The United Kingdom Immune Thrombocytopenia Registry (UKITP)

A brief overview of Primary ITP and the Registry to assist data entry staff

By the Registry Team

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What Is Primary ITP?

- Primary Immune Thrombocytopenia (ITP) is a rare disease (affects < 50 per 100,000 individuals)
- Primary ITP is an autoimmune condition in which platelets are destroyed by one's own immune system, thus leading to a low platelet count (thrombocytopenia).
- Platelet production is also thought to be impaired due to autoimmune pathophysiology.
- Primary ITP is distinguished from secondary ITP
- Primary ITP is diagnosed by exclusion of all known secondary causes of ITP
- Secondary ITP results from known causes, i.e. part of a known disease process (e.g. HIV, SLE, & AHIA) or drug-induced (e.g. quinine & heparin)
- The exact cause or trigger of the autoimmune mechanism in primary ITP is unknown

Signs and Symptoms

- Easy bruising
- Nosebleeds
- Skin rash of small red dots (petichiae)
- Prolonged bleeding from cuts & abrasions
- Excessive bleeding after major trauma
- Gastro-intestinal bleeding
- Intracranial haemorrhage (rare)

How is it treated?

- At low platelet count, patients bleed or are at risk of bleeding
- Treatment usually given when platelet count<$30x10^9$/L and/or patients bleeding and/or in preparation for a procedure

- First-line treatment
  - Corticosteroids (prednisone, dexamethasone, methylprednisolone)
  - Anti-D
  - IVIg

- Platelet transfusion for fast replacement of platelets

- Second-line treatments include
  - Azathioprine
  - Cyclosporin A
  - Cyclophosphamide
  - Danazol
  - Dapsone
  - Mycophenolate
  - Rituximab
  - Splenectomy
  - TPO receptor agonists (eltrombopag and romiplostim)
  - Vinca alkaloids

Aims of the Registry

- The registry was set up with the aim to gather sufficient sample size and long-term follow up data on this rare disease.
- This allows us to:
  - Conduct studies with adequate statistical power to detect clinically meaningful changes in outcomes
  - Increase the probability of identifying outcomes or events, particularly those that are rare
  - Have a representative sample with high external validity

Studies of UKITP Registry

- Epidemiological measures (e.g. incidence, prevalence, mortality)
- Natural history of ITP
- Treatment and practice patterns
- Clinical outcomes (including treatment effectiveness)
- Genotypes associated with ITP, disease severity and treatment response
- Future studies (in proposal)
  - Adverse events (not case by case but in aggregate data)
  - Patient-reported outcomes

Eligibility to participate

- Confirmed diagnosis with primary ITP
- 18 years old and above
- Consented to be part of the Registry

Recruitment – 2 routes

Route A: Local Recruitment (centre-led recruitment)

1. Collaborating centres identify potential participants, introduce them to the registry, and gain consent for their participation
2. Participants consent locally using study and tissue usage consent forms
3. Staff collect biological samples*** if consent provided by participant and send to Registry
4. Copies of consent forms, biological samples and details of participants (use local participant log which include Registry Identification Code, RIC) to be sent to Registry
5. Centre starts data collection process
   - send and receive data request to participants GP (using GP proformas available)
   - collect data from medical records (medical notes & electronic records) using data collections forms
   - Enter on the registry database (REDCap)

***TEMPORARILY ON HOLD: PLEASE DO NOT COLLECT BLOOD AND SEND TO THE REGISTRY UNTIL FURTHER NOTICE

Recruitment

Route B: By Invitation Pack** (central recruitment, i.e. by core registry staff)

1. Collaborating centres identify potential participants and introduce them to the registry
2. Participants agree to forward their details to the Registry team (use local participant log)
3. Registry uses details to send invitation pack to participants (Invitation pack consists of Participant information sheet, study consent form, tissue consent form, pre-paid self addressed envelope)
4. Signed consent forms from participants (study and subsequent tissue usage) received by Registry team
5. Copies of consent forms sent to collaborating centres through secure nhs.net email
6. Centres start data collection process
   - send data request to participants GP (using GP proformas available)
   - collect data from medical records (medical notes & electronic records) using data collections forms
   - Enter on the registry database (REDCap)
7. Centres collect biological samples*** during participants next routine visit and send sample to registry

** RESTRICTED TO ONLY A FEW CENTRES BEFORE LAST PROTOCOL UPDATE

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Data collection

Use online database: click here

- **Data collected include**
  - **Participant details (including their Consultant and GP)**
  - **Participant information**
  - **ITP diagnosis**
  - **Other medical conditions (comorbidities)**
  - **Family history (illnesses that run in the family)**
  - **ITP treatment**
  - **Bleeding events**
  - **Laboratory results**
    - **Haematological (including all platelet counts) levels**
    - **Biochemical levels**
    - **Immunological levels**

The Importance of Good Data

- Allow statistical analysis without issues
- Good data leads to robust findings
- Low quality and incomplete data can lead to wrong findings and wrong conclusion

Common data quality issues

- Common errors and how to correct them
  - Look out for values significantly outside the reference ranges and check with clinicians if in doubt that the values are correct
  - Check the data is entered in the correct units. If the unit is given but not correct, then try to convert it (see next slide)
  - See the Data Collection booklet for more tips on data correction (on database)
  - Dates: It is very important that correct dates are entered on the database after thorough checking of the medical records

    Note: Please select appropriate date status option available on the database while entering dates on the database, please refer to the data collection booklet

Unit Conversions

- If the units are given, but are not the correct units (with regards to the database), you need to convert them before uploading.
- For example, 1L = 10dL.
  - To convert from dL to L, divide by 10
  - To convert from L to dL, multiply by 10
- Likewise, there are 1000mg in 1g, and 1000mcg in 1mg.
  - Multiply by 1000 to convert to the smaller unit (g->mg and mg-> mcg)
  - Divide by 1000 to convert to the larger unit (mcg -> mg and mg -> g)

Unit Conversions (cont.)

- Hb: database requests g/dL, your centre uses g/L – please divide by 10 to convert from g/L to g/dL
- WBC & Neutrophils: database requests /nL (per nano litre), your centre uses 10^9/l please continue to use the same units as both of them are the same
- RBC: database requests /pl, your centre uses 10^{12}/L please continue to use the same units as both of them are the same
- Biochemical fields ALP, ALT and AST: U/L and IU/L are the same
- Immunological fields to convert g/L to mg/dL multiply by 100

Patient Information & Reference Ranges

- The following slides contain the reference ranges for a variety of numerical data collected for the registry
- It includes common drug treatment doses, blood results and biochemical values
- They act as guide for the expected range, so any values significantly outside these ranges will need to be checked. Remember these are reference ranges, and the values will be coming from patients who are unwell (ITP or comorbidities), so abnormal readings outside the ranges are likely
- Use best judgement for patient information (e.g. is the weight expressed for adult?)
- More detailed information can be found on the 'Guidance Notes for Data Collection'
- To assist with data entry on our database please refer to the document UKITP_Registry_Data_Entry_Guide_on_REDCap_Database

Treatment- Reference Ranges

Treatment	Dose Range
Prednisolone	0.5-2mg/kg/day
IVIg	0.4g/kg/week
Methylprednisolone	30mg/kg/day
Dexamethasone	20-40mg/day
Danazol	200mg/day
Dapsone	200mg/day
Azathioprine	1-2mg/kg

Treatment	Dose Range
Cyclophosphamide	1-2mg/kg/day
Vinca Alkaloids	1-2mg/week
Mycophenolate	1000mg BD
Eltrombopag	25 - 75mg/day
Cyclosporine	5mg/kg/day for 6 days, then 2.5-3mg/kg/day
Rituximab	375mg/m^2/week for 4 weeks (or 100mg tablet)
Romiplostim	1-10micrograms/kg/week (µg/kg/week)

Please refer to:

Provan et al. International consensus report on the investigation and management of primary immune thrombocytopenia. Blood. 2010. 115(2):168-86. PMID: 19846889
doi: 10.1182/blood-2009-06-225565

Haematological/Biochemical Ranges

Test		Lower Limit	Upper Limit	Units
Red Cell Count (RCC)	M	3.97	5.54	$x10^{12}/L$
	F	3.66	4.90	$x10^{12}/L$
Haemoglobin (Hb)	M	13.0	18.0	g/dL
	F	11.5	16.5	g/dL
White Blood Cell (WBC)		4.0	11.0	$x10^{9}/L$
Neutrophils		1.8	7.5	$x10^{9}/L$
Platelet		150	400	$x10^{9}/L$
Mean Platelet Volume (MPV)		7.2	11.7	fL
Direct Agglutination Test (DAT)		Positive/Negative		
Alanine Transaminase (ALT)		7	40	U/L
Aspartate Transaminase (AST)		13	40	U/L
Alkaline Phosphatase (ALP)		30	130	U/L
Bilirubin		-	<21	umol/L

- Thank you for your assistance.
- If you have any clinical-related queries, please contact your team's clinician
- If you have any concerns about adverse events data that you come across during data collection, please inform your team's clinician and the patient's clinicians immediately. Also inform the Medicine and Health product Regulatory Agency (MHRA). https://www.gov.uk/report-problem-medicine-medical-device
- If you have any queries with regards to the Registry, including our data entry database, please contact us at
  - uk-itp.registryteam@nhs.net