Postauthorisation Safety Study (PASS) of Avatrombopag and Haematological Malignancies in Patients With Primary Immune Thrombocytopaenia

First published: 30/09/2024

Last updated: 18/12/2024

Study Planned

Administrative details

EU PAS number

EUPAS1000000315

Study ID

1000000315

DARWIN EU® study

No

Study countries

- ☐ Denmark
- ☐ Sweden

Study description

Avatrombopag maleate (Doptelet®) is an orally administered thrombopoietin receptor agonist (TPO-RA) approved by the European Medicines Agency (EMA) for the treatment of primary immune thrombocytopaenia (ITP) in adults. It is also approved as second-line treatment. This postauthorisation safety study (PASS) will provide a descriptive analysis of haematological malignancies among patients exposed to avatrombopag using the Danish National Health Registers and the Swedish National Health Registers. This non-interventional, population-based, descriptive cohort study will use secondary data collection to estimate the incidence rate (IR) of haematological malignancies among patients with primary ITP who initiate avatrombopag. To contextualise this IR, the IR of haematological malignancies will also be estimated among patients with ITP who have not received avatrombopag. Finally, a standardised morbidity ratio will also be estimated.

Study status

Planned

Research institutions and networks

Institutions

RTI Health Solutions (RTI-HS)

- ☐ France
- ☐ Spain
- ☐ Sweden
- ☐ United Kingdom
- ☐ United Kingdom (Northern Ireland)
- ☐ United States

First published: 21/04/2010

Last updated: 13/03/2025

Institution | Not-for-profit | ENCePP partner

Aarhus University & Aarhus University Hospital DEPARTMENT OF CLINICAL EPIDEMIOLOGY

Denmark

First published: 20/07/2021

Last updated: 02/04/2024

Institution | Educational Institution | ENCePP partner

Centre for Pharmacoepidemiology, Karolinska Institutet (CPE-KI)

Sweden

First published: 24/03/2010

Last updated: 23/04/2024

Institution | Educational Institution | Laboratory/Research/Testing facility | Not-for-profit | ENCePP partner

Contact details

Study institution contact

Maria Foraster mforaster@rti.org

Study contact

mforaster@rti.org

Primary lead investigator

Maria Foraster 0000-0003-4450-4123

Primary lead investigator

ORCID number:

0000-0003-4450-4123

Study timelines

Date when funding contract was signed

Planned: 01/07/2024

Actual: 02/09/2024

Study start date

Planned: 28/01/2029

Data analysis start date

Planned: 01/10/2029

Date of final study report

Planned: 28/01/2030

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Swedish Orphan Biovitrum AB (publ)

Study protocol

5735_ITP PASS Protocol_v1.2_Final_20Dec2023_Redacted.pdf (883.6 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)

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:

Non-interventional, population-based, descriptive cohort study using routinely collected secondary data from the national health registers in Denmark and Sweden.

Main study objective:

The primary objective of the avatrombopag PASS is to estimate the IR of haematological malignancies among patients with primary ITP who initiate treatment with avatrombopag.

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Name of medicine

DOPTELET

Anatomical Therapeutic Chemical (ATC) code

(B02BX08) avatrombopag

avatrombopag

Medical condition to be studied

Haematological malignancy

Population studied

Short description of the study population

The study population will include adults with a new diagnosis of primary ITP recorded on at least 2 separate dates in 2006 or later. Two cohorts are defined: Avatrombopag Cohort and No Avatrombopag Cohort. For patients in the Avatrombopag Cohort, the date of the first dispensing/prescription of avatrombopag within the study period will be considered the index date (or day 0), contingent on meeting the other inclusion and exclusion criteria. Follow-up and outcome assessment will start on the day after the index date (day 1). Patients will be followed to the first of the following: occurrence of an outcome event, end of study period (initially planned for Q2 2027 in Sweden and Q1 2028 in Denmark), emigration, or death. For the No Avatrombopag Cohort, the date of the second diagnosis of primary ITP in the data source will be considered the index date (or day zero), and follow-up and outcome assessment will start on the day after the index date (day 1). Censoring events in the No Avatrombopag Cohort will be identical to those for the Avatrombopag Cohort except for the additional criterion that starting avatrombopag will end follow-up.

Age groups

Adult and elderly population (≥18 years)

Adults (18 to < 65 years)

Adults (18 to < 46 years)

Adults (46 to < 65 years)

Elderly (≥ 65 years)

Adults (65 to < 75 years)

Adults (75 to < 85 years)

Adults (85 years and over)

Special population of interest

Other

Special population of interest, other

The study population will consist of patients diagnosed with primary ITP, an acquired autoimmune disease

---

Estimated number of subjects

200

Study design details

Setting

Two cohorts are defined (details on eligibility criteria can be found in the protocol):

- Avatrombopag Cohort: Patients with a first ever dispensing/prescription of avatrombopag within the study period and who meet all the eligibility criteria before or on the index date (i.e., day 0 defined as the date of first dispensing/prescription of avatrombopag) will be assigned to the Avatrombopag Cohort.
- No Avatrombopag Cohort: Patients who are newly diagnosed with primary ITP

and who meet all eligibility criteria on the index date (i.e., day 0 defined as the date of the second diagnosis of primary ITP) will be assigned to the No Avatrombopag Cohort.
For both cohorts, follow-up and outcome assessment start on the day after the index date (day 1) and censoring criteria are identical (i.e., occurrence of an outcome event, emigration, death, or end of the study period); the No Avatrombopag Cohort has an additional censoring criterion that includes initiation of avatrombopag.
The study period is 6 years starting on the date avatrombopag was approved for reimbursement in Denmark (28 January 2022) and Sweden (18 June 2021) and ending in Q1 2028 in Denmark and Q2 2027 in Sweden. The study period includes a 5-year enrolment period, allowing for a minimum of 1-year follow-up for all included patients (up to 6 years of follow-up).

Comparators

To contextualize the primary analysis, the IR of haematological malignancies will also be estimated among patients newly diagnosed with ITP who have not received treatment with avatrombopag.

Outcomes

Haematological malignancies will be defined during follow-up as the first record of any of their individual components:
- Myeloproliferative neoplasms
- Myeloid and lymphoid neoplasms with eosinophilia and abnormalities of platelet-derived growth factor receptor alpha (PDGFRA), platelet-derived growth factor receptor beta (PDGFRB), or fibroblast growth factor receptor 1
- Myelodysplastic/myeloproliferative neoplasms
- Myelodysplastic syndrome
- Acute myeloid leukaemia and related precursor neoplasms

- Acute leukaemia of ambiguous lineage
- Precursor lymphoid malignancies
- Mature B-cell neoplasms
- Mature T-cell and natural killer (NK)–cell neoplasms
- Hodgkin lymphoma
- Histiocytic and dendritic cell neoplasms
- Post-transplant lymphoproliferative disorders

Data analysis plan

Patient attrition in each of the study cohorts will be reported. The characteristics of patients in the two study cohorts according to the covariables defined at the index date and annually up to 5 years after ITP diagnosis will be described. The observed number of incident haematological malignancies in each cohort (Avatrombopag Cohort and No Avatrombopag Cohort) will be reported. Crude IR estimates of haematological malignancies overall and by age categories, sex, and time since ITP diagnosis will be estimated for each cohort with 95% CIs. The expected number of events in the Avatrombopag Cohort will be estimated based on the IRs in the No Avatrombopag Cohort using indirect standardisation stratified by age categories, sex, and time since ITP diagnosis. The standardised morbidity (incidence) ratio (SMR), the ratio of the observed to expected number of cases, will be reported with 95% CIs and will represent the IRR of haematological malignancies in the Avatrombopag Cohort compared with the No Avatrombopag Cohort.

Documents

Study, other information

SobiITPPASS_DoIs_all.pdf (1.3 MB)

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)

Danish registries (access/analysis)

Sweden National Prescribed Drugs Register / Läkemedelsregistret

Sweden National Cancer Register / Cancerregistret

Landspatientregisteret (National Patient Register)

Data source(s), other

- The Swedish National Patient Register
- The National Hospital Medication Register (Denmark)
- The Danish Civil Registration System
- Income and education data from Statistics Denmark
- The Danish National Pathology Registry

Data sources (types)

Administrative healthcare records (e.g., claims)

Disease registry

Drug dispensing/prescription data

Electronic healthcare records (EHR)

Population 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

Unknown