An active surveillance, post-authorization safety study (PASS) of serious infection, malignancy, cardiovascular and other safety events of interest among patients treated with tofacitinib for moderately to severely active rheumatoid arthritis within the British Society for Rheumatology Biologics Register-Rheumatoid Arthritis (BSRBR-RA) (Safety of tofacitinib in BSRBR-RA)

First published: 05/09/2019

Last updated: 30/09/2026

Study | Finalised

Administrative details

EU PAS number

EUPAS31126

Study ID

49434

DARWIN EU® study

No

Study countries

United Kingdom

Study description

Tofacitinib is a potent, selective inhibitor of the Janus kinase (JAK) family of kinases with a high degree of selectivity relative to other kinases in the human genome. Tofacitinib was approved in the European Union (EU) in March 2017 at a dose of 5 mg administered twice daily (BID) for the treatment of adult patients with moderately to severely active RA who have responded inadequately to, or who are intolerant to, one or more disease modifying antirheumatic drugs (DMARDs).

To enable assessment of adverse outcomes of special interest including rare events and endpoints with long latency periods, Pfizer will implement a post approval, active surveillance study of tofacitinib exposed patients using actively collected prospective data in BSRBR RA.

Research Question: What are the rates of safety events of special interest in RA patients treated with tofacitinib in relation to other new advanced targeted therapies?

Study status

Finalised

Research institutions and networks

Institutions

Pfizer

First published: 01/02/2024

Last updated: 01/02/2024

Institution

British Society for Rheumatology Biologics Registers (BSRBR)

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Institution | Educational Institution | Other

Contact details

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Primary lead investigator

Cherise Wong

Primary lead investigator

Study timelines

Date when funding contract was signed
Planned: 08/05/2018

Actual: 08/05/2018

Study start date
Planned: 01/09/2019

Actual: 01/09/2019

Data analysis start date
Planned: 15/09/2025

Actual: 15/09/2025

Date of interim report, if expected
Planned: 14/03/2021

Actual: 14/03/2021

Date of final study report
Planned: 14/08/2026

Actual: 14/08/2026

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Pfizer 100%

Study protocol

A3921312_PROTOCOL_BSRBR PASS_v1.0 20 August 2019.doc.pdf (2.02 MB)

A3921312_PROTOCOL_V2.0_10SEP2021.pdf (479.68 KB)

A3921312_PROTOCOL VERSION 3.0_14Feb2022.pdf (526.64 KB)

Regulatory

Was the study required by a regulatory body?

No

Is the study required by a Risk Management Plan (RMP)?

EU RMP category 3 (required)

Other study registration identification numbers and links

A3921312

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:

Secondary use of data

Study design:

This is an active surveillance study using existing data within the existing British Society for Rheumatology Biologics Register for RA (BSRBR-RA), an ongoing prospective observational cohort study started in 2001.

Main study objective:

To evaluate the rates of serious infections, malignancy (overall, excluding NMSC), subtypes of lymphoma, lung cancer, CV, MACE, MI, VTE (DVT and PE) and other specified outcomes, including fractures, among patients with RA in an existing UK based register who initiate tofacitinib.

Rates will also be estimated among existing cohorts of patients treated with TNFi therapies to provide context for rates observed on tofacitinib. No a priori hypotheses will be tested in this descriptive study. Pending feasibility, rates of malignancy (overall, excluding NMSC), lung cancer, subtypes of lymphoma, serious infection, CV events, MACE, and MI, VTE, and other event rates, including fractures, will be compared between tofacitinib treated RA patients and the comparator cohorts using methods that adjust for sex, age, year of treatment start, treatment history, disease severity, comorbidities, and other potential confounders.

In response to the June 2021 signal evaluation procedure, subtypes of lymphoma, lung cancer, and MACE have been added as study endpoints (MI and lymphoma (overall) were already included as a study endpoint).

Further, rates of events, including serious infections, MACE, MI, VTE and malignancies excluding NMSC, will be estimated in elderly patients aged 65

years and older.

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Medicinal product name

XELJANZ

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

TOFACITINIB CITRATE

Anatomical Therapeutic Chemical (ATC) code

(L04AF01) tofacitinib

tofacitinib

Medical condition to be studied

Rheumatoid arthritis

Population studied

Short description of the study population

The active surveillance population includes rheumatoid arthritis patients already enrolled in the register who met the criteria for the cohorts as defined

in protocol section 9.3.2 as well as patients with rheumatoid arthritis, newly treated with tofacitinib following EMA approval and UK launch of the product (fully available January 2018) and registered with the BSRBR-RA.

Age groups

- 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

500

Study design details

Setting

The BSRBR-RA was established in 2001 to study the safety of biologic therapies in RA patients living in the UK. For the first 78 years the main focus was on the study of the safety profile of the first three TNFi agents (ie, ADA, ETA and INF) as a class and as individual therapies.

With the exception of the risk of developing tuberculosis, data within the BSRBRRA has not demonstrated any clear differences in AE profile between these agents.

At the time the register was established, the most appropriate comparison group for these three TNFi agents was patients with active RA receiving treatment with csDMARDs.

The register remains a relevant resource for studying the safety profile of new biologic, biosimilar and other targeted therapies as they receive National

Institute for Health and Clinical Excellence (NICE) approval and are used in real-world practice where patients have more diverse clinical background and comorbidities than a typical clinical trial population.

Unique features of BSRBR-RA include recruitment and collection of data from parallel comparison groups of patients consisting of (i) those with active RA who were treated with csDMARDs, and (ii) those with active RA who are biologic naïve treated with TNFi, a high proportion of recruited patients in the UK (>80%), and linkage with national mortality and malignancy registries. 9 Several studies have been conducted using data from the BSRBR-RA including work regarding risks of infections,10 and malignancies. 19,25 All patients within the BSRBR-RA provided informed and signed consent for participation (Study Reference 00/8/053).

External validity, ie, generalizability to RA patients who are not enrolled in the register, is maximised by encouraging physicians to enroll each and every patient meeting inclusion criteria, regardless of their baseline demographic or clinical characteristics or treatment history.

Comparators

Initiation of biologic (comparator cohort 1), discontinuation of biologic (comparator cohort 2)

Outcomes

1. Aplastic Anaemia, Pancytopaenia, Serious Neutropenia;
2. Cerebrovascular Accident;
3. Death;
4. Demyelination, Optic Neuritis;
5. Fractures;

6. Hepatitis B Reactivation;
7. Malignancy (overall, excluding NMSC);
8. Lymphoma (overall and independently by subtype, including non-Hodgkin lymphoma, Hodgkin lymphoma, and chronic lymphatic leukemia);
9. Lung Cancer;
10. NMSC;
11. Myocardial Infarction/Acute Coronary Syndrome;
12. Major Adverse Cardiac Events (MACE)
13. Pregnancy;
14. Progressive Multifocal Leukoencephalopathy (PML);
15. Pulmonary Embolism;
16. Serious Congestive Heart Failure;
17. Serious Infusion/Immunologic Reaction;
18. Serious Hypersensitivity Reaction;
19. Serious Infection;
20. Herpes Zoster;
21. Serious Hepatic Dysfunction/Failure;
22. Serious Lower Gastrointestinal Ulcer/Bleed/Perforation;
23. Serious Lupus/ Lupus-Like Illness;
24. Serious Skin Reaction (eg, Stevens Johnson syndrome, erythema multiforme, toxic epidermal necrosis);
25. Serious Haemorrhage;
26. Tuberculosis;
27. Venous thromboembolic events (DVT and PE);
28. All-cause mortality.

Data analysis plan

The initial analyses will consist of descriptive comparisons of baseline status and crude event rates between the different cohorts. The final analysis of endpoints will provide the rates of events overall and in subgroups defined by

baseline characteristics.
Pending feasibility, rates of malignancy, serious infection, CV and other event rates will be compared between tofacitinib treated RA patients and the comparator cohorts using methods that adjust for sex, age, year of treatment start, treatment history, disease severity, comorbidities, and other potential confounders.

Documents

Abstract of study report

A3921312_FINAL STUDY REPORT_27JUL2026.pdf (6.17 MB)

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)

British Society for Rheumatology Biologics Register for Rheumatoid Arthritis

Data source(s), other

BSRBR - Rheumatic and Musculoskeletal conditions

Data sources (types)

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