An Observational Study Assessing the Long-term Risk of Non-Melanoma Skin Cancer (NMSC) Among New Users of OpzeluraTM (Ruxolitinib) Cream in a Vitiligo Patient Population: Post-Authorization Safety Study (PASS)

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Study Planned

Administrative details

EU PAS number

EUPAS1000000413

Study ID

1000000413

DARWIN EU® study

No

Study countries

France

Germany

United States

Study description

This is a non-interventional, retrospective cohort study to evaluate the long-term risk of non-melanoma skin cancer (NMSC) among new users of Opzelura (ruxolitinib) cream in patients with vitiligo aged 12 years and older across the US, France, and Germany.

Opzelura (ruxolitinib) cream is a topical formulation of ruxolitinib phosphate, an inhibitor of the janus kinase (JAK) family of protein tyrosine kinases that was recently authorized for the treatment of non-segmental vitiligo.

As required by the European Medicines Agency, this study is being conducted as a post-authorization safety study (PASS) to assess the long-term risk of NMSC among new users of the Opzelura (ruxolitinib) cream for the treatment of vitiligo.

The primary objective of the study is to assess the long-term risk of NMSC among patients with vitiligo treated with Opzelura (ruxolitinib) cream compared to patients with vitiligo treated with other vitiligo-related treatments. Other vitiligo-related treatments include topical calcineurin inhibitors (TCI) / topical corticosteroids (TCS) and/or phototherapy.

Data is captured from two databases from US (PharMetrics Plus and US Ambulatory Electronic Medical Records [AEMR] Merged, and the Guardian Research Network [GRN] database) and two databases from the EU (German Statutory Health Insurance [SHI] and French Longitudinal Patient Data linked with French National Health Data System- Système National Des Données De Santé [SNDS]).

Study status

Planned

Research institutions and networks

Institutions

Incyte Corporation

Contact details

Study institution contact

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Study contact

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Primary lead investigator

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Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 27/07/2023

Actual: 27/07/2023

Study start date

Planned: 18/06/2025

Data analysis start date

Planned: 11/04/2025

Date of interim report, if expected
Planned: 15/07/2025

Date of final study report
Planned: 15/07/2031

Sources of funding

More details on funding

Incyte Corporation

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)

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 study is a non-interventional, retrospective cohort study to evaluate the long-term risk of NMSC among new users of Opzelura cream in patients with vitiligo aged 12 years and older. EMR and claims data from secondary databases in the US, France, and Germany are utilized in the study.

Main study objective:

The primary objective of the study is to assess the long-term risk of NMSC among patients with vitiligo treated with Opzelura (ruxolitinib) cream compared to patients with vitiligo treated with other vitiligo-related treatments. Other vitiligo-related treatments include TCI/TCS and/or phototherapy.

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Medicinal product name

OPZELURA

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

RUXOLITINIB

Anatomical Therapeutic Chemical (ATC) code

(D11AH09) ruxolitinib

ruxolitinib

Medical condition to be studied

Vitiligo

Population studied

Short description of the study population

The study population is drawn from nationally representative data sources in the US (IQVIA PharMetrics Plus and US AEMR Merged, and the GRN database) and the EU (German SHI and French LPD linked to SNDS).

The study includes adults and pediatric patients who are 12 years of age or older and with a vitiligo diagnosis identified by an ICD-10 diagnosis code of L80 and those who fulfill the eligibility criteria.

Approximately 29,000 unique patients with vitiligo in the PharMetrics Plus-AEMR Merged database and 4,000 unique vitiligo patients in the GRN database will be evaluated for inclusion in the study.

In the EU, approximately 10,710 patients from SHI (Germany) and 2,304 patients from SNDS (France) will be evaluated for inclusion in the study.

Age groups

- **Paediatric Population (< 18 years)**
- **Adult and elderly population (≥18 years)**
  - Adults (18 to < 65 years)
  - Elderly (≥ 65 years)

Study design details

Setting

The study includes the patients with a vitiligo diagnosis identified by an ICD-10 diagnosis code of L80 and those who fulfill the eligibility criteria.

Patients' records must meet all of the following inclusion criteria to be eligible in the study:

Patients aged 12 years or above in the index year; Patients with continuous enrollment in plans with both medical and drug coverage for at least 365 days prior to and including the index date;

Patients with a minimum of 365 days of follow-up time within 365 days of the index date;

and Patients with a vitiligo diagnosis code identified by ICD-10 code L80 in the outpatient sector or one main or secondary hospital diagnosis during the indexing period.

Patients diagnosed with atopic dermatitis, vitiligo-mimicking conditions, and any cancer type;

patients who use any chemotherapeutic agent in any formulation or any radiotherapy;

and patients with record of surgical graft procedures for vitiligo treatment, during the baseline period, on the index date, or during the latency period are excluded in the study.

Additionally, patients with the evidence of data quality issues during the index

year, including invalid health plan enrollment dates, missing or invalid age, and missing sex, are excluded in the study.
The baseline period is the time period of 365 days prior to and not including the index date (Day 0).
The indexing period starts from the date of Opzelura approval for vitiligo in the US and ends on 30 June 2026.
For French patients, the indexing period begins on the country-specific reimbursement date and ends in June 2026.
For German patients, the indexing period begins on the country's specific reimbursement date.
A patient's follow-up window starts from the day after the patient's index date until the end of patient follow-up which is 30 June 2029, or date of censoring, whichever occurs first.

Comparators

For the primary objective, patients with vitiligo treated with Opzelura (ruxolitinib) cream are compared to patients with vitiligo treated with other vitiligo-related treatments (including TCI/TCS and/or phototherapy).
For the secondary objectives, demographic and clinical characteristics of patients with vitiligo treated with Opzelura are compared to patients with vitiligo treated with other vitiligo-related treatments or no evidence of treatment.

Outcomes

The primary outcome is NMSC diagnosis.
To identify NMSC, the US data captures diagnosis of basal cell carcinoma (BCC), squamous cell carcinoma (SCC), and Merkel cell carcinoma (MCC).
Whereas the EU data only captures NMSC unspecified due to limitations in ICD-10 conventions in France and Germany.

Data analysis plan

Descriptive and comparative analyses will be conducted to evaluate the primary and secondary objectives of this study and will be presented by data source.

The unit of observation in this study will be the patient at risk for NMSC. Each exposed patient will be propensity score (PS) matched up to four of the unexposed patients, using nearest neighbor matching methodology.

Multivariable Cox models, adjusting for additional risk factors relevant to NMSC will be fitted within each data source to compare the primary safety outcomes of the treatment arms.

A per-protocol analysis will be conducted to assess the long-term risk of NMSC among the exposed and unexposed cohorts. Cox regression models will be used, with time dependent variables as necessary, to assess the long-term risk of NMSC among patients with vitiligo treated with Opzelura compared to patients with vitiligo treated with other vitiligo treatments.

Unadjusted HR and adjusted HRs of NMSC, with their 95% CIs will be provided.

PS will be constructed and used to match the exposed and unexposed cohorts using nearest neighbor methodology.

Demographic characteristics and clinical characteristics will be reported by treatment cohort using descriptive statistics. Comparisons of the demographic and clinical characteristics of patients with vitiligo treated with Opzelura to patients with vitiligo treated with other vitiligo-related treatments or no evidence of treatment will include independent sample t-tests or Mann-Whitney U tests for continuous variables in unmatched patients.

In matched patients, dependent sample t-tests may be used for the evaluation of continuous variables. The incidence rates per 1,000 person-years and corresponding 95% CIs will be calculated, separately among the treatment cohorts.

Crude and adjusted incidence rate ratios (IRRs) will be calculated comparing

patients with vitiligo treated with Opzelura to patients with vitiligo with no evidence of vitiligo-related treatments.

Summary results

TBD

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)

Système National des Données de Santé (French national health system main database)

Longitudinal Patient Data - France

Data source(s), other

United States - PharMetrics Plus and US Ambulatory Electronic Medical Records (AEMR) Merged, and the Guardian Research Network (GRN) database

Germany - German Statutory Health Insurance (SHI)

France - French Longitudinal Patient Data linked with French National Health Data System- Système National Des Données De Santé [SNDS].

Data sources (types)

Administrative healthcare records (e.g., claims)

Electronic healthcare records (EHR)

Use of a Common Data Model (CDM)

CDM mapping

Yes

Data quality specifications

Check conformance

Yes

Check completeness

Yes

Check stability

Yes

Check logical consistency

Yes

Data characterisation

Data characterisation conducted

Yes