# An Active Surveillance, Post Authorization Safety Study (PASS) of Serious Infection, Malignancy, Cardiovascular (CV) and Other Safety Events of Interest among Patients Treated with Tofacitinib for Moderately to Severely Active Rheumatoid Arthritis (RA) within the German Registry Rheumatoide Arthritis: Beobachtung der Biologika Therapie (RABBIT) (Safety of tofacitinib in RABBIT)

**First published:** 05/09/2019

**Last updated:** 01/10/2026

Study Ongoing

## Administrative details

**EU PAS number**

EUPAS31164

**Study ID**

49399

**DARWIN EU® study**

No

**Study countries**

Germany

**Study description**

Rationale and background: 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 the RABBIT registry.
Research Question: What are the rates of adverse outcomes of special interest in RA patients treated with tofacitinib in relation to those treated with biologic DMARDs (bDMARD) and non biologic DMARDs (nbDMARD)?

**Study status**

Ongoing

# Research institutions and networks

## Institutions

## Pfizer

**First published:** 01/02/2024

**Last updated:** 01/02/2024

Institution

## German Rheumatism Research Centre Berlin (Deutsches Rheuma-Forschungszentrum Berlin, DRFZ)

Germany

**First published:** 01/02/2024

**Last updated:** 01/02/2024

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

# Contact details


**Study institution contact**

Shahar Shmuel shahar.shmuel@pfizer.com

Study contact

shahar.shmuel@pfizer.com

**Primary lead investigator**

Andrea Leapley

Primary lead investigator

# Study timelines

**Date when funding contract was signed**
Actual: 19/04/2016

**Study start date**
Planned: 01/09/2019

Actual: 01/09/2019

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

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

# Sources of funding

- Pharmaceutical company and other private sector

## More details on funding

Pfizer

# Study protocol

A3921317_PROTOCOL_V1.0_21AUG2019.pdf (1.61 MB)

A3921317_PROTOCOL_V2.0_10SEP2021.pdf (482.5 KB)
A3921317_PROTOCOL- RABBIT PASS_v7.0_06JUL2025.pdf (728.39 KB)
A3921317_PROTOCOL- RABBIT PASS_v6.0_23FEB2025_CLEAN.pdf (717.49 KB)
Final_A3921317_PROTOCOL- RABBIT PASS_v5.0_10.18.2023_clean.pdf (650.14 KB)

A3921317_Amended Protocol_RABBIT PASS_Version 4.0_CLEAN_22Feb2023.pdf (759.97 KB)

A3921317_PROTOCOL- RABBIT PASS _V4.0_22FEB2023.pdf (377.9 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

A3921317

# 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 active surveillance study is using data from RABBIT, an ongoing, prospective observational cohort study started in 2001 with the primary aim of studying the safety of new therapies for RA during routine post-marketed clinical use. RABBIT is being conducted by German Rheumatism Research Center

**Main study objective:**

To evaluate the rates of serious infections, malignancy, CV, and other specified outcomes among patients with RA in a German register who initiate tofacitinib. Rates will also be estimated among existing cohorts of bDMARD and nbDMARD patients to provide context for rates observed on tofacitinib. No a priori hypotheses will be tested in this descriptive study

# 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

**Anatomical Therapeutic Chemical (ATC) code**

(L04AF01) tofacitinib

tofacitinib

**Medical condition to be studied**

Rheumatoid arthritis

# Population studied

**Short description of the study population**

The study population will comprise all patients with RA enrolled within RABBIT who receive tofacitinib following European Medicines Agency (EMA) approval and German launch. For contextualization purposes, the study population will also include RABBIT patients treated with bDMARDs and nbDMARDs.
As initiation of tofacitinib in
RABBIT will be from 01 May 2017 onwards, only treatments initiated after this date will be included in the final report.

**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)

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**Estimated number of subjects**

500

## Study design details

**Setting**

The German Biologics Register RABBIT has been active since May 2001 under the auspices of the “Kompetenznetz entzündlich-rheumatische Systemerkrankungen” (“Competence Network Rheumatology”).

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**Comparators**

The bDMARD comparator cohort will be presented in the final report, while the nbDMARD comparator cohort will be included in both interim and final report reports.

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**Outcomes**

Endpoints in RABBIT derive from physician reports of the occurrence of any AE or event of
interest.
The events of interest, based on previously identified risks in the treated and untreated RA population, include:
1. Serious infections (excluding TB): pneumonia, other infections of the respiratory
system, infections of the CNS, sepsis, bone or joint infections, OI, other infections.
2. TB.

3. Herpes Zoster.
4. Fractures.
5. Cardiac disorders: heart failure, coronary artery disease, myocardial infarction,
MACE, other cardiac disorders.
6. Hematologic disorders: bone marrow depression and hypoplastic anaemia, decreased
white blood cells, platelet disorders, other blood dyscrasia.
7. Disorders of the nervous system (excluding infections): stroke, central demyelination,
other disorders of the CNS, disorders of the peripheral nervous system, psychiatric
disorders.
8. Progressive multifocal leukoencephalopathy.
9. Allergic conditions and hypersensitivity.
10. Hepatic failure.
11. Gastrointestinal (GI) perforations: Lower intestinal perforations, Other GI perforations.
12. Pregnancy.
13. Thromboembolic events: deep vein thrombosis (DVT) and pulmonary embolism
(PE).
14. Operations and hospitalisations: bone and joint surgery and other joint therapeutic
procedures, other operations and (major) therapeutic procedures that lead to hospitalization.
15. Other serious diagnoses, symptoms, and syndromes.
16. NMSC.
17. Malignancies, (overall, excluding NMSC).

18. Lymphoma (overall and independently by subtype, including non-Hodgkin lymphoma, Hodgkin lymphoma, and chronic lymphatic leukemia).
19. Lung cancer.
20. All-cause Mortality.
21. Leukaemia (excl. B-CLL)
22. Other haematopietic neoplasms (malignant and benign)
23. Solid malignancies (overall))
24. Glioblastoma
25. Benign neoplasms
26. Unspecified neoplasms and precanceroses
27. Metastases, cancer related and morbidities and associated syndromes
28. Interstitial lung disease, pending

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**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

**Study report**

A3921317_FINAL STUDY REPORT_24JUL2026.pdf (6.55 MB)

# Data management

## Data sources

**Data source(s), other**

German Registry Rheumatoide Arthritis: Beobachtung der Biologika-Therapie (RABBIT)

**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