Postauthorisation Safety Study (PASS) of Avatrombopag in Patients With Severe Chronic Liver Disease (CLD)

First published: 18/09/2024

Last updated: 18/09/2024

Study Planned

Administrative details

PURI

https://redirect.ema.europa.eu/resource/1000000310

EU PAS number

EUPAS1000000310

Study ID

1000000310

DARWIN EU® study

No

Study countries

☐ Austria

☐ Denmark

☐ Netherlands

☐ Spain

Study description

This is a non-interventional, multinational descriptive cohort study conducted through secondary data collected via review of existing medical charts from patients managed in routine clinical practice at clinical sites in countries in Europe.

The study will collect patients' data from adult patients treated with avatrombopag or lusutrombopag or patients receiving platelet transfusions in preparation for an elective invasive procedure. The study will be conducted at approx. 10 to 15 clinical sites in selected European countries managing patients with severe CLD and severe thrombocytopenia.

The study size estimate is based on the number of patients treated with avatrombopag, and the actual study size will be determined mainly by the overall utilisation of avatrombopag in patients with severe CLD before elective invasive procedures at the selected sites in the selected countries. At each site, all eligible patients with severe CLD treated with lusutrombopag or receiving a platelet transfusion before elective invasive procedures will be also included. Based on the study feasibility assessment, most participating sites estimated that 1 to 5 potential patients of Child-Pugh class C or MELD score >24 will receive/have received avatrombopag during the study period due to the rarity of these patients undergoing elective procedures. Based on initial feasibility estimates, it is anticipated that approximately 30 patients with severe CLD receiving avatrombopag could be included in the study. A larger number of patients who received platelet transfusions have data available at the selected sites, and very few patients are expected to have received lusutrombopag as the label includes a warning for its use in patients in Child-Pugh class C. Differences in liver function test values before and after the procedure within

(not between) patients exposed to avatrombopag or lusutrombopag or receiving a platelet transfusion will be estimated.

Study status

Planned

Research institutions and networks

Institutions

Erasmus Medical Centre Rotterdam

First published: 01/02/2024

Last updated: 01/02/2024

Institution

Klinikum Klagenfurt Vienna in Austria, Hvidovre Hospital Copenhagen in Denmark; Hospital Universitario Puerta de Hierro, Madrid; Hospital Universitario de la Plana, Villareal, Castellón, Hospital Universitario Miguel Servet, Zaragoza

Hospital Universitario Insular de Gran Canaria, Las Palmas

Contact details

Study institution contact

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Primary lead investigator

Dr Jose Luis Calleja

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 12/06/2024

Actual: 12/06/2024

Study start date

Planned: 31/12/2024

Data analysis start date

Planned: 29/01/2027

Date of final study report

Planned: 31/03/2027

Sources of funding

- Pharmaceutical company and other private sector

Study protocol

0305735_Sobi_Doptelet CLD PASS protocol V2.0_FINAL 14Dec2023 - signed.pdf
(1.6 MB)

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:

Disease /health condition

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, multinational descriptive cohort study based on secondary data collected from patients' medical notes who are treated with avatrombopag or lusutrombopag and patients receiving platelet transfusions in routine clinical practice at sites in Austria, Denmark, Netherlands and Spain.

Main study objective:

The primary study objective is to estimate, among patients with severe CLD and severe thrombocytopenia who are scheduled for an elective invasive procedure, differences between LFT values measured before and after the elective invasive procedure, according to the treatment received (i.e., avatrombopag, lusutrombopag, or platelet transfusion).

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Name of medicine

DOPTELET

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

AVATROMBOPAG MALEATE

Anatomical Therapeutic Chemical (ATC) code

(B02BX08) avatrombopag

avatrombopag

Medical condition to be studied

Chronic disease

Thrombocytopenia

Additional medical condition(s)

severe chronic liver disease

Population studied

Short description of the study population

The source population will consist of patients under the care of physicians practising at hospitals or specialised outpatient settings (hospitals or specialty clinics) in European countries, where patients are being treated for severe thrombocytopenia due to severe CLD (chronic liver disease) in preparation for an elective invasive procedure.

The study population will comprise adult patients with documented severe CLD (Child-Pugh C or Model of End-Stage Liver Disease (MELD) score > 24) and severe thrombocytopenia (platelet count < 50 x 109/L) initiating treatment with avatrombopag or lusutrombopag or receiving a platelet transfusion in preparation for an elective invasive procedure during the study period.

Follow-up will start on the index date and end at the earliest of (1) 30 days after the date of the elective invasive procedure for patients who had a procedure

within 15 days of the end of treatment or 30 days after the last date of treatment for patients who did not have a procedure within 15 days after the end of treatment, (2) death, or (3) loss to 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

Hepatic impaired

Estimated number of subjects

30

Study design details

Setting

The study will be conducted in hospital or specialised outpatient settings (hospitals or specialty clinics) where patients with severe CLD and thrombocytopenia are treated in preparation for an elective invasive procedure. At each site, a study investigator will be identified to facilitate collection of patients’ data from medical records and, as needed, support the ethics committee submission as required by local policies. Access to data from both

hospital and outpatient/primary care settings would be desirable if postprocedure or posttreatment follow-up visits and laboratory test monitoring occur in a different healthcare setting (e.g., primary care).

Outcomes

The primary study outcome will be liver function measured through biochemical LFTs before and after the elective invasive procedure as recorded in each patient's medical record. The difference between LFT values measured before and after the procedure, i.e., preprocedure and postprocedure values, will be described according to the treatment received. The preprocedure LFT values used for this analysis will be the measurement before and closest to the procedure date, and the postprocedure LFT values will be the last one measured after the procedure within the defined follow-up window.

Secondary study outcomes will include (1) ascites and encephalopathy, which are considered significant complications of CLD to be assessed in the 3 treatment cohorts, and (2) ADRs attributed to avatrombopag. The frequency and severity of ascites and hepatic encephalopathy will be described before and after the procedure (and before and after treatment), according to the treatment received, based on information recorded in patients' medical records. Several clinical scales are available using various measures for grading ascites and hepatic encephalopathy that might be used in clinical practice. However, we propose to measure both ascites and encephalopathy following the classification of severity proposed in the Child-Pugh classification of cirrhosis (absent, slight, and moderate for ascites; none, grade 1 to 2, and grade 3 to 4 for encephalopathy). We anticipate that clinical use and actual recording of any measurement tool for ascites and encephalopathy in patients' records may be limited in routine clinical practice settings.

Data analysis plan

The analyses will be descriptive and will be performed separately for each exposure cohort. Patients initiating avatrombopag or lusutrombopag and patients undergoing platelet transfusions will be characterised in terms of demographic and clinical characteristics such as severity of CLD and thrombocytopenia, history of previous treatments with the same indication, comorbidities, use of comedications, and type of elective invasive procedure. For continuous variables, descriptive statistics will include the mean, SD, median, first and third quartiles, and minimum and maximum values. For categorical variables, descriptive statistics will include frequencies and percentages. For variables with missing data, the count and percentage of missingness will be reported for each variable. LFT values will be characterised by cohort and by period. Counts and proportions of patients that do not have LFTs recorded during follow-up will be calculated.

Data management

Data sources

Data sources (types)

Non-interventional study

Use of a Common Data Model (CDM)

CDM mapping

No

Data quality specifications

Check conformance

Yes

Check completeness

Yes

Check stability

Yes

Check logical consistency

Yes

Data characterisation

Data characterisation conducted

Not applicable