

Human medicinal product

Study type:

Non-interventional study

Scope of the study:

Effectiveness study (incl. comparative)

Safety study (incl. comparative)

Study design:

This study is a non-interventional, exploratory investigation of a cohort of patient registry data currently available in iMedWeb from Italian MS patients who received at least one course of cladribine tablets treatment in the cladribine clinical development trials.

Main study objective:

Clinical practice data from Italian MS patients who received at least one course of cladribine tablets treatment in pivotal clinical trials are continuously and consistently collected in digital database iMedWeb on entire Italian territory. Study will shed light whether long-termeffectiveness of cladribine tablets can be supported by data currently available in Italian MS patient registry.

Study Design

Non-interventional study design

Cohort

Other

Non-interventional study design, other

Non-interventional cohort RWE study

Study drug and medical condition

Medicinal product name

MAVENCLAD

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

CLADRIBINE

Anatomical Therapeutic Chemical (ATC) code

(L01BB04) cladribine

cladribine

Medical condition to be studied

Multiple sclerosis

Population studied

Short description of the study population

The study population will consist of Italian MS patients distributed across 26 Italian MS centers.

The selection of the MS patients will be based on the following criteria:

Inclusion criteria:

• Prior enrollment into oral cladribine pivotal clinical trials with at least one course of cladribine tablets treatment and participation in the clinical trial has ended

• Written informed consent was given to the patient registry

Exclusion criteria

• No exclusion criteria have been set-up for this non-interventional study.

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)

Estimated number of subjects

161

Study design details

Setting

The Italian digital patient registry iMedWeb continuously and consistently collects RWE data from 134 MS clinical centers spread across the entire Italian territory. The registry requires MS patients to provide a signed informed consent to allow their data upload into the registry. Only data from Italian MS patients who have participated into the cladribine tablets pivotal randomized clinical trials and who received at least one course of cladribine tablets treatment will be extracted in anonymized form from the registry for the analyses proposed in this study.

Outcomes

To assess the time-to-treatment change in clinical practice as surrogate marker for long-term effectiveness of cladribine in subjects with the clinical isolated syndrome (CIS) or remitting multiple sclerosis (RMS) phenotypes, Time-to-disability progression, Time-to-first EDSS ≥ 6.0, ≥ 7.0, Time-to-relapse during

observational period, Number of Disease Modifying Treatments (DMTs) after last cladribine tablets course in subjects with CIS, RRMS or SPMS Incidence of conversion of subjects with CIS to a clinically defined MS (CDMS)

Data analysis plan

Statistical testing will not be done as the nature of the study is descriptive and there is no hypothesis testing to be performed.Primary outcome time-to-treatment change as well as secondaryoutcome time-to-disability progression, time-to-first EDSS ≥ 6.0, time to-first EDSS ≥ 7.0 and time-to-relapse will be analyzed by means oftime-to-event analysis based on Kaplan-Meier method. Medianduration and its associated 95% Confidence Intervals (CIs) will beestimated from model. Analyses will be repeated by using gender, MS phenotype, RCT type and categorized age groups, EDSS score, number of relapses before RCT+1 and time since diagnosis as strata. Further, incidence of conversion from CIS to CDMS will be estimatedand number of treatments after last cladribine tablets course will betabulated.In case of unanticipated outcomes, additional ad hoc analyses will be performed to further investigate the data. Any missing data in RWE data will be assumed to be missing at random.

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)

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