Switch pattern of biological drugs for the treatment of inflammatory bowel diseases through the VALORE distributed database network

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Study Planned

Administrative details

EU PAS number

EUPAS1000000412

Study ID

1000000412

DARWIN EU® study

No

Study countries

☐ Italy

Study description

Due to their high cost, biological drugs threaten the sustainability of the Italian National Health Service and, therefore, it is crucial to ensure their appropriate use in clinical practice. Since 2006, following the patent expiry of some biologic drugs, the first biosimilar drugs have been introduced in the European market. They are defined by the European Medicines Agency as biologic drugs similar to the originator in terms of quality, efficacy and safety. In the context of inflammatory bowel diseases (IBDs) such as Crohn disease and ulcerative colitis, a large number of biosimilars concerning anti-TNF alpha inhibitors (adalimumab and infliximab) have been marketed, while for other more recent biological drug classes such as interleukin or integrin inhibitors patent expiry has not been occurred yet.

Switching between biological drugs, both originator and biosimilar, in patients affected by IBD is a frequent phenomenon in clinical practice (from 5 to 30% during the first year of therapy). Moreover, in September 2022 EMA stated that biosimilars are comparable to their reference products in terms of safety and immunogenicity and are therefore interchangeable. However, for a single molecule numerous biosimilars are marketed and switching patterns among biological drugs might be very various and complex. Nonmedical switching could also lead patients to a nocebo effect if not well motivated to patients who know little about biosimilars. For these reasons, it is essential to explore what is happening in clinical practice in patients affected by IBDs.

Study status

Planned

Research institutions and networks

Institutions

Pharmacology Unit - Veneto Pharmacovigilance Centre (Pharmacol UNIVR), University Hospital Verona

Italy

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

Contact details

Study institution contact

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Study contact

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Primary lead investigator

Andrea Spini

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 01/01/2019

Study start date
Planned: 01/09/2024

Data analysis start date
Planned: 01/10/2024

Date of final study report
Planned: 30/06/2025

Sources of funding

More details on funding

Agenzia Italiana del farmaco - progetti di farmacovigilanza multiregionali 2014-2016

Study protocol

240306_VALORE_Switch_protocol_MICI_vs_1.pdf (617.53 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:

Drug utilisation

Data collection methods:

Secondary use of data

Study design:

Descriptive, cohort, retrospective, multicenter study will be conducted.

Main study objective:

To describe the pattern of switch and swap among incident biological drug users approved for IBDs.

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Medicinal product name, other

Anti-TNF-alpha, anti-ILs and anti-Integrins approved for IBDs

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

ADALIMUMAB

GOLIMUMAB

INFLIXIMAB

USTEKINUMAB

VEDOLIZUMAB

Anatomical Therapeutic Chemical (ATC) code

(L04AB02) infliximab

infliximab

(L04AB04) adalimumab

adalimumab

(L04AG05) vedolizumab

vedolizumab

(L04AB06) golimumab

golimumab

(L04AC05) ustekinumab

ustekinumab

Medical condition to be studied

Inflammatory bowel disease

Population studied

Short description of the study population

The regional claims databases previously described will be considered. From this source, subjects will be included in the study based on the presence of all the following criteria: 1) At least two records of biological drugs (approved for IBDs – see table A1 of the appendix) dispensing during the study period (2010

to 2022). The first date of a biological drug dispensing will be considered as the index date and the biological drug as the index drug. Only incident users of biological drugs will be included, i.e. biological drugs users with no prior dispensings of a biological drug; 2) At least one year of look-back period in the database and at least one year of follow up after index date; 3) Patients with any of these indications: Crohn's disease and ulcerative colitis (see variable section for the identification of exposure and indication of use)

Age groups

Study design details

Setting

Italy

Data analysis plan

Cohort characterization

Incident users stratified by class of biological drugs (TNF-alpha inhibitors, anti-interleukin drugs and anti-integrin) and on the basis of occurrence of at least one switch/swap during follow up, will be characterized at baseline in terms of sex, age, type of index drug (originator/biosimilar), previous use of other drugs approved for IMID (cDMARDs, JAK-i, NSAIDs, corticosteroids), and comorbidities (hypertension, MACE, diabetes, previous infections, depression other IMIDs in the look-back period).

Pattern of switch and swap

The absolute frequency, mutually exclusive, in terms of single switch, single swap, multiple switches, by pharmacological class and active ingredient will be reported. This analysis will be performed 1) considering only the first one, three and five years of follow up after the index date (only patients with at least 1

year, three year and five years of follow up will be counted as denominator, respectively) and 2) for the entire duration of follow-up. Whether possible, the analysis will be stratified by sex (female/male) and age (≤18/19-44/45-64/65-79/≥80).

Time to switch and swap
Time to switch and swap will be described using a Kaplan Meier approach stratifying class of biological drugs/active ingredient according to indication. Time to 1) first medical switch/swap, 2) non-medical switch, 3) switch back, 4) multiple switches. Median time for such events will be also calculated.

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), other

VALORE distributed database network: claims data from 16 italian regions

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Data sources (types)

Administrative healthcare records (e.g., claims)

Use of a Common Data Model (CDM)

CDM mapping

Yes

CDM Mappings

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 extract-transform-load to a common data model