Association between previous biologic therapy exposure and incidence of life-threatening infections in patients with rheumatoid arthritis and psoriasis. A population-based cohort study.

First published: 09/04/2025

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Study Planned

Administrative details

PURI

https://redirect.ema.europa.eu/resource/1000000543

EU PAS number

EUPAS1000000543

Study ID

1000000543

DARWIN EU® study

No

Study countries

Spain

Study description

Since the advent of biologic agents targeting key proinflammatory pathways, the treatment of chronic inflammatory and autoimmune diseases has substantially changed.

Rheumatoid arthritis and psoriasis are two of the most common conditions for which these agents are administered.

Patients taking biologics are more prone to mild infections; however, since most trials conducted have been of short duration, long-term follow-up of these individuals is necessary.

Their association with serious infections has not yet been thoroughly analyzed.

In response to the need for further investigation into the long-term effects of biologic therapies, we propose a cohort study of patients with rheumatoid arthritis and/or psoriasis, comparing those exposed to biologic drugs with those who have not been exposed. We aim to analyze the association with potentially severe infections, including influenza, sepsis, pneumonia, and COVID-19.

Study status

Planned

Research institutions and networks

Institutions

Clinical Pharmacology, Vall d'Hebron Institut de Recerca (VHIR)

Spain

First published: 18/05/2021

Last updated: 20/05/2021

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

Fundació Institut Universitari per a la Recerca a l'Atenció Primària de Salut Jordi Gol i Gurina, IDIAPJGol

Spain

First published: 05/10/2012

Last updated: 23/02/2024

Institution | Educational Institution | Laboratory/Research/Testing facility | Not-for-profit | ENCePP partner

Contact details

Study institution contact

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Study timelines

Date when funding contract was signed

Planned: 01/12/2024

Actual: 01/12/2024

Study start date

Planned: 05/05/2025

Data analysis start date

Planned: 01/07/2025

Date of final study report

Planned: 31/12/2027

Sources of funding

- Other

More details on funding

Ciber INFEC (CENTRO DE INVESTIGACIÓN BIOMÉDICA EN RED. Enfermedades infecciosas): https://www.ciberinfec.es/en

Study protocol

Biologics_Protocol_v4.0_clean_20250221.pdf(1022.97 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:

Disease /health condition

Human medicinal product

Study type:

Non-interventional study

Scope of the study:

Safety study (incl. comparative)

Data collection methods:

Secondary use of data

Study design:

Population-based cohort study

Main study objective:

This study aims to evaluate the association between biologic exposure and the incidence of serious infections, including COVID-19, influenza, pneumonia, and/or septicaemia, in patients diagnosed with rheumatoid arthritis and/or psoriasis in the general population of Catalonia.

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Name of medicine, other

Biologic therapies

Population studied

Short description of the study population

Adult patients diagnosed with rheumatoid arthritis and/or psoriasis treated with biologic and non-biologic therapies in Catalonia, Spain.

Age groups

Adult and elderly population (≥18 years)

Adults (18 to < 65 years)

Adults (18 to < 46 years)

Adults (46 to < 65 years)

Elderly (≥ 65 years)

Adults (65 to < 75 years)

Adults (75 to < 85 years)

Adults (85 years and over)

Estimated number of subjects

25000

Study design details

Setting

Primary Care and Outpatients Specialized Care in Catalonia, Spain

Comparators

Biologic vs non-biologic therapies

Outcomes

The infections will be classified as potentially severe if they are associated with hospitalization or mortality: any infection that requires hospitalization or is associated with mortality, including pneumonia, influenza, septicaemia, and COVID-19.

Data analysis plan

The study population will be described overall and stratified by exposure status (exposed vs. unexposed individuals). Quantitative variables will be summarized using means with standard deviations (SD) or medians with interquartile ranges (IQR), depending on the distribution of the variable. Categorical variables will be presented as absolute and relative frequencies. Bivariate comparisons between groups will be conducted using Student's t-tests, Wilcoxon rank-sum tests, or Chi-square tests, as appropriate.

For the primary outcome, marginal structural models (MSMs) will be employed

to estimate the risk of treatment exposure while addressing confounding. Inverse probability of treatment weights (IPTWs) will be derived from propensity scores calculated using age, sex, socioeconomic deprivation score, previous life-threatening infections, and other relevant clinical factors. If necessary, weights will be truncated at the 1st percentile to stabilize estimates. Covariate balance before and after weighting will be evaluated using the standardized mean difference (SMD). Variables with SMD > 0.1 after weighting will be included in the MSM as additional covariates to achieve double robustness. IPTWs will then be applied in logistic regression models to estimate risk ratios (RRs) with 95% confidence intervals (CIs), using robust standard errors (SEs) to account for variability. Statistical significance will be determined using the Wald test at a 0.05 level. When assessing the association between prior biologic exposure and severity outcomes, patients will be assigned to the worst outcome observed (all-cause death > hospitalization > disease presence) to ensure a mutually exclusive classification.

Data management

Data sources

Data source(s)

The Information System for Research in Primary Care (SIDIAP)

Data source(s), other

Data from the Catalan Health Department on hospital discharges (CMBD-HA database) and on medicines dispensed at hospital pharmacies (MHDA database).

Data sources (types)

Administrative healthcare records (e.g., claims)

Drug prescriptions

Drug registry

Electronic healthcare records (EHR)

Population registry

Use of a Common Data Model (CDM)

CDM mapping

No

Data quality specifications

Check conformance

Yes

Check completeness

Yes

Check stability

Yes

Check logical consistency

Yes

Data characterisation

Data characterisation conducted

Yes

Data characterisation moment

after data extraction

Data characterisation details

Data quality processes will be implemented in each phase of the data flow cycle.
The quality controls will be carried out in the extraction and loading steps. To evaluate the integrity of the data, the elements present will be described by geographical areas, the professional registrar, the time and the function of distribution of the values.
The correction will be evaluated by checking the validity of atypical values, out of range values, format errors and logical date incompatibilities.
The integrity and correction measures will be used to inform decisions about the transformations necessary to improve the quality of the data (e.g. harmonisation, standardisation, cleaning) and the aptitude of the data for the purpose of specific research projects.