PRESTIGE-AF

PREVENTION OF STROKE IN INTRACEREBRAL HAEMORRHAGE SURVIVORS WITH ATRIAL FIBRILLATION

Predictive Modelling Substudy

Participant Information Sheet

WE INVITE YOU TO TAKE PART IN A SUBSTUDY OF PRESTIGE-AF

- Before you decide whether to take part, 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 friends and relatives if you wish.
- You are free to decide whether to take part in this substudy. If you choose not to take part, or you chose to withdraw at any time, this will not affect your participation in the PRESTIGE-AF Study and it will not result in any disadvantages for you.
- 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 prediction of individual risk of subsequent ischaemic or haemorrhagic stroke in patients with atrial fibrillation, 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 or 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 your treatment at hospital.

WHAT IS INVOLVED?

If you have decided that you wish to take part in PRESTIGE-AF, you will be asked to take some time to decide whether you are willing to take part in this substudy. If you agree to take part, you will have to complete and sign the informed consent form and will be given a copy to keep.

The only procedure for this substudy is a single collection of a blood sample which will be taken at your PRESTIGE-AF baseline study visit. Four blood tubes will be taken, which in total is 28 mL, which represents ~6 teaspoons of blood.

Biologic samples will be labelled only with your PRESTIGE-AF participant ID number (i.e. with a code that does not allow access to your identifiable information). Your blood samples will be stored securely and confidentially, firstly at the clinical site where you were

recruited. Then they will be securely shipped to the centralised PRESTIGE-AF Biobank, which is established in the Neurovascular Research Laboratory, Vall d'Hebron Institute of Research, Barcelona, Spain. The collection will be carried out in accordance with the national and European regulations in force and declared to the regulatory bodies.

Your blood sample will be used for determination of blood biomarkers and genetic variants. Blood biomarkers will be measured in the Neurovascular Research Laboratory, in Barcelona. In order to study the relationship between genetic biomarkers and health parameters, we will transfer genetic material, again without any identifiable information about you, to a DNA database called "DNA Banco Nacional" of Salamanca laboratory to perform DNA extraction and then to a genomic platform for genotyping (*genotyping* is the process of determining the genetic make-up of an individual by examining his/her DNA code in certain locations using biological assays). This genomic platform may be located in Europe or abroad. The remaining samples will be kept in the Neurovascular Research Laboratory in Barcelona to be used in future biomarker and genetic studies (which may comprise sequencing or epigenetic studies) on Ischaemic stroke and Intracerebral Haemorrhage (ICH), unless you decline. These future studies may comprise DNA sequencing (another method for examining someone's DNA code) - or epigenetic analyses (changes in the "packaging" of DNA that influence the function of genes).

Data already collected during your hospital treatment will also be analysed regarding the potential association of findings from neuroimaging (e.g. silent lesions, localisation and size of ICH) and the risk of future stroke. For this purpose, brain imaging data at baseline performed during your routine diagnostic work-up will be collected

and sent to the neuroimaging core lab at the University Graz to perform a detailed and centralized analysis.

Your clinical information regarding your comorbidities, stroke severity or other sociodemographic characteristics will be used to identify factors being related with an increased risk of suffering a new ischaemic stroke or ICH. This research will be undertaken by the Institute of Clinical Epidemiology and Biometry at the University of Wuerzburg, Germany. The institute 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 you personally from your participation in this substudy. However, if we are able to 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 participate in the substudy, it is possible that the analysis of biomarkers from biological samples might reveal information relevant to your health. In accordance with current legislation, you have 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 recruiting centre. The recruiting centre will provide this information to you or to your doctor. In the case you prefer not to be informed, your decision will be respected. However, when this information, according to the

judgment of the responsible doctor, is necessary to prevent a serious injury to your health or that of your biological family, a close family member or a representative will be informed.

We will not give you 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 your informed consent.

POTENTIAL RISK OF THE SUBSTUDY

There are no serious risks deriving from your 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.

COMPENSATION

You will not receive any financial compensation for taking part in this substudy. However, taking part should not cost you anything and you will be reimbursed for your travel expenses to the visits for the PRESTIGE-AF Study and provided with refreshments as appropriate.

ABOUT THIS SUBSTUDY

This Predictive Modelling research is a substudy of the PRESTIGE-AF clinical trial. As with the main study it is sponsored by Imperial College

London, which means that they are the responsible for the conduct of the study and all complaints procedures, legal rights and insurance procedures are the same for the substudy as for the main PRESTIGE-AF Study.

As with the main study, this substudy is funded by the European Union's Horizon 2020 research and innovation programme under grant agreement No. 754517.

CONFIDENTIALITY & DATA PROTECTION

Imperial College London is the sponsor for this study based in the United Kingdom. We will be using information from you and your medical records in order to undertake this study and will act as the data controller for this study. This means that we are responsible for looking after your information and using it properly. Imperial College London will keep identifiable information about you for 10 years after the study has finished.

Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible.

You can find out more about how we use your information by contacting us on hello@prestige-af.org

Your Local NHS Trust will collect information from you and your medical records for this research study in accordance with our instructions.

Your Local NHS Trust will keep your name, NHS number and contact details confidential and will not pass this information to Imperial College London. Your Local NHS Trust will use this information as

needed, to contact you about the research study, and make sure that relevant information about the study is recorded for your care, and to oversee the quality of the study. Certain individuals from Imperial College London and its delegates, as well as regulatory organisations may look at your medical and research records to check the accuracy of the research study. Imperial College London will only receive information without any identifying information. The people who analyse the information will not be able to identify you and will not be able to find out your name, NHS number or contact details.

Your Local NHS Trust will keep identifiable information about you from this study for 10 years after the study has finished.

DATA SHARING

When you agree to take part in a research study, the information about your health and care may be provided to researchers running other research studies in this organisation and in other organisations. These organisations may be universities, NHS organisations or companies involved in health and care research in this country or abroad. Your information will only be used by organisations and researchers to conduct research in accordance with the UK Policy Framework for Health and Social Care Research.

This information will not identify you and will not be combined with other information in a way that could identify you. The information will only be used for the purpose of health and care research, and cannot be used to contact you or to affect your care. It will not be used to make decisions about future services available to you, such as insurance.

This study is sponsored and is run by Imperial College London. However, there are 12 other European organisations in the Prestige AF Consortium with whom we will be sharing the pseudonymised results of this study. These organisations are other Universities and

Hospitals with specialist knowledge in different areas who will assist in the running of the study and the analysis and publishing of the data.

The aim of this research is to improve patient care and to help us do that we ask for you to consent to your data being used in future research studies. These studies would need to go through the same rigorous ethical screening procedure that we did, to get access to your data. All shared data will be pseudonymised, and no identifiable information will be given to anyone outside of the direct care team who look after you.

FURTHER INFORMATION

It is important that you have enough information to decide whether to take part. If you have any questions, please contact us hello@prestige-af.org

THANK YOU FOR TAKING THE TIME TO READ THIS INFORMATION.