Post-Authorisation Active Safety Surveillance Program Among Patients Treated With Tofacitinib for Polyarticular Juvenile Idiopathic Arthritis (pJIA) and Juvenile Psoriatic Arthritis (PsA) Within the United Kingdom (UK) Juvenile Idiopathic Arthritis (JIA) Biologics Register

First published: 06/11/2023

Last updated: 03/12/2024

Study Planned

Administrative details

EU PAS number

EUPAS107203

Study ID

107204

DARWIN EU® study

No

Study countries

☐ United Kingdom

Study description

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 (HZ), malignancy excluding nonmelanoma skin cancer (NMSC), NMSC, lymphoma, lung cancer, interstitial lung disease, fractures, gastrointestinal perforations, all-cause mortality, progressive multifocal leukoencephalopathy (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 UK JIA Biologics Register 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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Last updated: 01/02/2024

Institution

British Society for Rheumatology Biologics Registers (BSRBR)

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Institution | Educational Institution | Other

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: 21/12/2021

Actual: 21/12/2021

Study start date
Planned: 01/10/2026

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

A3921409_PROTOCOL- TOFA JIA UK REGISTER_V1.0_ 03MAY2023.pdf (630.84 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

A3921409

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 utilizing data from the UK JIA Biologics Register, which consists of the British Society for Paediatric and Adolescent Rheumatology Etanercept Cohort Study and the Biologics for Children with Rheumatic Diseases Study.

Main study objective:
To estimate the post-approval real-world IR of the following outcomes of interest among patients with pJIA or juvenile PsA who initiate tofacitinib (Tofacitinib cohort) and among patients with pJIA or juvenile PsA treated with approved bDMARDs (Comparator cohort):
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)

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 enrolled within the UK JIA Biologics Register who receive tofacitinib following product availability in the UK since 07 April 2022 through 01 July 2029. One comparator cohort comprised of patients with pJIA or juvenile PsA treated with approved bDMARDs (etanercept being the most prevalent bDMARD used within the UK registers) and identified from 01 January 2010 through 01 July 2029 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 07 April 2022 (corresponding to tofacitinib availability in the UK) to 01 July 2030 for the tofacitinib cohort and from 01 January 2010 to 01 July 2030 for the comparator cohort. This study is set within the UK JIA Biologics Register. Data from the UK JIA Biologics Register has contributed to a range of publications focusing on real-world biologic treatment effectiveness and safety. Historically and due to the nature of prior funding, data on children with JIA starting biologics, targeted therapies and MTX were captured in 2 parallel but identical studies, both based at The University of Manchester. The BSPAR Etanercept cohort study
collects data from children starting etanercept or methotrexate. The BCRD Study collects data from children starting non-etanercept bDMARDS, including other tumor necrosis factor (TNF) inhibitors such as adalimumab, JAK inhibitors or MTX. Both studies operate under the single banner of the UK JIA Biologics Register. Patients can contribute data to both studies and data captured using identical methods from the same hospitals are pooled for analyses.

Comparators

Patients with pJIA or juvenile PsA treated with approved bDMARDs (Comparator cohort):

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 UK (e.g., etanercept, adalimumab, abatacept, tocilizumab). 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 January 2010 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 during the study period from 01 January 2010 to 01 July 2029 and as captured in the UK JIA Biologics Register

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Outcomes

The following outcomes of interest will be examined in the interim and final study report. All outcomes, with the exception of growth or development disturbances, will be identified using the Medical Dictionary for Regulatory Activities (MedDRA) codes. Please see 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)
Hypersensitivity
Growth or development disturbances
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)

British Society for Rheumatology Biologics Register for Rheumatoid Arthritis

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