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Information for Prospective Participants

UK Adult Immune Thrombocytopenic Purpura (ITP) Registry

Invitation to participate in a research project

You are being invited to take part in a research study. Before you decide, it is important that you understand why this research is being conducted and what will be done. Please take time to read the following information carefully, to discuss it with us and others, and, finally, to decide whether or not you wish to take part. Feel free to ask us is there is any material that is unclear or on which you would like more information.

What is the UK adult ITP registry?

Immune (Idiopathic) thrombocytopenic purpura (ITP) is an uncommon disease characterised by a low platelet count. While we know that this condition results from the removal of antibody coated platelets by the immune system, we know very little regarding the underlying cause(s) of antibody attachment to platelets and, despite many years treating ITP adult patients, do not have definitive answers to such questions as when treatment is needed and which treatment may be best for a particular patient.

Individual hospitals will encounter only a small number of patients with uncommon diseases like ITP. This limited pool makes such conditions difficult to study, as generalisable results are only obtained through the study of a large number of people. A disease registry will allow us to build a complete picture of ITP through assembling information on patients across the United Kingdom. We would then have a sufficient number of patients to form distinct subgroups, such as individuals with mild and severe ITP or individuals responsive and nonresponsive to steroidal treatment, and may be able to link this clinical information with scientific findings. For example, we may find that adults with mild ITP have a particular profile or pattern within their immune response genes. Were such associations uncovered, they would help enable us to predict such valuable information as the severity of ITP a patient will likely have, his/her likely response to available treatments, and his/her risk of developing additional diseases. Worldwide, there have been very few studies on adult ITP; we hope that this registry will provide much of the information that we are currently lacking.

When you register through your haematologist, you will be asked to provide permission for study collaborators to collect ITP-related information from your medical records at regular intervals during study. The information that we will be collecting has been carefully determined and can be supplied to you upon request.

On most occasions, the information that we are collecting will be present in the medical records that are readily accessible by the registry staff or collaborating centres. In some circumstances, the information contained in them may not be complete or up to date as you may be receiving or have received treatment elsewhere. As your general practitioner is most likely to hold up-to-date information about your conditions and treatment, we will contact his/her team to request specific information for the sole purpose of this study. What we collecting is the same type of information that we collect at your referral centre for haematology care.

In addition, we will employ the NHS Data Linkage Service and Summary Care Records, which are used in clinical practice and research, to search for up-to-date information from certain electronic records held by the NHS and Office of National Statistics (ONS). It is important that we emphasise that only study-related information as per protocol will be searched through these different sources. In other words, it is not different to what becomes available to your haematologist and what you have agreed for collection. By engaging these resources, we will obtain the best data to generate robust and reliable findings which will in turn assist clinical

decision making. At the same time, we are improving our research methods alongside contemporary progresses made within the NHS to facilitate research on the whole, especially for nationwide studies like ours.

In addition, you will be asked to provide a small blood sample (15 mL, ~3 teaspoonsful) during a routinely scheduled blood testing (or a saliva sample [Oragene® kit]). Genetic material (DNA & RNA [where possible]) from this sample will be isolated and used for the molecular component of the study described later. In some instances, especially if you are seen at the Royal London Hospital, an additional 20mls of blood will be collected for T cell analysis (T cells are white blood cells involved in immune responses). The Chief Investigator's team will inform you if this is actually required at your hospital/clinic visit.

Data protection

The collection of information from medical records at The Royal London Hospital or through NHS IT services will be performed by the Chief Investigator's team, which includes the Lead Epidemiologist and Study Coordinator/Data Manager. For participants at all other centres, this data retrieval process from locally held medical records will be conducted by a member of your clinical care team. Access to records at these sites will be extended to the chief investigator's team but will be limited to monitoring and quality assurance purposes only.

Importantly, all information collected about you will be kept strictly confidential. Any published data will be anonymised so that you cannot be identified from it. During the study, we plan to share coded data with medical researchers at our sponsor, GlaxoSmithKline, and the Paediatric & Adult Intercontinental Registry on Chronic Idiopathic Thrombocytopenic Purpura (PARC-ITP) Study in Basel, Switzerland. These partnerships will increase our ability to investigate the natural progression, causes, and treatment of adult ITP while strengthening the accuracy of our findings. The information submitted to these two organisations will contain no personally-identifiable material, and all planned analyses utilising it will require favourable review from a research oversight body. As part of these collaborations, data will be shared with researchers in non-European Economic Area (EEA) countries which may not have laws protecting patient privacy to the same extent as the UK Data Protection Act or European Law.

Within these constraints, study personnel will take all reasonable steps to protect your privacy.

Molecular investigation of adult ITP

The molecular investigation of adult ITP will involve a scientific study of immune system molecules. The immune system consists of cells and proteins, and these proteins are coded for within our immune system genes. We know that individuals have minor variations in both the sequence and expression of these genes and would like to investigate whether these differences may be associated with observed differences in ITP severity and treatment effectiveness. We do not know what triggers ITP at present. It is one of a family of autoimmune diseases, disorders in which the immune system mistakenly attacks the body's own machinery. Studies of other autoimmune diseases suggest that one or more immune regulation genes may be overactive in ITP. We would, therefore, very much like to compare the activity of your immune regulation genes with activity patterns reported in healthy individuals and are hopeful that this comparison may yield causal hypotheses for further testing.

Immunological investigation of adult ITP

The immunological investigation of adult ITP will involve a scientific study of the immune systems cells and antibodies. We know that patients with ITP have different amounts of antibodies and that these antibodies can recognise different molecules on platelets or other self proteins (autoantibodies). We would like to investigate the white blood cells that produce platelet binding antibodies, those that clear platelets from the blood and those that regulate the overall immune response. Differences in these cells may be associated with the amounts of platelet antibodies in patients and may match up with ITP severity and treatment effectiveness. For example, ITP patients with a certain immune profile may benefit more from one therapy than another.

How may this research help?

Although this study is unlikely to have an immediate impact on you, it will likely benefit future patients by

1. helping us to find out what causes adult ITP.
2. enabling us to predict whether a particular case of ITP will be mild or severe and the risk of developing other illnesses.
3. resulting in a better understanding of which treatments to use in the future.

What are we asking from you?

If you agree to take part in this study, it will simply involve taking an extra 15 mL (~3 teaspoonsful) of blood on one occasion while you have your routine blood count at the outpatient clinic (or a saliva sample [Oragene® kit]). There are no hazards arising from this research apart from normal risks resulting from routine care; the amount of blood that we will take is very small and will not make you anaemic or feel in any way unwell. In some instances, especially if you are seen at the Royal London Hospital, an additional 20mls of blood will be collected for T cell analysis. The Chief Investigators team will inform you if this is required during your visit at the hospital.

Patients who would like to contribute to the Immune profiling part of the study, will be invited to contribute up to four blood samples of 50mls (10 teaspoons) over a six month period. These samples will be taken as part of routine bleeds. You will be free to decline further donations at any time. The additional amount of blood that we will take should not make you anaemic or feel unwell.

Of course, you do not have to join the study and may withdraw from it at any time. Please be assured that your decision not to take part will *not* affect your care in *any* way.

Should you decide to withdraw your consent to participate in this study the information you gave us before you left the study will still be used for research. Any remaining samples that can be linked to you will be destroyed at your request.

What will happen to my samples?

The tests for antibodies against platelets will be carried out at the NHS Blood & Transplant Service, Filton as part of the routine diagnostic service they provide or by other research laboratories were necessary. All obtained results will be coded in such a way that your identity will be unknown to researchers.

Tests on your samples will be undertaken using blood from the second or subsequent bleeds. These tests will partly be carried out in the laboratories at your hospital. Blood samples will also be transported to GSK laboratories, and other 3rd parties at GSKs discretion for analysis of how samples from patients with ITP vary and how they respond to proteins present in platelets. It may be necessary to store the blood samples but any remaining samples will be destroyed at the end of the study.

Duration of the study

The study will last a total of 11 years, concluding in 2018.

What will happen to the results of the study?

Results from the study will be published in peer-reviewed medical journals so that clinicians caring for adults ITP patients may be better able to manage their condition. Summary findings will additionally be published in *The Platelet*, the official newsletter of The ITP Support
Association, and presented at the Annual ITP Support Association Convention. Study participants and collaborators will be kept informed of study progress through a bi-monthly study newsletter that will be available on our online study site, www.ukitpregistry.com.

GSK plans to use the results from this study, and GSK or its collaborators may get patents, or sell drugs based upon this research in the future, or make profits other ways. You will not receive any financial benefit from these activities.

Who has reviewed the study?

The study has been carefully reviewed by our peers at the Institute of Cell and Molecular Science (ICMS) at Barts and The London School of Medicine and Dentistry, GlaxoSmithKline (GSK) Worldwide Epidemiology, the Joint Research Office for Barts and the London NHS Trust and Barts and The London School of Medicine and Dentistry, and the London Research Ethics Committee. These reviews have all been favourable.

What happens if there is a problem?

While we do not expect you to suffer any harm as a result of your participation in the study, it is important to note that no special compensation arrangement exists should it occur. Were you harmed as a result of someone's negligence, you may have grounds for legal action but may have to pay your own legal costs.

Should you wish to complain or have any concerns about any aspect of the way you have been approached or treated during the course of the study, normal National Health Service complaint mechanisms will be available to you. In such instances, we would ask that you please contact Patient Advisory Liaison Service (PALS) via telephone (+44 (0) 207 377 6335), minicom (+44 (0) 207 943 1350), or email (pals@bartsandthelondon.nhs.uk). You may alternatively visit with a PALS representative by asking at any reception centre in the hospital.

What can you do if you are worried or would like more information?

You will always be able to contact a member of the chief investigator's team to discuss your concerns and/or to get help:

	Chief Investigator /Consultant Haematologist	**Lead Epidemiologist**	**Data Manager & Study Coordinator**
Name	Dr. Daniel Hart	Mr Umesh Doobaree	Mr Raghava Nandigam
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Should you wish to discuss concerns over participation with a neutral party, please feel free to contact **Mrs. Shirley Watson, Chief Administrator of the ITP Support Association via phone (+44 (0) 123 437 6559)**; she will be happy to put you in contact with a clinical ITP expert not directly involved with our study. Though a financial sponsor of the molecular component of our study, the ITP Support Association remains first and foremost a patient support network and can be trusted in this regard as a provider of unbiased references.