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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

Registration date
11/07/2024

Overall study status
Completed

Last Edited
11/07/2024

Condition category
Haematological Disorders

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] 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

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Additional identifiers

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
Ethics approval required

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

Primary study design
Observational

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

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, Asnière, 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 Genesia analyser and STGDrugScreen® and STGThromboScreen® reagent (Diagnostica Stago®, Asnière, France).
Thrombin generation at time 0 will also be measured withThromboScreen® 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, Asnière, 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 (Cmax)
2. Time to reach peak concentration (Tmax)
3. Area under the concentration curve (AUC) extrapolated to infinity
4. The terminal elimination half-life
5. The apparent volume of distribution (Vd/F)
6. The apparent clearance (CL/F).

Pharmacodynamic study:
Thrombin generation will be measured at through (just before DOAC intake) and at peak (3 hours after DOAC intake) on the ST-Genesia 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 Thérasse, 1
Yvoir
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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)
Fund for Scientific Research (F.R.S.–FNRS), F.R.S. - FNRS, Fund for Scientific Research - FNRS, Belgian National Fund for Scientific Research, 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