Real-world comparative effectiveness of stroke prevention in patients with atrial fibrillation treated with Factor Xa nonvitamin-K oral anticoagulants (NOACs) vs. Phenprocoumon (ReLoaDeD)

First published: 11/06/2018

Last updated: 02/07/2024

Study | Finalised

Administrative details

EU PAS number

EUPAS24270

Study ID

38250

DARWIN EU® study

No

Study countries

Germany

Study description

Existing real-world studies have provided evidence that novel oral anticoagulants (NOACs) in general and rivaroxaban in particular are more effective and at least as safe as warfarin in non-valvular atrial fibrillation (NVAF) patients with renal impairment. Nevertheless, it is known that clinicians often hesitate to prescribe NOACs to patients with even moderate renal impairment. Therefore, it is important to investigate effectiveness and safety of rivaroxaban and other NOACs compared to vitamin-K antagonists in NVAF patients with renal dysfunction in real life setting. The primary objectives of this study are to describe the risk of ischemic stroke (IS)/ systemic embolism (SE) and intracranial hemorrhage (ICH) in patients with non-valvular atrial fibrillation (NVAF) and renal impairment initiating treatment with individual NOACs (rivaroxaban, apixaban, edoxaban) compared to phenprocoumon and to assess the healthcare resource consumption and costs.

Study status

Finalised

Research institutions and networks

Institutions

Bayer AG

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Institution

Contact details

Study institution contact

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Study contact

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Primary lead investigator

Bayer Clinical Trials BAYER AG

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 30/05/2018

Actual: 30/05/2018

Study start date

Planned: 15/06/2018

Actual: 15/06/2018

Date of final study report

Planned: 17/08/2020

Actual: 31/07/2020

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Bayer AG

Study protocol

OS_Protocol_ReLoaDed_Germany_v1.0_01JUNE2018_ENCePP.pdf (1.15 MB)

20031_OS_Protocol_ReLoaDed_Germany_v3.0_clean_23SEP2019_blackened.pdf (5.92 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 type list

Study topic:

Disease /health condition

Human medicinal product

Study type:

Non-interventional study

Scope of the study:

Effectiveness study (incl. comparative)

Other

If ‘other’, further details on the scope of the study

Persistency

Data collection methods:

Secondary use of data

Main study objective:

The primary objectives of this study are to describe describe the risk of ischemic stroke (IS)/ systemic embolism (SE) and intracranial hemorrhage (ICH) in patients with non-valvular atrial fibrillation (NVAF) and renal impairment initiating treatment with individual NOACs (rivaroxaban, apixaban, edoxaban) compared to phenprocoumon and to assess the healthcare resource consumption and costs.

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

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

RIVAROXABAN

APIXABAN

EDOXABAN

PHENPROCOUMON

Medical condition to be studied

Arrhythmia

Population studied

Short description of the study population

Patients with non-valvular atrial fibrillation (NVAF) and renal impairment initiating treatment with individual NOACs (rivaroxaban, apixaban, edoxaban). The source population of this study will include all insured members of approximately 64 German statutory health insurances (SHIs) contributing data to the InGef database.

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

Renal impaired

Estimated number of subjects

90.000

Study design details

Outcomes

- Risk of Ischemic stroke (IS) / Systemic embolism(SE) (as combined endpoint and alone), recurrent IS/SE (as combined endpoint), severe IS and intracranial hemorrhage (ICH) in patients with non-valvular atrial fibrillation (NVAF) and renal impairment determined by inpatient claims based diagnoses- Healthcare resource consumption and costs, - Risk of fatal bleeding, Kidney failure, Acute kidney injury (AKI) and IS, SE, Severe IS and recurrent IS/SE in patients with NVAF determined by inpatient claims based diagnoses- Risk of recurrent hospitalizations (in general and for IS/SE)- Risk of treatment discontinuation in patients with NVAF determined by pharmacy ClaimsThis study is registered under NCT03563937 on Clinicaltrials.gov

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Data analysis plan

Cox proportional hazards regression models will be applied in in each treatment group compared to phenprocoumon (reference) to estimate crude and confounder adjusted hazard ratios (HRs) of the above mentioned outcomes as well as treatment discontinuation with accompanying 95% confidence intervals and p-values. Kaplan-Meier cumulative incidence plots will be generated to characterize risk of outcome events of interest over time.In a second step, we will use the stabilized inverse probability of treatment weighting (IPTW) approach based on the propensity score to adjust for potential confounding resulting from imbalances in the baseline characteristics of different treatment groups.In a third step, we will additionally conduct a propensity score matched analyses for each comparison. A 1:1 matching will be performed using the nearest-neighbor approach with a caliper of 0.2 without replacement.

Documents

Study results

20031_EU PAS Abstract_2020-11-11.pdf (441.5 KB)

Study report

20031_OS_Report_V1.0_2020-07-31_redacted.pdf (955.18 KB)

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)

Administrative healthcare records (e.g., claims)

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