Queen Mary University of London

UK Adult ITP Registry *Update*

Welcome

It has been some time since we updated everyone on what's been going on with the Registry here at The Royal London Hospital.

Personnel at The London

There have been staffing changes with the arrival of Raghava Nandigam a year or so ago. He is the Data Manager and Study Coordinator. Those of you who have enrolled in the Registry will no doubt have contacted Raghava already. He has a long track record of data management and is responsible for keeping the whole database running, uploading and validating data, providing support for centres around the UK and providing the much needed documentation for local R&D departments.

A few months ago Umesh Doobaree started his PhD with us. Again, Umesh is a seasoned epidemiologist who is going to carry on form where Ameet Sarpatwari left off. Umesh plans to use the data in the Registry to analyse long-term outcomes, co-morbidities, risk of thromboembolism, and genetic studies in our large ITP cohort. Umesh has provided a run-through of his planned research later in the newsletter.

We appointed the first ITP Clinical Nurse Specialist, Louise Taylor, who is the first point of contact for many patients with ITP. Louise has spearheaded the Nursing Education programme, and advises on TPO receptor agonist administration and ITP management in general. She sees many ITP patients on the Day Unit here at The London. For a full run down on all her recent activities.

We have moved into the new hospital here at the Royal London and we have an excellent team headed up by Sister Marlene Johnson who runs the Day Unit.

Laboratory research

Jointly with Dr Dan Pennington, a Senior T cell Immunologist at The Blizard Institute, we were awarded a research grant by The Barts & The London Charity to look at the role of T cells in ITP. To date, most research focus has been on B lymphocytes but it looks as though for many patients it may be the T cells that are causing the ITP. We have appointed an experienced post doctoral scientist, Dr Saleha Hassan, who will be analysing the T cells in terms of their abnormal function as well as their genes to see if they are causing ITP in some of our patients. If a patient does have a T cell form of ITP they may not respond to steroids or IVIg but may need T cell type treatment. As we learn more I will provide updates via the newsletter.

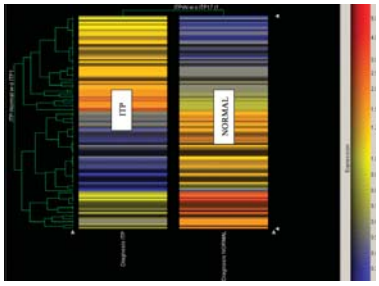
Genetics: DNA polymorphisms

We received a grant from The ITP Support Association a couple of years ago and we examined the DNA from a number of patients looking for changes within specific genes to see if there were any obvious changes which might be linked to ITP. These results showed that within the TNF-α gene there was a definite polymorphism linked to ITP. The paper was published in the journal *Hematology*, volume 16, page 243 (2011).

Genetics: Exome sequencing

There is a large genome centre at Barts and we are planning to look at the exomes of 200 patients with ITP (exomes are the coding regions of our genes) to see if we can identify any new genes that might be implicated in the development of ITP.

Dr Nichola Cooper from The Hammersmith Hospital is planning to look more at B cells in ITP and examine closely their role in patients taking part in the Registry. Her work will be carried out both at The Hammersmith and The Blizard Institute here at The London. Again, all data will be reported back here.



Thanks!

The Registry has more than 1000 patients. Many of these come from The Royal London but around 65% have been enrolled by participating centres who have signed up to take part in the Registry. We would like to extend our warm thanks to all of those clinicians, nurses and others who are helping collect data.

If there is anything we can do to help you more please contact us.

ITP Clinical Centre Network

Following discussions with the ITP Patients' Support Association we set out with a number of other clinicians interested in ITP to develop a structure that would help improve access throughout the UK to newer treatments and to clinical studies. We felt that it was a requisite that patients, where ever they lived, could be treated locally and would be offered options, and could have discussions that reflected modern thinking on treatment.

We identified many centres that have been active in entering patients to the ITP Registry held at Barts Health, and others that would have if resources had been available, and have now developed a network of ITP Clinical Centres that geographically cover England but also have centres in all the devolved countries (*http://itpsupport.org.uk/itpforum/centres.htm*). Each centre is led by an enthusiastic clinician with an interest in ITP. We hope that each of the centres can act as a hub locally to support neighbouring hospitals in developing clinical and research studies.

In order to support the centres we have set up the UK ITP Forum, where all are represented, which has met on a number of occasions and also has regular telecon links. The Forum is chaired by Paula Bolton-Maggs and Quentin Hill is the secretary and there is a web page for the Forum on the ITP Registry, which also links to the ITP Patients Association site.(*http://itpsupport.org.uk, http://ukitpregistry.com*)

Although there is little funding currently available to support the initiative our experience in North East London is that organised data collection can be accepted for portfolio funding from the NIHR Clinical Research Network and this provides support both for the data collection and for other initiatives. The ITP Registry is recognised by the NIHR for portfolio funding and anyone entering patients into the registry can apply locally for a share of the funds. The CRN has been reorganised this year into 25 local clinical research networks each with 6 Divisions supporting different specialist clinical areas, of which Non-Malignant Haematology is one with Cancer. The funding is no longer given to Trust R&D departments but is allocated through the divisional model as activity based funding to support named individuals who are working on NIHR Portfolio studies. This is to ensure that appropriate posts are funded and will enhance transparency. While activity may not be sufficient to support a whole post part-time posts can be created, or by linking with other non-malignant haematology projects funding support can be increased and posts shared. These can be used for research nurses, data managers etc. We have also had discussions with other bodies for support and may be able to develop pilot projects in some centres.

We hope that as the network structure of centres matures it will be a focus for clinical and research studies. It will enhance support of both the childhood and adult registries and increase the data available for review. Already a number of projects have been discussed, including individual centre feedback, drug side-effects, co-morbidities and long term clinical outcomes. Some of these are part of the on-going review of the Adult registry but there is a large amount of data available to interested individuals.

It is not anticipated that the current list of centres will be exclusive and we are keen to include any centre where there is a commitment to improve patient care in ITP and to support the aims of the group.

Professor Adrian Newland

ITP Clinical Nurse Specialist

I was employed as an ITP Research Nurse in 2010 and took over the trials for TPO receptor agonists, romiplostim and eltrombopag. As the trials came to an end and romiplostim was approved by NICE, I developed the role from focusing mainly on research in ITP to all inclusive care of patients that were prescribed Nplate. I guided the patients through their training in self administration. This role developed into a Nurse Specialist role and I added all ITP patients into the role. I am actively involved in recruiting patients onto the UK Adult ITP Registry and discuss the research objectives with patients who attend the Thursday morning ITP clinic. I also consent patients for the Registry and take blood samples as part of the Registry studies.

A major part of my role is the running of clinical trials for ITP and haemophilia. I am responsible for the smooth running of the studies, obtaining blood samples and reviewing patients taking part in studies regularly.

I am also a nurse member of many ITP specialist groups, which include consultants and patient advocates.

As the CNS for ITP at Royal London, I was asked to join a European ITP Advisory Group. This Advisory Group has been developing Nursing Education on ITP.

We have published *Immune Thrombocytopenia: A Practical Guide for Nurses and Other Healthcare Professionals*. This has been well received and is now published in 7 languages. The PDF version is available at: *http://newsletter.ebmt.org/march11/Nurses%20Group/Resources/ITP_Practical_Guide_06-01-11.pdf*.

Part of my role as the RLH ITP nurse is to raise the awareness of ITP in the healthcare community and to develop and educate ITP nurses. I am also the first point of contact for the ITP patients at the RLH. My contact details can be found at the back of the newsletter.

I work very closely with Dr Provan, Prof Newland and all the staff at the ITP registry.

Louise Taylor

Lead Epidemiologist Report

As this is my first newsletter, I should perhaps introduce myself. I joined Drew's and Adrian's team as the Lead Epidemiologist for the UKITP Registry after having worked in the private sector over the last 7 years. Coming back to mainstream academia and field research was a very important and decisive moment in my career. I bring along my experience of working in cancer, cardiovascular and rare disease epidemiology. Becoming an Epidemiologist was a change of heart from becoming a Psychologist after having studied the latter for some years. Before and during my formative years in psychology and epidemiology, I practised for quite some time as an Intensive Care Nurse in several university hospitals within inner and outer London.

Now that I am at the Registry, I am learning a great deal under the leadership of prominent experts on this rare disease called ITP. The more I learn the more I find unanswered questions about ITP, whether about its aetiology, descriptive epidemiology or treatment. However, one thing that I understood clearly is the ethos behind the creation of this registry, which is to answer many of these questions using large scale, real-life data. The registry, drawing on its blood/saliva bank, is also well positioned to undertake research to uncover potential biological pathways in disease expression.

Since I started, I have been busy planning with the team so that we can start the epidemiology programme using our own data. It became apparent during that process that we had to also engage data from other resources that were not available to us (e.g. General Practices and Health and Social Care Information Centre (HSCIC)). We know that good quality data and sound methodology contribute to robust findings on which important decisions can be reliably made. To achieve this we revised the data collection process, applied to the Ethics Committee, Confidentiality Advisory Group (CAG) and other bodies to ensure all approvals are in place, and also redesign other elements of the registry. We are now only waiting for CAG to respond back to us with their final approval to engage the data from the HSCIC.

Apart from the setting up process, this first phase of our programme will see the description of the demographic and clinical characteristics of our cohort while focusing on occurrence of comorbid illnesses. How certain haematological markers of ITP, including platelet count, behave over time and in relation to other characteristics will be described. We will also look at the influence of potential contributory factors toward the occurrence of thromboembolic events and bleeding using multivariate modelling.

The next phase of our programme is to describe treatment patterns and their effectiveness. With adequate support we also anticipate to undertake health outcome studies, including quality of life outcomes reported by patients at various stages of their care pathway. The latter is an area of interest among doctors and nurses in view of choosing the best treatment strategies for their patients. We will also bring genetic epidemiology methodologies into our aetiologic research activities and construct geno-phenotypic models to predict disease severity and response to treatment. Undertaking this programme is also a personally exciting and challenging moment too, as it will be generating novel data that I will be integrating into my own research thesis.

The Registry is therefore undergoing a pivotal moment. We are also undertaking a data updating process nationally. Our data entry database has also been revised to receive new data, especially on risk factors for thromboembolism and bleeding. So far, we have received very good response from all our centres. At this year's BSH meeting, we received very encouraging feedback and there was a wide interest for more up-to-date evidence on treatment effectiveness.

We have also been busy working on our studies too. A systematic review is in its final stage of completion and we aim to publish our findings in due course. While undertaking all the above activities, we are also addressing the requests of several haematology teams outside of the United Kingdom to join our Registry. This is an exciting time for the Registry because this improves our scope of recruiting more participants and bringing in more data on various therapeutic agents and patterns. An increase in sample size, especially for a rare disease, will also ensure that we have strong statistical power to undertake comparative studies as well as increase their likelihood of detecting rare events (e.g. bone marrow fibrosis). The other advantage of using our registry is that the external collaborators, whether national or international, can access to their own data for their own research.

On the whole, we are very enthusiastic with the progress made so far and are very grateful and thankful to our external centres to make this possible. We shall report back to you all in due time with our findings.

Umesh Doobaree

Study Coordinator Report

The UK Adult ITP Registry

The UK Adult ITP Registry has successfully been recruiting patients since its re-initiation in 2007 under the direction of Dr Drew Provan (Chief Investigator), and Professor Adrian Newland (Co-Investigator).

Current Scenario and Latest Developments

To date, 1,152 adult patients with primary ITP have registered with the Registry, with comprehensive clinical data (e.g., demographics, bleeding events, co-morbid conditions, ITP-specific treatments, and laboratory results) having been collected on 896 (78%) of these participants. Recruitment is currently undertaken at 40 NHS collaborating trusts in the UK with participants from more than 100 hospitals; registry is open for collaboration with new centres nation-

ally and internationally. Though these statistics make Registry one of the largest databases on adults with primary ITP in the world, substantial work is still required to collect sufficient information for more detailed analyses on disease progression in primary ITP, including the identification of patients more likely to suffer major bleeding and thromboembolic events.

Recently there have been lot of developments in the registry; we have been working hard in (a) creating a streamlined process for patient recruitment at The Royal London Hospital, (b) redesigning our online database, (c) conducting analyses of extracted data and (d) increasing the number of participating centres nationally and internationally.

Our decision to redesign our existing online database was based on our desire to create a more user-friendly system and update the database with the additional fields required for data collection, which we believe will help patient recruitment, international collaboration, and analyses. The ITP Registry database is live and in the future we hope to include ITP researchers from other countries (*www.itpregistry.org*).

Raghava Nandigam

Thank you!

We would like to take this opportunity to thank all the participants who have consented to participate in the study as well as our collaborating centres for supporting us in running a successful research project. Should you wish to take part in the Registry or have any queries regarding research undertaken, please do not hesitate to contact a member of our team, whose details can be found at our study website: *www.ukitpregistry.com*.

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