Net clinical benefit of vitamin K antagonists versus direct oral anticoagulants for nonvalvular atrial fibrillation

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Study Planned

Administrative details

PURI

https://redirect.ema.europa.eu/resource/103473

EU PAS number

EUPAS103472

Study ID

103473

DARWIN EU® study

No

Study countries

☐ Spain

Study description

AIM: to assess the net clinical benefit (combined risk of suffering acute non-fatal atherothrombotic events, major bleeding or death) asociated with the exposure of vitamin K antagonists (VKA) or direct oral anticoagulants (DOAC) in patients with nonvalvular atrial fibrillation (NVAF). DESIGN: retrospective cohort study based on the information provided by BIFAP (Database for Pharmacoepidemiological Research in Primary Care). Subjects: adults with NVAF and at least one prescription of VKA and/or DOAC between 2010 and 2021. Primary composite outcome: risk of suffering acute non-fatal atherothrombotic events, major bleeding or death with VKA or DOAC. Primary safety outcome: risk of suffering major bleeding. Secondary result outcomes: risk of primary outcome combined for each active principle. Risk of each individual component of the composite primary outcome. DATA ANALYSIS: 1. Primary outcome incidences per 1000 person-years by sex and age group. 2. Outcome analysis through multilevel survival models. 3. Outcome analysis by subgroups: >74 years, naïve to anticoagulants, secondary prevention, chronic renal failure. 4. Sensitivity analysis of the primary composite outcome by: time of exposition to the anticoagulant, diary dosis of DOAC, level of effective anticoagulation with VKA, ischaemic and bleeding risk. 5. Analysis of the primary composite outcome for edoxaban by renal function. 6. Sensitivity analysis of major bleeding excluding traumatic major bleedings.

Study status

Planned

Research institutions and networks

Institutions

Servicio Navarro de Salud-Osasunbidea

Spain

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Institution | Hospital/Clinic/Other health care facility

Contact details

Study institution contact

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Study contact

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Primary lead investigator

Luis Carlos Saiz

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 01/01/2023

Study start date

Planned: 01/03/2023

Date of final study report

Planned: 01/03/2024

Sources of funding

- Other

More details on funding

Government of Navarre

Study protocol

Memoria NACOs BIFAP v4. 06-05-2022.pdf(1.17 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 type:

Non-interventional study

Scope of the study:

Assessment of risk minimisation measure implementation or effectiveness

Effectiveness study (incl. comparative)

Main study objective:

To assess the net clinical benefit (combined risk of suffering acute non-fatal atherothrombotic events, major bleeding or death) asociated with the exposure of vitamin K antagonists (VKA) or direct oral anticoagulants (DOAC) in patients with nonvalvular atrial fibrillation (NVAF).

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Anatomical Therapeutic Chemical (ATC) code

(B01AA03) warfarin

warfarin

(B01AA07) acenocoumarol

acenocoumarol

(B01AE07) dabigatran etexilate

dabigatran etexilate

(B01AF01) rivaroxaban

rivaroxaban

(B01AF02) apixaban

apixaban

(B01AF03) edoxaban

edoxaban

Medical condition to be studied

Atrial fibrillation

Transient ischaemic attack

Ischaemic stroke

Pulmonary embolism

Myocardial infarction

Additional medical condition(s)

Major bleeding

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

500000

Study design details

Outcomes

Primary composite outcome: risk of suffering acute non-fatal atherothrombotic events, major bleeding or death with VKA or DOAC. Primary safety outcome: risk of suffering major bleeding. - Risk of primary outcome combined for each active principle. Risk of each individual component of the composite primary outcome. - Risk of each individual component of the composite primary outcome.

Data analysis plan

1. Primary outcome incidences per 1000 person-years by sex and age group. 2. Outcome analysis through multilevel survival models. 3. Outcome analysis by subgroups: >74 years, naïve to anticoagulants, secondary prevention, chronic renal failure. 4. Sensitivity analysis of the primary composite outcome by: time of exposition to the anticoagulant, diary dosis of DOAC, level of effective anticoagulation with VKA, ischaemic and bleeding risk. 5. Analysis of the primary composite outcome for edoxaban by renal function. 6. Sensitivity analysis of major bleeding excluding traumatic major bleedings.

Data management

Data sources

Data sources (types)

Other

Data sources (types), other

Prospective patient-based data collection

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