Safety and Effectiveness of Rivaroxaban and Apixaban compared to warfarin in non-valvular atrial fibrillation patients in the routine clinical practice in the UK (SiERRA UK)

First published: 18/02/2019

Last updated: 10/07/2024

Study Finalised

Administrative details

EU PAS number

EUPAS28234

Study ID

43877

DARWIN EU® study

No

Study countries

United Kingdom

Study description

A recent cohort study in the UK showed that amongst patients with a history of non-valvular atrial fibrillation (NVAF) using non-vitamin K antagonists oral anti-coagulants (NOAC) without an apparent indication for dose reduction, the reduced dose was prescribed in approximately 30% of patients receiving apixaban and 10% of patients receiving rivaroxaban in the new users of both-agents. We hypothesize that patients dosed inappropriately could have higher rates of stroke and systemic embolism or bleeding. This population-based retrospective cohort study investigates safety and effectiveness in new users of rivaroxaban and apixaban versus new users of warfarin in a cohort of non-valvular atrial fibrillation (NVAF) patients from the THIN database (secondary data) in the UK, who received appropriately and inappropriately standard and reduced doses of each drug in accordance with the label. Safety and effectiveness of rivaroxaban, apixaban and warfarin are assessed based on the risk of intracranial hemorrhage and hemorrhagic strokes (safety) and ischemic stroke, systemic embolism and myocardial infarction (effectiveness). Secondary objectives comprise the assessment of the mentioned risks in subpopulations of patients with renal impairment or diabetes, mortality rates, and drug utilisation as well as patient characteristics before and after the first intracranial hemorrhage or ischemic stroke.

Study status

Finalised

Research institutions and networks

Institutions

Fundación Centro Español de Investigación Farmacoepidemiológica (CEIFE)

Spain

First published: 15/03/2010

Last updated: 15/02/2024

Institution | Not-for-profit | ENCePP partner

Contact details

Study institution contact

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Study contact

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Primary lead investigator

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Study timelines

Date when funding contract was signed

Actual: 03/01/2019

Study start date

Planned: 28/02/2019

Actual: 28/02/2019

Date of final study report

Planned: 31/07/2021

Actual: 22/09/2021

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Bayer AG

Study protocol

Study 20343_Study protocol_v1.0_2018-11-12_Redacted.pdf (997.49 KB)

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 type list

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

Drug utilisation

Effectiveness study (incl. comparative)

Data collection methods:

Secondary use of data

Main study objective:

Primary objectives are to assess the safety and effectiveness of rivaroxaban, apixaban and warfarin in patients with non-valvular atrial fibrillation (NVAF), who appropriately and inappropriately received standard and reduced doses of each NOAC in accordance with the label.

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Medicinal product name

ELIQUIS

XARELTO

Anatomical Therapeutic Chemical (ATC) code

(B01AA03) warfarin

warfarin

(B01AF01) rivaroxaban

rivaroxaban

(B01AF02) apixaban

apixaban

Medical condition to be studied

Ischaemic stroke

Population studied

Short description of the study population

In the UK, nearly all residents are registered in a general medical practice that uses a system of electronic medical records. THIN is a structured, de-identified electronic medical record database in the UK. The population included in THIN is representative of the UK as a whole in terms of age, sex and geographic distribution. THIN now collects data from around 500 practices, covering about 5% of the general population of the UK population (including practices in England, Wales, Scotland, and Northern Ireland).

Inclusion criteria

-Patients aged >=18 years of age

-NVAF

-New users of Rivaroxaban, Apixaban, Warfarin

-At least one year enrollment with the general practice (GP)

-One year since first health contact recorded in THIN prior to the first prescription of a study drug

Exclusion criteria

-Patients with other recent indications of OAC initiation as described in section 9.1.

-Individuals on more than one OAC on the start date.

-Users of Rivaroxaban apart from 15/20mg daily dose

-Users of Apixaban apart from 5/10mg daily dose

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

Renal impaired

Special population of interest, other

Ischaemic stroke

Estimated number of subjects

40.000

Study design details

Outcomes

Risk of intracranial hemorrhage / Risk of ischemic events, Risk of intracranial hemorrhage in NVAF-patients with renal impairment or diabetes / Risk of ischemic events in NVAF-patients with renal impairment or diabetes / All-cause mortality / Drug utilisation / Drug utilisation after first intracranial hemorrhage or ischemic stroke / Patient characteristics / Patient characteristics after first intracranial hemorrhage or ischemic stroke

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Data analysis plan

Descriptive statistics will be used to summarize the characteristics of the study population. 95% confidence intervals will be computed for descriptive variables. We will analyze safety, effectiveness, and all-cause mortality associated to use of the study drugs in three independent nested-case control analyses. These three analyses will include all cases identified in each follow-up (respectively: intracranial hemorrhage events, ischemic events, and deaths) and an analysis-specific group of controls. These control groups will comprise a random sample of members of all three cohorts, frequency-matched by age, sex and calendar year to each set of cases. Unconditional logistic regression models will be used to obtain odds ratio estimates of oral anticoagulant use adjusted by baseline variables described above and oral anticoagulant use at index date.

Documents

Study results

20343_EU-PASS_Abstract_Redacted.pdf (425.44 KB)

Study report

SIERRA Study Report SB_27 Sep 2021.pdf (4.16 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)

THIN® (The Health Improvement Network®)

Data source(s), other

THIN

Data sources (types)

Electronic healthcare records (EHR)

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

No