Effectiveness and safety of non-vitamin K anticoagulants (NOACs) versus warfarin in frail patients with nonvalvular atrial fibrillation (AF): a nationwide cohort study

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Study Ongoing

Administrative details

EU PAS number

EUPAS39592

Study ID

41003

DARWIN EU® study

No

Study countries

Denmark

Study description

Growing evidence suggests that frail patients with AF are less likely to receive adequate oral anticoagulant therapy (OAC), although frail patients present higher thrombotic risk and mortality. Part of this care gap may be explained by the scarce data on the safety and effectiveness of NOACs versus warfarin in frail AF patients. Therefore, this study aimed (1) to present population characteristics and rates of effectiveness and safety outcomes among frail patients with non-valvular AF in Denmark according to OAC treatment regimen (no OAC, warfarin, or NOAC) and (2) to investigate the comparative effectiveness and safety of NOACs (Dabigatran, Rivaroxaban, and Apixaban, as a class) versus warfarin in a Danish nationwide cohort of frail patients with non-valvular AF. Non-interventional, observational cohort studies based on secondary data collection from Danish nationwide administrative databases will be used for the investigations. The source population comprise all residents of Denmark between 2013-2018. The study population will comprise all frail patients with an inpatient or outpatient primary or secondary discharge diagnosis of non-valvular AF. Frail patients will be identified using the ICD-10 based Hospital Frailty Risk Score (HFRS).

Study status

Ongoing

Research institutions and networks

Institutions

Aalborg University Hospital

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Institution

Thrombosis and Drug Research Unit

Contact details

Study institution contact

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Primary lead investigator

Anette Arbjerg Højen

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 01/02/2021

Actual: 19/04/2021

Study start date

Planned: 22/02/2021

Actual: 20/04/2021

Data analysis start date
Actual: 07/05/2021

Date of final study report
Planned: 30/09/2021

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Bayer AG, Berlin, Germany

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 type:

Non-interventional study

Scope of the study:

Assessment of risk minimisation measure implementation or effectiveness

Effectiveness study (incl. comparative)

Main study objective:

(1) To present population characteristics and rates of effectiveness and safety outcomes among frail patients with non-valvular atrial fibrillation in Denmark according to OAC treatment regimen (no OAC, warfarin, or NOAC). (2) To investigate the comparative effectiveness and safety of NOACs versus warfarin in a Danish nationwide cohort of frail patients with non-valvular atrial fibrillation.

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Anatomical Therapeutic Chemical (ATC) code

(B01AA03) warfarin

warfarin

(B01AE07) dabigatran etexilate

dabigatran etexilate

(B01AF01) rivaroxaban

rivaroxaban

(B01AF02) apixaban

apixaban

Medical condition to be studied

Atrial fibrillation

Additional medical condition(s)

All frail patients with an inpatient or outpatient primary or secondary discharge diagnosis of non-valvular atrial fibrillation. Frail patients will be identified using the Hospital Frailty Risk Score (HFRS). HFRS, a score utilizing ICD-codes, was developed to identify patients at low (HFRS <,5), intermediate (HFRS 5-15) and high risk (HFRS >15) of frailty.

Population studied

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)

Estimated number of subjects

30.000

Study design details

Outcomes

The primary effectiveness outcome is a diagnosis of stroke or systemic embolism. The primary safety outcome is major bleeding recorded as intracranial, gastro-intestinal, and major bleeding in various anatomical positions and reported in total as ‘any bleeding’. All-cause death was also included as an outcome.

Data analysis plan

Substudy 1: Patient baseline characteristics will be described for the overall study population and according to age (≥80 or <80). Cumulative incidence functions will be used to visualize how risk of outcomes evolve over time since AF diagnosis according to OAC regimen and age group using the Aalen–Johansen estimator assuming death as competing risk. The absolute risk of each study outcome according to OAC regimen and age group will be calculated at 1 year after AF diagnosis. Substudy 2: Patient baseline characteristics will be described for the study population according to baseline treatment group. To compare the risk of each endpoint among NOAC users with warfarin users reference), pooled logistic regression models will be used to estimate treatment effects by means of hazard ratios for the effectiveness and safety outcomes (both an ITT and PP approach). To allow an unbiased comparison of the treatment groups, we plan to use inverse probability of treatment weighting (IPTW).

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)

Danish registries (access/analysis)

Data source(s), other

Danish Registries (access/analysis)

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