PRESTIGE-AF

PREVENTION OF STROKE IN INTRACEREBRAL HAEMORRHAGE SURVIVORS WITH ATRIAL FIBRILLATION

Predictive Modelling of Risk Substudy

Personal Legal Representative Information Sheet and Consent Form

Chief Investigator: Prof Roland Veltkamp

WE INVITE YOU TO CONSIDER A SUBSTUDY OF PRESTIGE-AF

You are being asked to consider this substudy on behalf of a patient, who is your relative, partner or close friend, because they are unable to make the decision for themselves.

- You are free to decide if you wish to make this decision or not.
- You are being asked to consider what the patient would want and should set aside your own personal views when making this decision.
- Before you decide whether to enrol the patient into the study , it is important for you to understand why the research is being done and what it will involve.
- Please take time to read the following information carefully. Discuss it with the patient if this is appropriate and with other relatives or friends.
- You are free to decide whether the patient should take part in this trial. If you choose for the patient not to take part, this will not affect the care they get from their doctors or their participation in the main PRESTIGE-AF Study.
- If you do decide for the patient to take part, you can withdraw them from the trial at any time without them being disadvantaged and without giving a reason.

- If in the future, the patient regains capacity to make their own decisions, they will be given all of the information and asked to decide if they want to take part or not. They will be free to withdraw from the trial and can do so without disadvantage.
- Ask us if there is anything that is not clear or if you would like more information.

BACKGROUND

The PRESTIGE-AF Study offers a unique opportunity to develop tools for the prediction of individual risk of subsequent ischaemic or haemorrhagic stroke in patients with atrial fibrillation (AF), who have had a previous intracerebral haemorrhage (ICH) or bleeding within their brain. We will explore risk prediction using biomarkers, genetic variants, information from clinical data and brain imaging.

Biomarkers are molecules that can be measured in blood, giving doctors some information about their patient's status. Some examples of biomarkers are cholesterol and blood sugar levels. In addition, small variations in our genetic material (DNA, or desoxyribonucleic acid) are also related to specific diseases or a different response to therapeutic interventions.

In this substudy, we aim to search for blood biomarkers and genetic variants related to the risk of suffering a new ischaemic stroke, ICH, or related to the response to anticoagulant medications.

Within this substudy, we will also assess the additive value of the information from blood biomarkers and genetic variants for predicting future events in addition to clinical information as well as results from brain imaging routinely collected during the patient's treatment at hospital.

WHAT IS INVOLVED?

The only additional procedure for this substudy is a single collection of a blood sample which can be taken at the patient's PRESTIGE-AF Study visit at the same time as their main study blood test.

If you decide to enrol the patient into the substudy up to 5 tubes of blood will be collected (up to 34 ml) which is about 7 teaspoons.

Blood based biomarkers change over time, therefore we would like to take their sample at the start of the study so that we have a true baseline measure. If for any reason you do not want them to have the sample taken during screening or at the enrolment visit, we can also take it at their one month follow up visit.

There are some situations where we can only take blood for the genetics part of the substudy. For example, if the research site does not have correct storage for biomarker samples or if the patient is having your sample taken after the one month visit, (because their biomarkers may have changed). If they take part in the genetic component only, 3 tubes of blood will be drawn (18 ml).

If for any reason you do not think the patient would want to provide a genetic sample, they can take part in the biomarkers part of the substudy only, this will be 4 tubes of blood (28ml).

WHAT WILL HAPPEN TO THE SAMPLES

The patient's sample will be labelled with your PRESTIGE-AF participant number with no identifiable information about them. Blood samples will be held securely at the hospital until they are transferred to the PRESTIGE-AF biobank at the Neurovascular Research Laboratory, Vall d'Hebron Institute of Research (VHIR), in Barcelona, Spain. All transportation of samples will be made securely and in accordance with UK and EU guidance.

Their samples will be analysed to identify biomarkers and genetic variants related to the risk of stroke or to the response to anticoagulant medications. For the biomarker component, blood based biomarkers will be measured at VHIR. For the genetic component their samples will be transferred to a DNA database (DNA

Banco Nacional, in Salamanca, Spain) where DNA extraction will be performed. Then, they will be shipped to a genomic platform (which may be outside of the UK and EU) where genotyping will take place. (*genotyping* is the process of determining the genetic make-up of an individual by examining the DNA code in certain locations using biological assays).

If you consent to the patient taking part in future research, any remaining blood sample left, after the analysis is complete, will be kept in the Neurovascular Research Laboratory in Barcelona to be used in future studies that may include genetic analysis.

PREDICTIVE MODELLING ANALYSIS

We will analyse data collected in the main PRESTIGE-AF study to look for potential associations. This research will be undertaken by the Institute of Clinical Epidemiology and Biometry at the University of Wuerzburg, Germany. We will also assess the additional effect of adding information from blood biomarkers, genetic variants and neuroimaging information to the routine clinical information for identifying the best models to forecast new ischaemic stroke or ICH in future ICH patients.

POTENTIAL BENEFITS OF THE SUBSTUDY

There are no potential benefits for the patient for taking part in this substudy. However, if we can identify new biomarkers and genetic variants as well as new clinical and brain imaging information related to the response to oral anticoagulants, these results will be useful in the future to reduce the risk of suffering an ischaemic stroke or an ICH in patients with atrial fibrillation (AF), as well as to prevent side effects related with anticoagulants.

If you decide to enrol them into the substudy, the analysis of biomarkers from biological samples might reveal information relevant to their health. In accordance with current legislation, the patient has the right to be informed of the data obtained in the course of study.

At the end of the study, we will send a report with the results of the biomarkers analysed to your doctor. If the patient prefers not to be informed, their decision will be respected. However, when this information, according to the judgment of the responsible doctor, is necessary to prevent a serious injury to their health or that of their biological family, a close family member or a representative will be informed.

We will not give the patient any individual results from the genetic analyses that will be performed. We currently consider that outside of a clinical setting (in the context of genetic diagnosis) reporting of genetic results is of questionable value, and might even be harmful, for instance by causing undue alarm. We will however continuously monitor the situation regarding the way genetic results are presented, as scientific progress is made, and, if necessary, we will contact the local regulatory ethics committee for advice. Please note that if any change in strategy regarding reporting of genetic results was considered in the future, we would again seek informed consent from either you or the patient (if they have regained the ability to make the decision).

POTENTIAL RISK OF THE SUBSTUDY

There are no serious risks deriving from the patient's participation in this substudy. Blood sampling can cause a burning sensation at the location where the needle is inserted into the skin and cause a small bruise. In very few cases a mild local infection that disappears within a few days can develop. More rarely, people may experience dizziness at the time of blood taking.

WHAT IF SOMETHING GOES WRONG?

Imperial College London holds insurance policies which apply to this study. If the patient experiences harm or injury as a result of taking part in this study, they will be eligible to claim compensation without having to prove that Imperial College is at fault. This does not affect their legal rights to seek compensation.

If they are harmed due to someone's negligence, then they may have grounds for a legal action. Regardless of this, if you or they wish to complain, or have any concerns about any aspect of the way the patient has been treated during the course of this study then the investigator should immediately be informed *(prestige-af@imperial.ac.uk)* The normal National Health Service mechanisms are also available to you and the patient. If you or the patient are still not satisfied with the response, you may contact the Imperial College, Research Governance and Integrity Team.

HOW WILL WE USE INFORMATION ABOUT YOU

Imperial College London is the sponsor for this study and will act as the data controller for this study. This means that we are responsible for looking after the patient's information and using it properly. Imperial College London will keep their personal data for:

- 15 years after the study has finished in relation to data subject consent forms
- 15 years after the study has completed in relation to primary research data.

We will need to use information from the patient, their medical records, their GP or other healthcare providers for this research project.

This information will include:

- The patient's name
- Their contact details
- Their NHS Number
- Health information

People will use this information to do the research or to check the patient's records to make sure that the research is being done properly.

People who do not need to know who the patient is will not be able to see their name or contact details. Their data will have a code number instead.

We will keep all information about the patient safe and secure.

Some of their information will be sent to countries in the European Union. They must follow our rules about keeping the patient's information safe.

Once we have finished the study, we will keep some of the data so we can check the results. We will write our reports in a way that no-one can work out that the patient took part in the study.

LEGAL BASIS

As a university we use personally-identifiable information to conduct research to improve health, care and services. As a publicly-funded organisation, we have to ensure that it is in the public interest when we use personally-identifiable information from people who have agreed to take part in research. This means that when you agree for the patient to take part in a research study, we will use their data in the ways needed to conduct and analyse the research study.

Health and care research should serve the public interest, which means that we have to demonstrate that our research serves the interests of society as a whole. We do this by following the UK Policy Framework for Health and Social Care Research.

INTERNATIONAL TRANSFERS

There may be a requirement to transfer information to countries outside the European Economic Area (for example, to a research partner). Where this information contains the patient's personal data, Imperial College London will ensure that it is transferred in accordance with data protection legislation. If the data is transferred to a country which is not subject to a European Commission (EC) adequacy decision in respect of its data protection standards, Imperial College London will enter into a data sharing agreement with the recipient

organisation that incorporates EC approved standard contractual clauses that safeguard how the patient's personal data is processed.

SHARING YOUR INFORMATION WITH OTHERS

For the purposes referred to in this privacy notice and relying on the bases for processing as set out above, we will share the patient's personal data with certain third parties.

- Other College employees, agents, contractors and service providers (for example, suppliers of printing and mailing services, email communication services or web services, or suppliers who help us carry out any of the activities described above). Our third party service providers are required to enter into data processing agreements with us. We only permit them to process the patient's personal data for specified purposes and in accordance with our policies.

- This clinical trial is part of a large European Union funded project. We are working with the following research collaborators across Europe who are all specialists in different fields. In order to answer the questions of our research we are all working together and therefore the patient's data will be shared with:

    - University Hospital Würzburg, Germany
    - Julius-Maximilans Universitaet Würzburg, Germany
    - Medizinische Universitaet Graz, Austria
    - Kings College London, UK
    - Fundacio Hospital Universitari Vall d'Hebron- Institut de Recerca, Spain
    - Universite de Bordeaux, France
    - Azienda Ospedaliera di Perugia, Italy
    - Region Nordjylland (North Denmark Region) , Denmark
    - Stroke Alliance for Europe, Belgium
    - Heidelberg University Hospital, Germany
    - University of Liverpool, UK

If you would like to find out more about the PRESTIGE-AF Project and what each partner does there is more information on our website www.prestige-af.org

WHAT ARE YOUR CHOICES ABOUT HOW YOUR INFORMATION IS USED

The patient can stop being part of the study at any time, without giving a reason, but we will keep information about them that we already have.

- We need to manage their records in specific ways for the research to be reliable. This means that we won't be able to let you or the patient see or change the data we hold about them.

- If you agree to the patient take part in this study, you will have the option for them to take part in future research using their data saved from this study.

WHERE CAN YOU FIND OUT MORE ABOUT HOW YOUR INFORMATION IS USED

You can find out more about how we use the patient's information

- at www.hra.nhs.uk/information-about-patients/
- by asking one of the research team
- by sending an email to hello@prestige-af.org
- www.prestige-af.org/privacy-cookie-policy/

COMPLAINTS

If you, or the patient, wish to raise a complaint on how we have handled their personal data, please contact Imperial College London's Data Protection Officer via:

- email at dpo@imperial.ac.uk
- telephone on 020 7594 3502 and/or

- via post at Imperial College London, Data Protection Officer, Faculty Building Level 4, London SW7 2AZ.

If you, or the patient, are not satisfied with our response or believe we are processing their personal data in a way that is not lawful you or the patient, can complain to the Information Commissioner's Office (ICO). The ICO does recommend that you seek to resolve matters with the data controller (us) first before involving the regulator.

FUNDER

A group of international researchers formed the PRESTIGE AF consortium, which applied for research funding. This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No. 754517.

ETHICAL REVIEW

This research was designed and reviewed by a consortium of experts within the field. There are several monitoring boards in place that will continue to review the trial throughout, to ensure the safety of participants.

This research has been reviewed and approved by the London Surrey Borders Research Ethics Committee and the Medicines and Healthcare Products Regulatory Agency. The Health Research Authority has approved this research to be conducted within the UK National Health Service.

FURTHER INFORMATION

It is important that you have enough information to decide whether to take part. If you have any questions, please contact the study team: prestige-af@imperial.ac.uk

Thank you for taking the time to read this information.

CONSENT FORM

Principal Investigator: Participant ID:	Please Initial box
I confirm that I have read this information sheet and I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.	☐
I understand that I am giving this consent based on what I believe would be my relative/friend/partner's wishes. In my opinion they would be willing to participate.	☐
I understand that participation is voluntary and I or the person I am consenting for are free to withdraw at any time, without giving any reason, without medical care or legal rights being affected.	☐
I understand that sections of any of my relative/friend/partner's medical notes may be looked at by responsible individuals from NHS or from regulatory authorities where it is relevant to my taking part in this research.	☐
I give permission for these individuals to access my relative/friend/partner's records that are relevant to this research.	☐

I agree to my relative/friend/partner taking part in the whole substudy / biomarkers component only / genetics component only *(delete as applicable)*	
I agree that my relative/friend/partner's consent will override my consent when they are able to give informed consent.	
I give/do not give *(delete as applicable)* consent for remaining blood samples and information collected about my relative/friend/partner to be used to support other research in the future, including those outside of the EEA.	

_____

Name of Participant

_____	_____	_____
Name of Investigator taking consent	Date	Signature

_____	_____	_____
Name of legal Representative	Date	Signature

When completed: 1 for Participant, 1 for investigator site file, 1 to be kept in medical notes

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