Observational Study of Effectiveness and Safety of Recombinant Zoster Vaccine (Shingrix)® in Moderately-to-Severely Active Ulcerative Colitis (UC) or Rheumatoid Arthritis (RA) Patients Treated with Tofacitinib (Xeljanz)® in Real- World Clinical Care Settings

First published: 19/01/2024

Last updated: 06/12/2024

Study Ongoing

Administrative details

EU PAS number

EUPAS48998

Study ID

199015

DARWIN EU® study

No

Study countries

United States

Study description

This study plans to evaluate the effectiveness and safety of the RZV (“Shingrix ® vaccine”) in real-world patients with ulcerative colitis (UC) and rheumatoid artiritis (RA) treated with tofacitinib.

Study status

Ongoing

Research institutions and networks

Institutions

Pfizer

First published: 01/02/2024

Last updated: 01/02/2024

Institution

Optum

Germany

First published: 03/01/2012

Last updated: 07/02/2014

Institution Other ENCePP partner

Contact details

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Primary lead investigator

Michelle Iannacone

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 06/04/2022

Actual: 06/04/2022

Study start date

Planned: 02/01/2024

Actual: 01/03/2024

Date of final study report

Planned: 14/09/2025

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Pfizer 100%

Study protocol

A3921427_PROTOCOL- XELJANZ SHINGRIZ PASS_V2.1_05OCT2023.pdf(2.46 MB)

Regulatory

Was the study required by a regulatory body?

Yes

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

Non-EU RMP only

Other study registration identification numbers and links

A3921427

Methodological aspects

Study type

Study type list

Study topic:

Human medicinal product

Study type:

Non-interventional study

Scope of the study:

Effectiveness study (incl. comparative)

Safety study (incl. comparative)

Data collection methods:

Secondary use of data

Study design:

This is a non-interventional observational cohort study to evaluate the effectiveness and safety of RZV in real-world patients with ulcerative colitis (UC) or rheumatoid arthritis (RA) receiving ongoing treatment with tofacitinib.

Main study objective:

The primary objective for effectiveness in this study is:
To estimate and compare the incidence rate of HZ among patients with UC or RA being treated with tofacitinib who receive two doses of RZV relative to the incidence rate among patients with UC or RA being treated with tofacitinib who do not receive RZV.

The secondary objective for effectiveness in this study is:
To estimate and compare the incidence rate of HZ among patients with UC or RA being
treated with tofacitinib who receive at least one dose of RZV relative to the incidence rate among patients with UC or RA being treated with tofacitinib who

do not receive RZV.

The secondary objectives for safety in this study are:
1. To estimate and compare the incidence rate of UC disease flares among patients with UC being treated with tofacitinib who receive at least one dose of RZV relative to the incidence rate among patients with UC being treated with tofacitinib who do not receive RZV.
2. To estimate and compare the incidence rate of RA disease flares among patients with RA being treated with tofacitinib who receive at least one dose of RZV relative to the incidence rate among patients with RA being treated with tofacitinib who do not receive RZV.

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

Colitis ulcerative

Rheumatoid arthritis

Population studied

Short description of the study population

As this study aims to assess the effectiveness and safety of Recombinant Zoster Vaccine (RZV) among patients receiving ongoing treatment with tofacitinib, we will identify current users of tofacitinib rather than new users or initiators as the source population to identify patients with and without RZV vaccine.

A patient will be considered to be a current user of tofacitinib if they have a tofacitinib on-treatment period on or after 20 October 2017. The date of tofacitinib dispensing will serve as the first day of the on-treatment period. The duration of the on-treatment period will be defined by the days' supply for the dispensing plus a grace period of 30 days to account for non-adherence. A patient will continue to be considered a current user if the time between the current and subsequent dispensing of tofacitinib is less than or equal to the days' supply plus 30 days. Otherwise, the on-treatment period will cease at the end of the 30-day grace period, and the patient will no longer be considered a current user of tofacitinib. (It should be noted that discontinuation of tofacitinib is not a censoring criterion. Patients who were previously included in one of the exposure cohorts while they were on-treatment for tofacitinib will continued to be followed if their tofacitinib on-treatment period ends.) If the patient restarts treatment with tofacitinib (ie, has another on-treatment period) after the end of a previous on-treatment period, the patient may be included in the study if they continue to meet the other eligibility criteria.

If there are consecutive dispensings of tofacitinib with overlapping days' supply, the duration of the on-treatment period will be the sum of the days' supply from each dispensing plus 30 days if the dose of tofacitinib is the same for both dispensings, as it is likely that this represents an early refill. However, if the dose of tofacitinib is different for the subsequent dispensing, the end date for the earlier dispensing will be set to the day prior to the dispensing date of the subsequent dispensing when calculating the duration of the on-treatment period.

Once patients who are current users of tofacitinib on or after 20 October 2017 have been identified, the source population will be restricted to those who are 18 years and older and have a diagnosis of UC or RA on or after 20 October 2016.

Age groups

Adults (18 to < 65 years)

Study design details

Setting

The source population will consist of adult patients 18 years and older treated with tofacitinib with moderately to severely active UC or RA between 20 October 2017 (the date of RZV approval in the US) and 31 July 2023 (or most recent available data at the time the data are extracted). Severity of UC and RA will not be measured directly; rather, it will be assumed based on the indications for tofacitinib treatment.

Comparators

Optum will identify a cohort of patients without exposure to RZV among patients who are current users of tofacitinib. To minimize the immortal time bias that may be introduced when exposure is defined based on information accrued during follow-up, these patients will be randomly drawn from time-matched vaccination risk sets that are defined as sequential 4-week windows during which they were eligible for inclusion in the RZV cohorts, but without any RZV exposure during the window. Matching within this narrow caliper of calendar time limits the potential immortal time introduced by using future information (ie, lack of RZV receipt) to classify patients at the time of cohort entry. A cohort entry date will be randomly selected from this time window. In addition, other factors, such as duration of tofacitinib use, will be considered for matching upon feasibility, which will be described in the statistical analysis plan (SAP).

To construct the vaccination risk sets, separate 4-week windows will be created, starting on the study initiation date (20 October 2017) through the end of the study period. Among patients who are current tofacitinib users within a given 4-week window, patients without any RZV exposure who meet the study inclusion criteria and exclusion criteria at the beginning of the 4-week window will be identified. These patients will be eligible to be sampled as comparator patients for each RZV initiator identified with receipt of a second RZV dose during the same 4-week window.

Up to 2 comparators for each RZV initiator will be selected, matched on data source (the Optum Research Database or the Optum Medicare Advantage and and Medicare Part D Database) and other factors considered upon feasibility. Patients will be sampled with replacement. This process will be repeated for each 4-week window during the study period; as such, it is possible that a

patient could be sampled as a comparator multiple times during the study.

Outcomes

The primary outcome for this study is the occurrence of new herpes zoster (HZ) infection. The secondary outcome for this study is disease flare: UC flare within the UC cohorts and RA flare within the RA cohorts.

Data analysis plan

There will be 4 propensity score models that, separately, will estimate propensity scores that discriminate between (1) receipt of two doses of RZV and non-receipt of RZV in UC cohorts, (2) receipt of two doses of RZV and non-receipt of RZV in RA cohorts, (3) receipt of at least one dose of RZV and non-receipt of RZV in UC cohorts, and (4) receipt of at least one dose of RZV and non-receipt of RZV in RA cohorts. If there are confounders identified that would only be appropriate to include in one model and not the other, separate propensity score models for the outcomes HZ and disease flare will be considered. Once the final models have been generated, propensity scores will be estimated for each patient.

Data management

Data sources

Data source(s), other

Optum Research Database

Optum Medicare Advantage and Medicare Part D Database

Data sources (types)

Administrative healthcare records (e.g., claims)

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