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

**First published:** 09/02/2023

**Last updated:** 23/04/2024

Study Planned

## Administrative details

**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

**First published:** 01/02/2024

**Last updated:** 01/02/2024

Institution | Hospital/Clinic/Other health care facility

# Contact details

**Study institution contact**

Santi Arana saranab.md@gmail.com

Study contact

saranab.md@gmail.com

**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