Drug-drug interactions between dicloxacillin/flucloxacillin and DOACs

First published: 16/11/2020

Last updated: 23/04/2024

Study Planned

Administrative details

EU PAS number

EUPAS38060

Study ID

38061

DARWIN EU® study

No

Study countries

Denmark

Netherlands

Study description

Direct oral anticoagulants (DOACs) are a group of anticoagulants that include dabigatran, rivaroxaban, apixaban, and edoxaban. They are used to reduce the

risk of stroke and systemic embolism (SE) in patients with non-valvular atrial fibrillation (NVAF) and as prophylaxis against deep vein thrombosis (DVT) and pulmonary embolism (PE). They were developed as alternatives to vitamin-K antagonists (VKA) such as warfarin, and studies have shown that they are just as safe and effective in prevention of stroke in patients with NVAF. DOACs are more convenient than warfarin due to wider therapeutic range meaning that routine blood tests are not required. Previous studies have investigated co-administration of dicloxacillin and warfarin, which leads to higher risk of strokes and SE. Wether or not a similar association between DOACs and dicloxacillin/flucloxacillin exists, has never been assessed. With this cohort study we aim to investigate if co-administration of dicloxacillin/flucloxacillin leads to increased risk of strokes or SE in patients using DOACs.

Study status

Planned

Research institutions and networks

Institutions

University of Southern Denmark (SDU)

Denmark

First published: 01/02/2024

Last updated: 27/03/2024

Institution | Educational Institution

Division of Pharmacoepidemiology & Clinical Pharmacology (PECP), Utrecht Institute for Pharmaceutical Sciences (UIPS), Utrecht University

Netherlands

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Institution | Educational Institution | ENCePP partner

Pharmacoepi center, University of Southern Denmark

Denmark

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Institution | Educational Institution | ENCePP partner

Contact details

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Study contact

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Primary lead investigator

Anton Pottegård

Primary lead investigator

Study timelines

Date when funding contract was signed
Planned: 13/11/2020

Study start date
Planned: 01/01/2021

Date of final study report
Planned: 02/08/2021

Sources of funding

- Other

More details on funding

None

Study protocol

Protocol-EU-PAS.pdf (717.17 KB)

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

Main study objective:

To investigate if co-administration of dicloxacillin/flucloxacillin leads to increased risk of strokes or systemic embolism in patients using DOACs

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Anatomical Therapeutic Chemical (ATC) code

(B01AE07) dabigatran etexilate

dabigatran etexilate

(B01AF01) rivaroxaban

rivaroxaban

(B01AF02) apixaban

apixaban

(B01AF03) edoxaban

edoxaban

(J01CE02) phenoxymethylpenicillin

phenoxymethylpenicillin

(J01CF01) dicloxacillin

dicloxacillin

(J01CF05) flucloxacillin

flucloxacillin

Medical condition to be studied

Ischaemic stroke

Embolism arterial

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)

Special population of interest

Hepatic impaired

Immunocompromised

Pregnant women

Renal impaired

Estimated number of subjects

200000

Study design details

Outcomes

To estimated the hazard ratios (HR) for the four DOACs (dabigatran, rivaroxaban, apixaban, edoxaban) with a 95% CI comparing the group treated with dicloxacillin/flucloxacillin vs. group treated with phenoxymethylpenicillin, and vs. no treatment with antibiotics. - To calculate number needed to treat for one additional patient to be harmed (NNTH) - Performing subgroup analysis (age, sex, or intake of dicloxacillin or flucloxacillin) - Extend follow-up period from 5-20 days to 5-30 days - Analyze if indication for DOAC treatment had any influence - Subgroup analysis excluding specific patient groups

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Data analysis plan

Risks, hazard ratio using Cox regression, odds ratio using conditional logistic regression

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)

PHARMO Data Network

Data source(s), other

Danish Registries (access/analysis), PHARMO Data Network

Data sources (types)

Administrative healthcare records (e.g., claims)

Drug dispensing/prescription data

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