Post-Authorisation Active Safety Surveillance Program Among Patients Treated With Tofacitinib for Polyarticular Juvenile Idiopathic Arthritis (pJIA) and Juvenile Psoriatic Arthritis (PsA) Using Nationwide Swedish Healthcare Registers

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Study Planned

Administrative details

EU PAS number

EUPAS107199

Study ID

107200

DARWIN EU® study

No

Study countries

Sweden

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, NMSC, lymphoma, lung cancer, all-cause mortality, interstitial lung disease, gastrointestinal perforations, PML, myocardial infarction (MI), and cardiovascular risk (excluding MI). Within the JIA population, additional events of interest include growth or developmentdisturbances 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 nationwide Swedish healthcare registers 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

Karolinska Institutet

Sweden

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Institution | Educational Institution

Contact details

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Primary lead investigator

Sampada Gandhi

Primary lead investigator

Study timelines

Date when funding contract was signed
Planned: 07/12/2021

Actual: 07/12/2021

Study start date
Planned: 01/03/2026

Date of interim report, if expected
Planned: 30/08/2026

Date of final study report
Planned: 01/05/2031

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Pfizer 100%

Study protocol

A3921408_PROTOCOL- TOFA JIA SWEDISH REGISTER_V1.0_ 03MAY2023.pdf

(600.92 KB)

Regulatory

Was the study required by a regulatory body?

Yes

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

EU RMP category 3 (required)

Other study registration identification numbers and links

A3921408

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 8-year active surveillance, secondary data collection study of patients with pJIA or juvenile PsA using data from existing nationwide cohorts from the years 2022-2030 in Sweden.

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

Medicinal product name

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 idiopathic arthritis

Juvenile psoriatic arthritis

Population studied

Short description of the study population

The study population will comprise all patients with pJIA or juvenile PsA who receive tofacitinib and are identified from nationwide Swedish healthcare registers following product availability in Sweden since 18 March 2022 through 01 July 2029.

Age groups

- Children (2 to < 12 years)
- Adolescents (12 to < 18 years)

Study design details

Setting

The study period will be defined from 18 March 2022 (corresponding to tofacitinib availability in Sweden) to 01 July 2030 (covering the data available through register linkages on this date) Sweden is a Scandinavian country with 10 million inhabitants. A population-based cohort study conducted in the southernmost county of Sweden reported a mean annual incidence rate for JIA

to be 12.8/100,000 children < 16 years (95% CI: 11.3–14.5), with the highest age-specific annual incidence at the age of 2 years (36/100,000) during the years 2002-2010.
Another longitudinal, prospective, population based incidence study reported annual incidence rates of JIA according to the ILAR criteria ranging from 7 patients/100,000 in Iceland and 23/100,000 in the Trondheim region of Norway, with an annual incidence of 15 per 100,000 per year (95% CI: 12-18). Swedish health care is tax funded and offers universal access. Hospital referral is based on geography rather than insurance status. Patients with JIA are typically treated by rheumatologists, the vast majority of whom work in public and hospital based clinics.

Health and demographic information is collected in a series of registers with a high degree of completeness resulting from the mandatory and semi-automated registration of their data. Based on each Swedish resident's unique personal identification number, issued to all Swedish residents alive in 1947 or born/immigrated thereafter, linkage of data from different registers is possible. The registers are maintained by governmental bodies, who may perform data linkages and provide de-identified data for research purposes.

Comparators

Patients with pJIA or juvenile PsA treated with approved bDMARDs:
1. Diagnosis of pJIA defined as oligoarthritis, polyarthritis (RF+), or polyarthritis (RF-) or a diagnosis of juvenile PsA defined using ICD-10-SE codes listed in protocol Section 9.2.1.1 and as recorded in the NPR.
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 Sweden (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 18 March 2022 to 01 July 2029 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 and identified by dispensation of bDMARD in the Prescribed Drug Register during 18 March 2022 and 01 July 2029.

Outcomes

The following outcomes of interest will be examined in the interim and final study report. All outcomes will be identified using ICD-10-SE codes. Please see protocol Annex 1 for relevant ICD-10-SE codes.
Venous thromboembolism
Serious infections and other important infections (including opportunistic infection and tuberculosis)
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)
Fractures
PML
All-cause mortality
HZ reactivation
NMSC
Interstitial lung disease

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)

Sweden National Prescribed Drugs Register / Läkemedelsregistret

Sweden National Cancer Register / Cancerregistret

Swedish Cause of Death Register

Data source(s), other

Swedish National Patient Register Sweden, Swedish Contagious Disease Register Sweden, Swedish JIA Clinical Register Sweden

Data sources (types)

Disease registry

Drug dispensing/prescription data

Electronic healthcare records (EHR)

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