Post-Authorisation Active Safety Surveillance Program Among Patients Treated With Tofacitinib for Polyarticular Juvenile Idiopathic Arthritis (pJIA) and Juvenile Psoriatic Arthritis (PsA) Within the German Biologics in Pediatric Rheumatology Registry (BiKeR) and Juvenile Arthritis Methotrexate/Biologics Long-term Observation (JuMBO) Registries (BiKeRJuMBO)

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Last updated: 05/12/2024

Study Planned

Administrative details

EU PAS number

EUPAS107192

Study ID

107193

DARWIN EU® study

No

Study countries

☐ Germany

Study description

Juvenile idiopathic arthritis (JIA) is a heterogenous group of conditions, defined as arthritis persisting for 6 weeks or longer with no other identifiable cause and onset prior to age 16. JIA is the most common pediatric rheumatic illness, with an annual incidence in developed countries of 2 to 20 per 100,000 children and a prevalence of 16 to 150 per 100,000. Tofacitinib (Xeljanz®) is an oral Janus Kinase (JAK) inhibitor approved in the European Union (EU) in adult populations for the treatment of moderate to severe rheumatoid arthritis (RA), active PsA, and moderate to severe ulcerative colitis (UC). The important identified and potential risks associated with use of tofacitinib listed in the Risk Management Plan (RMP) include (but not limited to): venous thromboembolism, serious infections (including tuberculosis), herpes zoster or HZ, fractures, malignancy excluding NMSC and NMSC, lymphoma, lung cancer, interstitial lung disease, gastrointestinal perforations,all-cause mortality, PML, myocardial infarction (MI), and cardiovascular risk (excluding MI). Within the JIA population, additional events of interest include growth or development disturbances, and response to vaccination. Furthermore, drug hypersensitivity is considered as an identified risk and listed in the Summary of Product Characteristics (SmPC) but does not meet the criteria to be included in the RMP. As part of the tofacitinib pharmacovigilance plan, Pfizer will implement a post-approval, active surveillance study of patients with pJIA or juvenile PsA initiating tofacitinib and those treated with approved bDMARDs using prospectively collected data included in the BiKeR and JuMBO registries from Germany to actively monitor the safety events of interest in the post-approval real-world setting, including

events associated with long-term use.

Study status

Planned

Research institutions and networks

Institutions

Pfizer

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Institution

Biologika in der Kinderrheumatologie-Register (BIKER) at the Asklepios Klinik Sankt Augustin

Germany

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Institution | Hospital/Clinic/Other health care facility

Juvenile Arthritis Methotrexate/Biologics Long-term Observation (JuMBO) Register

Contact details

Study institution contact

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Primary lead investigator

Sampada Gandhi

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 22/11/2021

Actual: 22/11/2021

Study start date

Planned: 01/03/2026

Date of interim report, if expected

Planned: 30/08/2026

Date of final study report

Planned: 01/05/2033

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Pfizer 100%

Study protocol

A3921407_PROTOCOL- TOFA JIA BIKERJUMBO_V1.0_ 03MAY2023.pdf (674.18 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

A3921407

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 cohort study utilizing data from patients with pJIA or juvenile PsA from the two German registries separately, namely the BiKeR and JuMBO registries.

Main study objective:

To estimate the incidence rate of the following outcomes of interest among patients with pJIA or juvenile PsA who initiate tofacitinib and patients with pJIA or juvenile PsA treated with approved bDMARDs: venous thromboembolism, serious infections and other important infections, all malignancies combined (excluding NMSC), lymphoma (examined separately), and lung cancer (examined separately).

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Name of medicine

XELJANZ

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

TOFACITINIB CITRATE

Anatomical Therapeutic Chemical (ATC) code

(L04AA29) tofacitinib

tofacitinib

Medical condition to be studied

Juvenile psoriatic arthritis

Juvenile idiopathic arthritis

Population studied

Short description of the study population

The study population will comprise all patients with pJIA or juvenile PsA enrolled within the BiKeR and JuMBO registries who receive tofacitinib following product availability in Germany on 01 March 2022 through 01 July 2031. One comparator cohort comprised of patients with pJIA or juvenile PsA treated with approved bDMARDs will be assembled to provide context for rates observed among patients treated with tofacitinib.

Age groups

Children (2 to < 12 years)

Adolescents (12 to < 18 years)

Study design details

Setting

The study period will be defined from 01 March 2022 (corresponding to Tofacitinib availability in Germany) to 01 July 2032. The German BiKeR registry is a longitudinal multicenter observational registry that is an initiative of the Centre for Pediatric Rheumatology Sankt Augustin supported by the German Society for Childhood Rheumatology [Gesellschaft für Kinder- und Jugendrheumatologie (GKJR)]. The registry was set up in 2001 by pediatric rheumatologists in Germany to prospectively monitor the long term safety and effectiveness of biologics in treatment of JIA. During the first six years of BiKeR, one-third of patients were lost to follow-up for age-related reasons. It is recognized that follow-up of patients beyond adolescence is necessary to yield scientifically rigorous long-term safety information about bDMARDs in JIA patients. Therefore, JuMBO was launched as the BiKeR follow-up register for adult JIA patients in 2007. In general, BiKeR and JuMBO registries have been used in previously published studies to assess the safety and effectiveness of DMARDs in JIA patients and these registries aim to provide results that help to guide therapeutic decisions by providers for affected children, families; to improve post-marketing drug surveillance; and to reduce cost.

Comparators

BiKeR comparator cohort: Patients with pJIA or juvenile PsA treated with approved bDMARDs

1. Diagnosis of pJIA defined as extended oligoarthritis, Polyarthritis (RF+), or Polyarthritis (RF-) or juvenile PsA by a rheumatologist
2. Patients younger than 16 years at diagnosis of pJIA or juvenile PsA
3. Patients aged 2-17 years at initiation of any bDMARD approved for pJIA or juvenile PsA treatment in Germany (e.g., etanercept, adalimumab, abatacept, tocilizumab, golimumab). This is first use of unique bDMARD, not restricted to first bDMARD use (i.e., not restricted to bDMARD naïve patients). For example,

a patient starting etanercept for the first time during the period of 01 March 2022 to 01 July 2031 will be eligible regardless of this patient’s prior use of another bDMARD, for example tocilizumab.
4. Patients initiating a bDMARD as a monotherapy or in combination with MTX identified from the BiKeR registry between 01 March 2022 through 01 July 2031

JuMBO Comparator Cohort: Patients with pJIA or juvenile PsA treated with approved bDMARDs
1. Must be previously enrolled in BiKeR registry
2. Diagnosis of pJIA defined as extended oligoarthritis, Polyarthritis (RF+), or Polyarthritis (RF-) or juvenile PsA by a pediatric or adult rheumatologist
3. Patients younger than 16 years at diagnosis of pJIA or juvenile PsA
4. Patients aged 2-17 years at initiation of any bDMARD approved for pJIA or juvenile PsA treatment in Germany (e.g., etanercept, adalimumab, abatacept, tocilizumab, golimumab). This is first use of unique bDMARD, not restricted to first bDMARD use (i.e., not restricted to bDMARD naïve patients). For example, a patient starting etanercept for the first time during the period of 01 March 2022 to 01 July 2031 will be eligible regardless of this patient’s prior use of another bDMARD, for example tocilizumab.
5. Patients initiating a bDMARD as a monotherapy or in combination with MTX identified from the JuMBO registry between 01 March 2022 through 01 July 2031

Outcomes

All outcomes, with the exception of growth or development disturbances, will be identified using the Medical Dictionary for Regulatory Activities (MedDRA) codes in both registries. Please see protocol Annex 1 for relevant MedDRA codes.
• Venous thromboembolism
• Serious infections and other important infections (including opportunistic infection, tuberculosis and

vaccine preventable infections)

• All malignancies combined (excluding NMSC)

• Lymphoma (examined as a separate outcome)

• Lung cancer (examined as a separate outcome)

• Gastrointestinal perforations

• Major adverse cardiac events (including MI)

Data analysis plan

Crude incidence rates (IRs) of events overall and stratified by baseline characteristics such as disease activity, subtype of JIA, treatment type defined as monotherapy or combination therapy with MTX on the index date, and prior JIA therapy in both tofacitinib cohort and comparator cohort will be calculated. A comparative analysis will examine the risk of the outcomes of interest among patients from the tofacitinib cohort compared to the patients from the comparator cohort adjusting for confounding by baseline characteristics. Propensity scores will be estimated using baseline characteristics described in the study protocol. Propensity score adjusted IR (per 100 PY) and associated 95% CI will be calculated for the outcomes of interest, for which there are adequate data using an exact Poisson method. Where there are adequate data to compare the risk between cohorts, multivariable Cox proportional hazards models will be fit to compare risk of the outcome of interest.

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)

Biologika in der Kinderrheumatologie

Data source(s), other

Juvenile Arthritis Methotrexate/Biologics Long-term Observation Register (JuMBo)

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