

Study of direct oral anticoagulants (medications that help prevent blood clots) in lung transplant patients

Submission date 27/11/2023	Recruitment status No longer recruiting	<input type="checkbox"/> Prospectively registered
Registration date 11/07/2024	Overall study status Completed	<input type="checkbox"/> Protocol
Last Edited 11/07/2024	Condition category Haematological Disorders	<input type="checkbox"/> Statistical analysis plan
		<input type="checkbox"/> Results
		<input type="checkbox"/> Individual participant data
		<input type="checkbox"/> Record updated in last year

Plain English summary of protocol

Background and study aims.

Direct oral anticoagulants (DOAC) have transformed the landscape of oral anticoagulant therapy for almost a decade. They are increasingly used in clinical practice, mainly for stroke prevention in atrial fibrillation and the treatment of venous thrombosis.

Venous thrombosis is a common complication after lung transplantation and 25% of lung transplant patients also develop atrial flutter or fibrillation. Oral anticoagulation is therefore often necessary in these patients.

DOAC pharmacology may be affected by physiological changes that occur after lung transplantation, and they are subject to some interactions with drugs given to prevent rejection, which have been little studied. This raises questions about the optimal management of anticoagulant therapy in lung transplant patients, which we are regularly facing in our clinical practice.

The main objective of the study will be to describe the pharmacology of DOAC in lung transplant patients. A secondary objective will be to evaluate clinical outcomes (bleeding and thrombosis) during a 12-months follow-up. Taken together, these data will answer the question: "How best can we safely use DOAC in lung transplant patients?".

Who can participate?

Any adult lung transplant patient taking a direct oral anticoagulant (apixaban, dabigatran etexilate, edoxaban, or rivaroxaban) for (i) the treatment and secondary prevention of VTE or (ii) stroke prevention in NVAF may participate. However, they must be able to come to the CHU UCL Namur for 24 hours to have the necessary blood samples taken.

What does the study involve?

This study involves taking several blood samples over 24 hours to establish the pharmacological profile of DOACs in lung transplant recipients.

What are the possible benefits and risks of participating?

This is an observational study with no direct benefit to participants. Improved knowledge of the pharmacology of DOAC in lung transplant patients will help to improve their use in this

population in the future.

The potential harm to participants is no different from that of a conventional blood collection (e.g., hematoma or transient pain at the puncture site).

Where is the study run from?

CHU UCL Namur in Belgium.

When is the study starting and how long is it expected to run for?

August 2021 to November 2025.

Who is funding the study?

Fonds de la Recherche Scientifique - FNRS (Belgium).

Who is the main contact?

Dr Michael Hardy, michael.hardy@uclouvain.be

Contact information

Type(s)

Public, Scientific, Principal investigator

Contact name

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Additional identifiers

Clinical Trials Information System (CTIS)

Nil known

Protocol serial number

MH 001

Study information

Scientific Title

Pharmacokinetics and pharmacodynamics of direct oral anticoagulants in lung transplant patients: a prospective study

Acronym

ATRAP

Study objectives

The main objective of the study is to describe the pharmacokinetic and pharmacodynamic profile of direct oral anticoagulants (DOAC) in lung transplant patients. A secondary objective is to evaluate clinical outcomes (bleeding and thromboembolic events) during follow-up.

Taken together, these data will answer the question: "How best can we safely use DOAC in lung transplant patients?".

Ethics approval required

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Ethics approval(s)

approved 01/03/2022, Ethics Committee of the CHU UCL Namur (Avenue Docteur G. Thérassé, 1, Yvoir, 5530, Belgium; +32 81 42 21 11; comite.ethique.g@chuclnamur.uclouvain.be), ref: B0392022000001

Study design

Single-centre prospective observational cohort study with a 12-month follow-up period.

Primary study design

Observational

Study type(s)

Treatment, Safety, Efficacy

Health condition(s) or problem(s) studied

Direct oral anticoagulant use in lung transplant patients

Interventions

Pharmacokinetic study

Apixaban, edoxaban and rivaroxaban plasma levels will be estimated using a calibrated chromogenic anti-Xa assay, the STA®-Liquid anti-Xa (Diagnostica Stago, Asnières, France).

Dabigatran plasma levels will be estimated with an ecarin-based assay (STA®-ECA II, Diagnostica Stago).

Pharmacodynamic study:

Thrombin generation will be assessed using the ST Genesis analyser and STGDrugScreen® and STGThromboScreen® reagent (Diagnostica Stago®, Asnières, France).

Thrombin generation at time 0 will also be measured with ThromboScreen® reagent after DOAC removal using the DOAC-Stop® system (Haematex, Sydney, Australia) to assess the thrombin generation underlying DOAC.

Pharmacogenetic study:

The single nucleotide polymorphism (SNP) CYP3A5*3 (rs776746), known to influence tacrolimus dose requirement, will be screened.

Intervention Type

Other

Primary outcome(s)

Pharmacokinetic study:

Concentration-time data will be analyzed using non-compartmental PK to derive PK parameters. DOAC concentrations will be measured in the morning just before DOAC intake (T0), then 1, 2, 3, 4, 6 and 8 hours after DOAC intake. Whenever possible, DOAC concentrations will also be measured the next morning just before DOAC intake (T24) to assess inter-individual variability. Apixaban, edoxaban and rivaroxaban plasma concentrations will be estimated using a calibrated chromogenic anti-Xa assay, the STA®-Liquid anti-Xa (Diagnostica Stago, Asnières, France), using dedicated calibrators from Stago. Dabigatran plasma levels will be estimated with an ecarin-based assay (STA®-ECA II, Diagnostica Stago).

1. Peak concentration (C_{max})
2. Time to reach peak concentration (T_{max})
3. Area under the concentration curve (AUC) extrapolated to infinity
4. The terminal elimination half-life
5. The apparent volume of distribution (V_d/F)
6. The apparent clearance (CL/F).

Pharmacodynamic study:

Thrombin generation will be measured at trough (just before DOAC intake) and at peak (3 hours after DOAC intake) on the ST-Genesis system with STG-DrugScreen and STG-ThromboScreen reagent and the following parameters will be evaluated:

1. Lag time
2. Peak height
3. Time to peak
4. Endogenous thrombin potential (ETP)
5. Velocity index

Key secondary outcome(s)

Clinical outcomes during the 12-month follow-up period (or until the end of the study, depending on which comes first) measured using patient records:

1. Any documented thromboembolic event
2. Any documented bleeding event

Completion date

02/11/2025

Eligibility

Key inclusion criteria

1. ≥ 18 years old;
2. Medical history of lung transplant;
3. DOAC prescription (apixaban, dabigatran etexilate, edoxaban or rivaroxaban) for (i) the treatment and secondary prevention of VTE or (ii) stroke prevention in NVAF.
4. DOAC taken for at least three days.
5. Both inpatients and outpatients are considered for inclusion.

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Adult

Lower age limit

18 years

Upper age limit

99 years

Sex

All

Key exclusion criteria

Patient hospitalized in intensive care unit at inclusion.

Date of first enrolment

02/11/2022

Date of final enrolment

02/11/2024

Locations

Countries of recruitment

Belgium

Study participating centre

CHU UCL Namur

Avenue Docteur G Thérassé, 1

Yvoir

Belgium

5530

Sponsor information

Organisation

CHU UCL Namur

ROR

<https://ror.org/00ntbvq76>

Funder(s)

Funder type

Government

Funder Name

Fonds De La Recherche Scientifique - FNRS

Alternative Name(s)

Belgian National Fund for Scientific Research, F.R.S. - FNRS, Fund for Scientific Research - FNRS, Fund for Scientific Research (F.R.S.-FNRS), FNRS

Funding Body Type

Government organisation

Funding Body Subtype

Local government

Location

Belgium

Results and Publications

Individual participant data (IPD) sharing plan

Storing in a publicly available repository.

IPD sharing plan summary

Stored in publicly available repository