

UKITP PROSPECTIVE PATIENT OVERVIEW (3.24)



Information for Prospective Participants UK Adult Immune Thrombocytopenic Purpura (ITP) Registry

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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 if 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.~~ we know very little regarding the underlying cause of platelet removal, despite many years treating ITP adult patients. We also do not have definitive answers to questions such as when treatment is needed and which treatment benefits which ITP patients.

ITP is a rare disease. Individual hospitals will encounter only a small number of ITP patients which makes it difficult to observe patterns within ITP patients. Our aim, at the UK ITP Registry, is to collect data from ITP patients from all over the country, in order to build a broad picture of ITP so that we can see emerging patterns. Collecting data from a large group of patients allows us to discover subgroups of ITP patients. For example, it could be the case that people with a certain characteristic do not respond well to steroids, or a certain characteristic may be linked to more severe disease. 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.

If you consent to be part of the Registry, your haematologist's team will collect ITP-related information from your medical records. In order to build a complete picture, we like to retrieve data from different sources, each of which will be explained below. We ask for your permission to use each source of data separately. You are free to not consent to any or all of the sources below.

~~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~~

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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.

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Hospital Records

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With your permission, your haematologist's team will collect data from your hospital medical records. This gives us the bulk of information we need including which treatments you've had and any previous bleeds.

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.

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General Practitioner (GP) data

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We also ask if you will allow us to contact your GP and get a copy of your GP medical notes. We often find that GP records may have some ITP-related information that can't be found in your hospital notes. In particular, past treatments that you may have had at a different hospital. The information we request is the same as what we are looking for in your medical notes, but we ask to see the GP notes in case there is any extra information available. You can ask your local team to see the GP Proforma (version 1.29) if you want to see the information we extract. You are free to decline access to your GP records.

NHS Data Linkage Service and Summary Care records

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). Again this is to find the same ITP-related information, but offers us another source for completeness of historical data.

By engaging these resources, we will obtain the best data to generate robust and reliable findings which we hope will assist future clinical decision making.

In addition, you will be asked to provide a small blood sample (4 to 8 mL, about 1 to 2 teaspoonful) during a routinely scheduled blood testing. Genetic material (DNA & RNA) from this sample will be isolated, saved and used for studies described later.

You may be asked if you are willing to consent to donate an additional 20-50 mls of blood. This will only be participants from The Royal London Hospital. If you have consented to this, the team will tell you this is going to happen before your hospital/ clinic appointment.

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 on pregnancy and newborn

Dr Sue Robinson, Consultant Haematologist at Guy's and St Thomas' NHS Foundation Trust, has a specific interest in obstetric haematology and will collaboratively lead a study on pregnancy and newborn's health in ITP patients with the Chief Investigator Dr Vickie McDonald.

Recommendations for the management of ITP in pregnancy are largely based on expert opinion because of a lack of observational studies or randomised clinical control trials. The ITP Registry has been expanded to look at the management of pregnancy in ITP patients. If you are a female participant we would like your permission to monitor how your ITP is managed during your pregnancies. This would include getting some information from your medical records on how your new born child is after birth- only up to 3 months post birth. The data collected regarding your baby will be minimal. This is a data collection study. Allowing us to collect your data will not affect yours or your baby's care in any way.

If you received maternity care outside the health organisation where you receive your haematology care, your maternity records will be held at this external organisation. Therefore, the team extracting the relevant study related materials will request for your maternity notes to be sent to them. By agreeing to be part of this sub study, you therefore accept that your maternity will be requested and accessed for data extraction.

If you would like any further information in relation to this part of the study, please address your queries to:

Dr Susan Robinson (Sub-Investigator - ITP Registry – Pregnancy Section)
Guys & St Thomas NHS Foundation Trust,
Haematology Department
Great Maze Pond
London
SE1 9RT
Telephone: +44(0)2071883423

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Email: Susan.Robinson@gstt.nhs.uk

Data management and 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.

Barts Health NHS Trust is the sponsor for this study based in the United Kingdom. We will be using information from your medical notes 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. Barts Health will keep identifiable information about you for 20 years from study closure in accordance with the Research Governance Framework and Trust Policy.

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.

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Data retrieval from your medical records will be done locally at your hospital. 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. [NHS site] will use your name, NHS number and contact details 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. Individuals from Barts Health and regulatory organisations may look at your medical and research records to check the accuracy of the research study. [NHS site] will pass these details to Barts Health along with the information collected from you and your medical notes. The only people in Barts Health who will have access to information that identifies you will be people who need to contact you to audit the data collection process. 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.

Under strict control, the UK ITP Registry may collaborate with fellow researchers outside of Queen Mary University of London in order to conduct some studies, especially those that require expertise and facilities not available at the University. If this collaboration is deemed necessary, the UK ITP

Registry will enter into a data sharing agreement with these researchers where anonymised information may be shared for a defined period of time.

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

Blood Samples

ITP is a variable disease. We don't understand why the disease can affect people differently, nor do we understand why some people respond to certain treatments whilst others do not. We want to investigate whether variations in genes that make up our immune system may contribute to the differences seen in ITP.

In order to do this, we ask you if you are willing to donate 4-8 ml (1 to 2 teaspoons) of blood on one occasion. Blood samples will be labelled with an anonymised code and sent to the Royal London Hospital. We will extract the DNA from this blood and store the DNA at the Royal London Hospital for future studies. Any blood not used for DNA extraction will be discarded. You can be part of the ITP Registry without consenting to donate a blood sample.

As well as wanting to understand if different genes contribute to ITP, we want to know if certain cells in your blood contribute to ITP. To do this, only participants from the Royal London Hospital will be invited to take part in a sub-study looking at the cells in your blood. In order to be part of it, you will be asked to donate four blood samples of 50ml (10 teaspoons) over a six month period. You will be free to decline further donations at any time. This is still a small amount of blood and you should not experience any side effects from donating this amount.

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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.

What will happen to my samples?

Blood samples will be sent by your haematology team to UK ITP Registry at the Royal London Hospital where they will be stored. Samples may be sent to other institutions for specialised tests if the facilities are not available at the Royal London Hospital. Samples will be sent to other centres anonymised and all results obtained will be coded in such a way that your identity will be unknown to researchers.

Leaving the Registry

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. If you would like to withdraw, please inform your local site staff or email the registry directly (uk-itp.registryteam@nhs.net).

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.

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~~Helping us to find out what causes adult ITP.
2. ~~enabling~~Enabling us to predict whether a particular case of ITP will be mild or severe and the risk of developing other illnesses.
3. ~~resulting~~Resulting in a better understanding of which treatments to use in the future.
- 3-4. ~~Helping us understand the outcome of pregnancy in ITP and which treatments to use in the future.~~

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Duration of the study

The Registry has ethics to run until 2020.

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.

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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.~~ Barts Health NHS Trust has agreed that if you are harmed as a result of your participation in the study, you will be compensated, provided that, on the balance of probabilities, an injury was caused as a direct result of being part of this study. These special compensation arrangements apply where an injury is caused to you that would not have occurred if you were not in the study. These arrangements do not affect your right to pursue a claim through legal action.

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 please contact Queen Mary University of London on 020 7882 7250 to initiate the complaint procedure . You may also~~ contact Patient Advisory Liaison Service (PALS) via telephone (+44 (0) 207 377 6335), minicom (+44 (0) 207 943 1350), or email

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(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 (please see below) 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 (012-3437-6559); 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.

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Central Research Team

Contact details

UK Registry Coordinating Team
Dr Vickie McDonald
(Consultant Haematologist and Chief Investigator)

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