Post-Authorization Safety Study (PASS): Investigating the occurrence of major bleedings in real life, in patients with atrial fibrillation (AF) treated with the combination of apixaban and dronedarone compared against patients on warfarin and dronedarone

First published: 14/11/2016

Last updated: 02/04/2024

Study Finalised

Administrative details

EU PAS number

EUPAS15449

Study ID

28182

DARWIN EU® study

No

Study countries

Sweden

Study description

Apixaban is used to prevent stroke (caused by blood clots in the brain) and blood clots in other organs in adults with atrial fibrillation (AF). In addition, Swedish patients with paroxysmal AF are frequently treated with dronedarone as a way to prevent the occurrence of attacks of AF. There are hospitals in Sweden using the combination of apixaban and dronedarone in patients while others have decided to continue using the older drug warfarin to prevent stroke in combination with dronedarone, until there is more data available of using apixaban in combination with dronedarone. This is a Swedish retrospective cohort study using national register linkage data. Data from three registers will be extracted and linked, a dispensed drug register, a patient register, and a cause of death register. The primary objective of this study is to compare the occurrence of major bleedings in patients with AF treated with the combination of apixaban and dronedarone versus the combination of warfarin and dronedarone. Other objectives include the occurrence of intracranial haemorrhage, gastrointestinal bleedings, and all-cause mortality.

Study status

Finalised

Research institutions and networks

Institutions

Friberg Research AB, Karolinska Institute

Sweden

First published: 19/03/2014

Last updated: 20/08/2024

Institution | Educational Institution | Hospital/Clinic/Other health care facility | Laboratory/Research/Testing facility

Contact details

Study institution contact

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Study contact

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Primary lead investigator

Angelo Modica

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 01/04/2016

Actual: 13/04/2016

Study start date

Planned: 16/01/2017

Actual: 30/03/2017

Data analysis start date
Planned: 01/11/2016

Actual: 30/03/2017

Date of final study report
Planned: 28/02/2017

Actual: 09/06/2017

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Pfizer

Study protocol

Study B0661075 Final Protocol 06-Apr-2016.pdf (2.89 MB)

PASS Protokoll studie B0661075_FINAL 2016-10-18_amended 2017-05-05.pdf (2.92 MB)

Regulatory

Was the study required by a regulatory body?

No

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

Not applicable

Methodological aspects

Study type

Study topic:

Disease /health condition

Human medicinal product

Study type:

Non-interventional study

Scope of the study:

Assessment of risk minimisation measure implementation or effectiveness

Data collection methods:

Secondary use of data

Main study objective:

To compare the occurrence of major bleedings in patients with atrial fibrillation (AF) treated with the combination of apixaban and dronedarone versus the combination of warfarin and dronedarone.

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

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

APIXABAN

DRONEDARONE

WARFARIN

Medical condition to be studied

Atrial fibrillation

Population studied

Short description of the study population

Patients with Atrial fibrillation (AF) treated with the combination of apixaban and dronedarone or the combination of warfarin and dronedarone.

Patients with following criteria were included:

1. Have ≥1 AF diagnosis registered in the Patient register
2. Age ≥18 years
3. Had a filled prescription for apixaban or warfarin during the identification period

Age groups

- Adults (18 to < 46 years)
- Adults (46 to < 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

Atrial fibrillation patients

Estimated number of subjects

3000

Study design details

Outcomes

The main bleeding endpoint is “major bleeding” defined as: - Any intracranial bleeding, or - Hospitalization with a bleeding diagnosis- Fatal bleed defined by a diagnosis in the Cause of Death register (underlying cause of death or first contributory cause of death), or a hospital discharge code of "4" indicating death during hospital stay in conjunction with a bleeding diagnosis. Secondary bleeding endpoints are:- Any hospitalization with a diagnosis of: - Intracranial bleed - Gastrointestinal bleed - Urogenital bleed - Other bleed - Contacts without overnight stay a bleeding diagnosis in principal or first secondary position.Death by any reason in the Cause of Death register.

Data analysis plan

Detailed methodology for summary and statistical analyses of data collected in this study will be documented in a Statistical Analysis Plan (SAP), which will be dated, filed and maintained by Pfizer. For descriptive analyses describing the two cohorts at baseline, Chi2 and t-tests will be used. For time dependent analyses, made in analogy with the intention to treat principle, censoring will be made at the event, death and end of observation period. For time dependent analyses made in analogy with the on treatment principle, additional censoring will be done when a patient no longer is on combination treatment. For the assessment of bleeding events during follow up, uni and multivariable Cox regression will be used. Introduction of covariates will be done stepwise. Propensity score matching will be used. All tests will be two-sided. Confidence intervals are 95% and p-values <0.05 will be considered as significant.

Documents

Study results

Apixadron NI PASS Study Report Final_shorter version to EU PAS Registry 2017-09-15_1-60.pdf (1.31 MB)

Study publications

Friberg L. Safety of apixaban in combination with dronedarone in patients with ...

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)

Other

Data sources (types), other

Swedish prescribed drug registerThe Swedish National Board of Health and Welfare's National Patient RegisterThe Swedish National Board of Health and Welfare's Cause of Death Register

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