Shortening the time to confirm or to rebut Adverse events of interest related to innovative Therapies for immune-mediated inflammATory dIseases: cross-talking between different data sOURces. SATURATIOn study.

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Study Planned

Administrative details

EU PAS number

EUPAS1000000207

Study ID

1000000207

DARWIN EU® study

No

Study countries

France

Study description

To identify or to rebut adverse events of interest (AEs) is a challenging aim. Twenty years after the introduction of Tumor necrosis factors inhibitors (TNFi) for immune-mediated inflammatory diseases (IMIDs), the association between AEs and TNFi according to the underlying pathology is still not clear. Currently, several databases relying on different recording methods are used in pharmacoepidemiology to detect AEs. Jointly analyzing these different data sources (integrative approach) is often discussed as a way to improve the detection of AEs. However, synthesizing all these replicative results is highly time-consuming and requires a heavy workload, thus leading to delayed conclusions. The French National Health Data System (SNDS) has been used in France to conduct real-life studies on large, unbiased and nationally representative samples, especially regarding the safety of drugs. Our hypothesis is that assessing AEs related to biologics through the SNDS would yield earlier as reliable results as those obtained through an integrative approach. The aim of SATURATIOn is to shorten the time to confirm or to rebut adverse events of interest associated with innovative therapies for IMIDs by using SNDS data. To achieve this objective we propose a 4-year program comprising 3 Work Packages. In WP1, we will use an integrative approach in order to identify AEs related to biologics/target therapies (systematic reviews and network meta-analyses based on trials and observational studies); ii) in WP2, we will identify the same AEs related to the same therapies using SNDS data; machine learning will be used to improve high-dimensional proxy confounder adjustment ; iii) In WP3, we will compare the results from the integrative approach and from the French health-insurance data regarding AEs. Overall, the main interest of the SATURATIOn phamacoepidemiological project is to allow the fast generation of appropriate analyses for confirming the occurrence of biologics-related AES.

Study status

Planned

Research institutions and networks

Institutions

Assistance Publique - Hôpitaux de Paris (AP-HP)

France

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Institution | Hospital/Clinic/Other health care facility

University Paris Est Créteil

Networks

COCHRANE COLLABORATION

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Network

Contact details

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Primary lead investigator

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Study timelines

Date when funding contract was signed

Planned: 01/07/2024

Study start date

Planned: 02/09/2024

Data analysis start date

Planned: 02/09/2024

Date of interim report, if expected

Planned: 01/11/2025

Date of final study report

Planned: 01/09/2028

Sources of funding

- Other public funding (e.g. hospital or university)

More details on funding

- We obtained funding from the National Agency for Safety of Medicines and Health products to conduct a three-year PhD program (November 2023) to conduct the WP2
- We obtained funding from the Univeristy Paris Est Créteil to conduct a three-year PhD program (November 2023) to conduct the WP2
- WP1 will be conducted by the permanent researchers of the team

Study protocol

DARWIN_EU.pdf (475.75 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

Study type:

Non-interventional study

Scope of the study:

Safety study (incl. comparative)

Data collection methods:

Combined primary data collection and secondary use of data

Study design:

(1) Systematic review and network meta-analysis assessing the risk of Adverse events of interest in adult patients receiving biologics/targeted therapies for PsO, PsA, AS, or IBD comparing them against each other.
(2) Nationwide “exposed/unexposed” cohort study using the French health-insurance

Main study objective:

The aim of SATURATIOn is to shorten the time to confirm adverse events of interest related to innovative therapies for immune-mediated inflammatory diseases using the French National health-insurance data.

Study Design

Non-interventional study design

Cohort

Systematic review and meta-analysis

Study drug and medical condition

Medicinal product name

CIMZIA

COSENTYX

ENBREL

HUMIRA

ILUMETRI

JAKAVI

KYNTHEUM

OLUMIANT

REMICADE

RINVOQ

SIMPONI

SKYRIZI

STELARA

TALTZ

TREMFYA

Medicinal product name, other

Biosimilars of these drugs when available

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

ADALIMUMAB

BARICITINIB

BRODALUMAB

CERTOLIZUMAB PEGOL

ETANERCEPT

GOLIMUMAB

GUSELKUMAB

INFLIXIMAB

IXEKIZUMAB

RISANKIZUMAB

RUXOLITINIB PHOSPHATE

SECUKINUMAB

TILDRAKIZUMAB

UPADACITINIB

USTEKINUMAB

Anatomical Therapeutic Chemical (ATC) code

(L01EJ01) ruxolitinib

ruxolitinib

(L04AA37) baricitinib

baricitinib

(L04AA44) upadacitinib

upadacitinib

(L04AB) Tumor necrosis factor alpha (TNF-alpha) inhibitors

Tumor necrosis factor alpha (TNF-alpha) inhibitors

(L04AB01) etanercept

etanercept

(L04AB02) infliximab

infliximab

(L04AB04) adalimumab

adalimumab

(L04AB05) certolizumab pegol

certolizumab pegol

(L04AB06) golimumab

golimumab

(L04AC) Interleukin inhibitors

Interleukin inhibitors

(L04AC05) ustekinumab

ustekinumab

(L04AC10) secukinumab

secukinumab

(L04AC12) brodalumab

brodalumab

(L04AC13) ixekizumab

ixekizumab

(L04AC16) guselkumab

guselkumab

(L04AC17) tildrakizumab

tildrakizumab

(L04AC18) risankizumab

risankizumab

(L04AF) Janus-associated kinase (JAK) inhibitors

Janus-associated kinase (JAK) inhibitors

Medical condition to be studied

Psoriasis

Psoriatic arthropathy

Ankylosing spondylitis

Inflammatory bowel disease

Population studied

Short description of the study population

Intervention group: Adult patients receiving TNFi for psoriasis (PsO), psoriatic arthritis (PsA), ankylosis spondylitis (AS), inflammatory bowel diseases (IBD)

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)

Study design details

Setting

France

Comparators

Comparator group: Patients receiving other biological/targeted therapies (listed above) or placebo (only for RCTs) for the same diseases, with the same severity as in the intervention group to avoid selection bias.
Details of the two groups and preliminary data are available in the protocol (Table 1).

Outcomes

Primary outcomes will be the following incident AEs of interest:
• Heart failures and Major Adverse Cardiovascular Events (MACEs) (including nonfatal stroke, nonfatal myocardial infarction or cardiovascular death),
• Serious infections (any infection meeting the regulatory definition of a serious adverse event, SAE)
• Malignancies excluding non-melanoma skin cancer (NMSC) and carcinoma in

situ of the cervix,

• Psychiatric disorders (depression, suicidal ideation behaviour; neurotic, stress-related, or somatoform disorders; and personality and behavioural disorders)

Secondary outcomes

• NMSC and carcinoma in situ of the cervix,

• Demyelinating diseases and auto-immune diseases

• Pulmonary embolism and leg veinous thrombo-embolic events

• All reported events defined as SAEs.

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 source(s)

Système National des Données de Santé (French national health system main database)

Data source(s), other

Already published trials and already published observational studies

Data sources (types)

Administrative healthcare records (e.g., claims)

Clinical trial

Non-interventional study

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

Unknown