LOOK-UP: Active pharmacovigilance study of the medicine Rinvoq™ (upadacitinib)

First published: 03/07/2024

Last updated: 14/03/2025

Study Finalised

Administrative details

PURI

https://redirect.ema.europa.eu/resource/1000000227

EU PAS number

EUPAS1000000227

Study ID

1000000227

DARWIN EU® study

No

Study countries

☐ Portugal

Study description

The LOOK-UP is an investigator-initiated clinical study with the aim of monitoring the post-marketing safety of the medicine Rinvoq™ (upadacitinib), which is indicated for the treatment of rheumatoid arthritis, psoriatic arthritis, axial spondyloarthritis, atopic dermatitis, ulcerative colitis, and Crohn's disease. The Marketing Authorisation Holder is AbbVie Deutschland GmbH & Co. KG.

Study status

Finalised

Research institutions and networks

Institutions

Porto Pharmacovigilance Centre, Faculty of Medicine, University of Porto (UFPorto)

Portugal

First published: 17/11/2010

Last updated: 12/06/2023

Institution | Educational Institution | ENCePP partner

Medicines Risk Management Department, Infarmed

Portugal

First published: 11/12/2021

Last updated: 14/12/2021

Institution | EU Institution/Body/Agency | ENCePP partner

Contact details

Study institution contact

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Primary lead investigator

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Primary lead investigator

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Study timelines

Date when funding contract was signed

Planned: 01/03/2024

Study start date

Planned: 31/03/2024

Actual: 31/03/2024

Data analysis start date

Planned: 01/11/2024

Date of interim report, if expected

Planned: 31/12/2024

Actual: 31/12/2024

Date of final study report

Planned: 28/02/2025

Actual: 28/02/2025

Sources of funding

- National competent authority (NCAs)

More details on funding

INFARMED - Portuguese Authority of Medicines and Health Products, I.P.

Study protocol

StudyProtocol_31.06.2024.pdf(314.53 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:

Human medicinal product

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:

An ambispective, multicentric cohort observational study, conducted as a Phase 4 post-authorisation safety study (PASS).

Main study objective:

Quantify the incidence of adverse events in patients with a medical prescription for Rinvoq™.

Particular attention will be given to serious adverse events already described in the previous literature (malignant neoplasms, excluding non-melanoma skin cancer; non-melanoma skin cancer (NMSC); major adverse cardiovascular events (MACE); venous thromboembolism (VTE); serious and opportunistic infections, including herpes zoster and tuberculosis; gastrointestinal perforations; hepatic injuries, including drug-induced liver injury; bone fractures; all-cause mortality).

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Name of medicine

RINVOQ

RINVOQ 15 MG - PROLONGED-RELEASE TABLET

RINVOQ 30 MG - PROLONGED-RELEASE TABLET

RINVOQ 45 MG - PROLONGED-RELEASE TABLET

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

UPADACITINIB

Anatomical Therapeutic Chemical (ATC) code

(L04AF03) upadacitinib

upadacitinib

Medical condition to be studied

Rheumatoid arthritis

Crohn's disease

Dermatitis atopic

Colitis ulcerative

Psoriatic arthropathy

Population studied

Short description of the study population

Patients will be included retrospectively and prospectively from the study start date from hospitals in the Porto district who cumulatively meet the following inclusion criteria:
(i) medical prescription of Rinvoq™ from 1 January 2024;
(ii) 18 years or older at the time of recruitment;
and (iii) explicit consent to participate in the study.

Patients will be excluded if, at the time of recruitment:
(i) they present any degree of cognitive impairment that prevents them from responding to a questionnaire administered by telephone;
(ii) they are participating in a phase I, II, or III clinical trial;
(iii) their life expectancy is less than 1 month;
or (iv) they do not have a valid telephone contact.

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)

Special population of interest

Frail population
Hepatic impaired
Renal impaired

Study design details

Setting

The centers involved in the study will be exclusively hospital institutions.
For the purposes of practicality and logistical efficiency, the selection of participating hospitals will be limited to the area affiliated with UFPorto, specifically the Porto district.

Comparators

NA

Outcomes

Primary outcome: incidence of adverse events that arise during the established follow-up period, coded according to MedDRA terminology.

Exploratory outcome: Rate of non-compliance with PRAC recommendations, i.e., quantify the frequency with which patients with identified risk factors receive a prescription for Rinvoq™ despite the existence of viable therapeutic alternatives.
Patients with risk factors are considered to be:
(i) patients aged 65 years or older;
(ii) current smokers or those with a long history of smoking;
(iii) individuals at high risk of serious cardiovascular problems, such as heart attacks or strokes;
or (iv) those more likely to develop cancer.

Data analysis plan

A descriptive analysis of the variables of interest will be conducted.
Categorical variables will be presented through absolute and relative frequencies, and continuous variables through descriptive statistics such as mean and standard deviation, quartiles, median, and minimum and maximum values.

Sociodemographic data will be described using the above measures according to the characterisation of each variable.
Clinical history information for each patient will also be detailed. Univariate and multivariate regression analyses will be conducted to evaluate the relationship between risk factors and adverse events, depending on the sample size to confer statistical power to these tests.
To address the primary objective of the study, incidence rates of adverse events will be estimated overall, as well as by subgroups.
Sub-analyses stratified by clinical interest variables such as severity of events, dosage of Rinvoq™ (15mg, 30mg, 45mg), allergy history, among others, will be conducted.
Survival analysis will be performed to evaluate the time to occurrence of adverse events, allowing the identification of temporal patterns in adverse events, considering the possibility of data censoring (for example, when patients are no longer followed in the study due to dropout or other reasons).
Kaplan-Meier curves will be used to graphically illustrate the cumulative probability of non-occurrence of adverse events over time.
Additionally, statistical tests such as the log-rank test will be used to compare survival curves between different patient subgroups, identifying significant differences in adverse event incidence between these groups.
When appropriate, Cox proportional hazards modelling will be used to evaluate the impact of specific variables such as age, sex, comorbidities, and other relevant factors on the risk of adverse events.
Finally, subgroup and sensitivity analyses will also be considered.

Data management

ENCePP Seal

This study has been awarded the ENCePP seal

Conflicts of interest of investigators

DeclarationofInterests-Annex5_signed.pdf(404.15 KB)

Composition of steering group and observers

Composition of Steering Group and Observers_signed.pdf(586.39 KB)

Signed code of conduct

ENCePPCoCAnnex3_DeclarationofcompliancewiththeENCePPCodeofConduct_signed.pdf (349.91 KB)

Signed code of conduct checklist

ENCePPCoCAnnex2_ChecklistofCodeofConduct_signed.pdf(415.8 KB)

Signed checklist for study protocols

ENCePPChecklistforStudyProtocols_signed.pdf(402.83 KB)

Data sources

Data sources (types)

Administrative healthcare records (e.g., claims)

Electronic healthcare records (EHR)

Non-interventional study

Patient surveys

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

Not applicable