# Comparative Effectiveness and Safety of Drugs used in Rare Neuromuscular and Neurodegenerative Diseases (CAESAR)

**First published:** 10/11/2020
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Study | Planned

## Administrative details

**PURI**
https://redirect.ema.europa.eu/resource/37984

**EU PAS number**
EUPAS37983

**Study ID**
37984

**DARWIN EU® study**
No

**Study countries**
Italy

**Study description**
CAESAR is an Italian multicenter retrospective cohort study on Rare Neuromuscular and Neurodegenerative diseases (RND), based on information available in regional administrative healthcare databases. The aims are 1) to describe the prescriptive patterns of drugs used for the treatment of patients affected by RND and identify patient characteristics associated to these patterns in the three Italian regions (Tuscany, Umbria, Lazio), accounting for over 10 million residents, and 2) to perform a comparative evaluation of the effectiveness and safety of drugs used for the treatment of RND, with a focus on specific active agents. The study population will be enrolled in the period 2009-2019, with a

two-year look-back and at least 1 year of follow-up, including patients, resident in one of the three regions and affected by Amyotrophic lateral sclerosis (ALS), Progressive muscular atrophy (PMA), Pseudobulbar palsy, Progressive bulbar palsy (PBP), Primary lateral sclerosis (PLS), Other motor neuron disease, Myasthenia gravis (MG). Patients will be defined from Hospital discharge records (ICD-9-CM codes), disease specific copayment exemptions, and, as far as possible, disease specific drug treatments. Drug utilisation patterns will be based on drugs (ATC codes) prescribed to outpatients using the DDDs. Safety and effectiveness will be investigated using a new-user approach and applying both, intention-to-treat and as-treated analysis. Clinical data available in two of the participating regions for ALS patients will be used to 1) validate the algorithm used for patient identification, 2) validate the exposure definition, and 3) perform external adjustment. Data and analysis ill be managed through a common data model, with shared data scripts, performing the analysis at regional level (in-house) and pooling aggregated anonymous data to obtain overall results.

**Study status**
Planned

# Research institution and networks

## Institutions

### Department of Epidemiology of the Regional Health Service - Lazio

Italy
**First published:** 23/03/2010
Last updated
22/06/2018

Institution

ENCePP partner

EU Institution/Body/Agency


### Department of Epidemiology of the Regional Health Service - Lazio

Italy
**First published:** 23/03/2010
Last updated
22/06/2018

Institution

ENCePP partner

EU Institution/Body/Agency

## Neurofarba Department, Pharmacovigilance Unit, University of Florence

Italy
**First published:** 21/02/2014
Last updated
03/03/2014

Institution
Educational Institution
ENCePP partner

## Unit of adverse drug reactions monitoring (UADRM), University Hospital of Pisa

Italy
**First published:** 08/01/2014
Last updated
16/02/2024

Institution
Educational Institution
Hospital/Clinic/Other health care facility
ENCePP partner

## National Center for Disease Prevention and Health Promotion, National Institute of Health Rome, Italy, University of Florence, Neurofarba Department Florence, Italy, Unit of Adverse Drug Reactions Monitoring, University Hospital of Pisa Pisa, Italy, Scarab Lab Florence, Italy, Umbria Region, Regional Pharmacovigilance Center Perugia, Italy, Umbria Region Perugia Hospital - Neuropathophysiology Perugia, Italy

# Contact details

**Study institution contact**
Ursula Kirchmayer

Study contact

u.kirchmayer@deplazio.it
**Primary lead investigator**
Ursula Kirchmayer
Primary lead investigator

## Study timelines

**Date when funding contract was signed**
Planned:
23/09/2020
Actual:
23/09/2020

**Study start date**
Planned:
01/03/2021

**Data analysis start date**
Planned:
01/06/2021

**Date of interim report, if expected**
Planned:
25/10/2021

**Date of final study report**
Planned:
24/10/2022

## Sources of funding

- Other

## More details on funding

Italian Medicines Agency, Regional Drug Departme

## 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 type:**
Non-interventional study

**Scope of the study:**
Drug utilisation
Effectiveness study (incl. comparative)

**Main study objective:**
Objective 1. describe the prescriptive patterns of the study drugs in patients affected by RND and identify patient characteristics associated to these patterns in the three Italian regions (Tuscany, Umbria, Lazio), accounting for over 10 million residents. Objective 2. comparative evaluation of the effectiveness and safety of drugs used for the treatment of RND, with a focus on specific agents

## Study Design

**Non-interventional study design**
Cohort

## Study drug and medical condition

**Medical condition to be studied**
Amyotrophic lateral sclerosis
Progressive muscular atrophy
Pseudobulbar palsy
Progressive bulbar palsy

Upper motor neurone lesion
Motor neurone disease
Myasthenia gravis

**Additional medical condition(s)**
Other RNDs might be included during the study

# Population studied

**Age groups**
Term newborn infants (0 – 27 days)
Infants and toddlers (28 days – 23 months)
Children (2 to < 12 years)
Adolescents (12 to < 18 years)
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**
5000

# Study design details

**Outcomes**
Overall and cause specific mortality, Admission to intensive care unit, Remission from corticosteroid use, discontinuation after a period of prescriptions with corticosteroids for systemic use, Adverse drug reactions (serious infections, autoimmune disease) - to be defined, Respiratory failure and tracheotomy (for ALS patients), Thymoma, thymectomy, myasthenia gravis crisis, use of intravenous immunoglobulins, plasmapheresis (for MG patients)

**Data analysis plan**
Data will be organised and managed through a common data model. Analysis will be performed running the shared scripts at local level and pooling aggregated data at the end. Drug utilization will be defined on the basis of DDDs, using different indicators: prevalence of use (by dividing the number of drug users by the overall resident population), prevalence of use among patients in the cohort (by disease for single drugs), DDDs per 1000 users per day (the mean number of doses consumed every day by 1000 patients included in the cohort). CER will be performed through a propensity matched cohort design (head-to-head comparison between different drug groups/drugs). Patients in the compared exposure groups will be propensity matched. A group of patients not treated with any of the drugs will also be defined and compared. Intention-to-treat and As-treated analyses will be performed using Cox proportional Hazard models (HRs and 95%CIs).

# Data management

**Data source(s)**
Mortality Information System
Drug claims information system
Hospital Information System
Healthcare Emergency Information System
ARS Toscana

**Data source(s), other**
MIS, PHARM, HIS, HEIS, ARS

**Data sources (types)**
Administrative data (e.g. claims)
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