Real-life anticoagulants comparative benefit-risk in nonvalvular atrial fibrillation (NVAF) in France (ENGEL 2)

First published: 04/04/2016

Last updated: 23/07/2024

Study Finalised

Administrative details

EU PAS number

EUPAS13017

Study ID

49819

DARWIN EU® study

No

Study countries

☐ France

Study description

The research question is to compare the 1-year and long-term benefit-risk between each of direct oral anticoagulant (DOAC) (Pradaxa®, Xarelto®) vs vitamin K (VKA) for new users in nonvalvular atrial fibrillation (NVAF). The main objective is to compare the 1-year risk of major bleeding, stroke and systemic embolism (SSE) (prior named “arterial thrombotic events” as in the protocol and the study report “One-year of follow-up”), myocardial infarction (MI) and death for each DOAC (dabigatran, rivaroxaban) vs VKA in NVAF during drug exposure. The secondary objectives are to compare healthcare resources use and their related costs during drug exposure on the 1-year of follow-up, and the long-term risk (2 and 3-year) of the same outcomes for each DOAC vs VKA and for dabigatran vs rivaroxaban according to the initial DOAC doses. This is a cohort study in the French natiowide claims database including new users of DOAC or VKA in NVAF in 2013 with a follow-up until 31 December 2016, and 3 years history. The index date will be that of the first dispensing of DOAC or VKA in 2013. Data will be extracted from 2010 to 2016. Outcomes analysis will be performed during drug exposure for matched patients on high-dimensional propensity score (hdPS), and all patients with hdPS adjustment.

Study status

Finalised

Research institutions and networks

Institutions

Bordeaux PharmacoEpi, University of Bordeaux

France

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Institution | Educational Institution | Hospital/Clinic/Other health care facility | Not-for-profit | ENCePP partner

Contact details

Study institution contact

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Study contact

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Primary lead investigator

Nicholas Moore

Primary lead investigator

Study timelines

Date when funding contract was signed

Actual: 19/12/2014

Study start date

Actual: 05/04/2016

Data analysis start date

Actual: 25/04/2016

Date of interim report, if expected
Actual: 25/10/2018

Date of final study report
Planned: 31/10/2019

Actual: 20/12/2019

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Boehringer Ingelheim France

Regulatory

Was the study required by a regulatory body?

Yes

Is the study required by a Risk Management Plan (RMP)?

Not applicable

Other study registration identification numbers and links

ClinicalTrial.gov: NCT02785354

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

Disease epidemiology

Drug utilisation

Effectiveness study (incl. comparative)

Data collection methods:

Secondary use of data

Main study objective:

The main objective is to compare the one-year risk of major bleeding, risk of stroke and systemic embolism (SSE), risk of myocardial infarction (MI) and risk of death for each DOAC (Pradaxa®, Xarelto®) versus VKA in NVAF during drug exposure.

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Anatomical Therapeutic Chemical (ATC) code

(B01AA) Vitamin K antagonists

Vitamin K antagonists

(B01AE07) dabigatran etexilate

dabigatran etexilate

(B01AF01) rivaroxaban

rivaroxaban

Medical condition to be studied

Atrial fibrillation

Population studied

Short description of the study population

Participants with nonvalvular atrial fibrillation treated with direct oral anticoagulants (DOAC) (Pradaxa®, Xarelto®) and vitamin K (VKA) utilizing French nationwide claims database identified from 2013 to 31 December 2016.

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

Special population of interest, other

Patients with nonvalvular atrial fibrillation

Estimated number of subjects

150000

Study design details

Outcomes

Clinically relevant bleeding (CRB) as a hospitalisation with primary diagnosis of haemorrhagic stroke, or other critical organ or site bleeding, or other bleedings, SSE as a hospitalisation of ischemic/undefined stroke or systemic arterial embolism, Acute coronary syndrome (ACS) as a hospitalisation of MI or unstable angina, All-cause of death, Composite criterion of CRB/SSE/ACS/death. To compare the long-term risk (2-year and 3-year) of outcomes for each DOAC (Pradaxa®, Xarelto®) versus VKA and for Pradaxa® versus Xarelto® according to the initial dose (standard or reduced dose), drugs use (exposure duration, number of dispensations, medication possession ratio, withdrawal and switch), Healthcare resources use and their related costs on the 1-year of follow-up.

Data analysis plan

Statistical analysis will be carried out according to a documented and approved Statistical Analysis Plan (SAP). The SAP describes statistical analysis as foreseen at the time of planning study. Statistical analysis will be performed after database lock using SAS® software. Blind double programming will be used for the main outcome measures.Primary outcomes will be analysed using survival methods: Kaplan Meier estimate and cumulative incidence function estimate for cumulative incidence of clinical outcomes, Cox proportional hazard risk model and Fine and Gray model to compare incidence of each outcome between treatment groups, for hdPS matched patients, and all patients with hdPS

adjustment.The analysis of healthcare costs during the drug exposure will be performed as an “intent-to-treat” analysis on the 1-year follow-up period. Costs will be estimated according to treatment group from national health insurance and collective perspectives.

Documents

Study publications

Blin P, Dureau-Pournin C, Cottin Y, Bénichou J, Mismetti P, Abouelfath A, Lassa…

Blin P, Dureau-Pournin C, Bénichou J, Cottin Y, Mismetti P, Abouelfath A, Lassa…

Blin P, Dureau-Pournin C, Cottin Y, Bénichou J, Mismetti P, Abouelfath A, Lassa…

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