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

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## Administrative details

EU PAS number
EUPAS1000000310
Study ID
1000000310
DARWIN EU® study
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

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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  $< 50 \times 109$ /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

### **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 sources (types)** 

Non-interventional study

Use of a Common Data Model (CDM)

**CDM** mapping

No

Data quality specifications

Yes			
Check compl	eteness		
Yes			
Check stabili	ty		
Yes			

### **Check logical consistency**

**Check conformance** 

Yes

## Data characterisation

### **Data characterisation conducted**

Not applicable