# Association between use of direct oral anticoagulants (DOACs) and increased risk of interstitial lung disease

**First published:** 08/05/2024

**Last updated:** 06/10/2025

Study Finalised

## Administrative details

**EU PAS number**

EUPAS1000000133

**Study ID**

1000000133

**DARWIN EU® study**

No

**Study countries**

- [ ] Germany
- [ ] Italy
- [ ] Spain
- [ ] United Kingdom

**Study description**

New user active comparator cohort study examining the association between direct oral anticoagulant (DOAC) use and incidence of ILD compared to users of vitamin K antagonists among people with atrial fibrillation and venous thromboembolism.

**Study status**

Finalised

# Research institutions and networks

## Institutions

### European Medicines Agency (EMA)

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

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Institution

# Contact details

**Study institution contact**

Daniel Morales daniel.morales@ema.europa.eu

Study contact

daniel.morales@ema.europa.eu

**Primary lead investigator**

Daniel Morales

Primary lead investigator

## Study timelines

**Date when funding contract was signed**
Planned: 24/03/2023

**Study start date**
Planned: 24/03/2023

Actual: 24/03/2023

**Date of final study report**
Planned: 01/03/2024

Actual: 11/07/2024

## Sources of funding

- EMA

## More details on funding

EMA in house resources

## Study protocol

PROTOCOL-DOAC-ILD.pdf (225.76 KB)

## Regulatory

**Was the study required by a regulatory body?**

Yes

**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:**

Safety study (incl. comparative)

**Data collection methods:**

No individual level data collected for the purpose of the study

**Study design:**

New user active comparator cohort study

**Main study objective:**

Assess whether use of factor Xa (FXa) inhibitors (edoxaban, apixaban and rivaroxaban) or direct thrombin inhibitor (dabigatran) associated with an increased risk of interstitial lung disease (ILD) when compared with patients treated with vitamin K antagonists (VKA), among patients with Atrial Fibrillation (AF), Deep Vein Thrombosis (DVT) and Pulmonary Embolism (PE).

## Study Design

**Non-interventional study design**

Cohort

## Study drug and medical condition

**Medicinal product name, other**

DOACs and vitamin-k antagonists

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

APIXABAN

DABIGATRAN

EDOXABAN

RIVAROXABAN

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**Anatomical Therapeutic Chemical (ATC) code**

(B01) ANTITHROMBOTIC AGENTS

ANTITHROMBOTIC AGENTS

(B01AE07) dabigatran etexilate

dabigatran etexilate

(B01AF01) rivaroxaban

rivaroxaban

(B01AF02) apixaban

apixaban

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**Medical condition to be studied**

Interstitial lung disease

# Population studied

**Short description of the study population**

People with atrial fibrillation

People with venous thromboembolism

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**Age groups**

- **Adult and elderly population (≥18 years)**
  - Adults (18 to < 65 years)
    - Adults (18 to < 46 years)
    - Adults (46 to < 65 years)
  - Elderly (≥ 65 years)
    - Adults (65 to < 75 years)
    - Adults (75 to < 85 years)
    - Adults (85 years and over)

# Study design details

**Setting**

Primary care data sources

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**Comparators**

Vitamin-K antagonists

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**Outcomes**

Interstitial lung disease (ILD)

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**Data analysis plan**

Propensity score matched cohort study with use of propensity score diagnostics to assess adequate confounding control.
Use of Cox regression to estimate hazard ratios for incident ILD among the target cohort (DOAC users) and control cohort (VKA users).

## Documents

**Study report**

DOACs and ILD Study Report.pdf (1.52 MB)

# 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)**

IQVIA Medical Research Data - OMOP

IQVIA Disease Analyzer Germany

THIN® (The Health Improvement Network®)

**Data source(s), other**

The Health Improvement Network (THIN®) Italy

The Health Improvement Network (THIN®) Spain

## Use of a Common Data Model (CDM)

**CDM mapping**

Yes

## Data quality specifications

**Check conformance**

Unknown

**Check completeness**

Unknown

**Check stability**

Unknown

**Check logical consistency**

Unknown

## Data characterisation

**Data characterisation conducted**

Yes

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**Data characterisation moment**

after data extraction

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**Data characterisation details**

Inspection of code frequencies, comparison with expected incidence.