International IBD Genetics Consortium

PRED4

Thiopurine Induced Leucopaenia

Case Report Form

Please stick study label here

On completion, please return to:
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Thiopurine Induced Leucopaenia
Introduction

Please complete all boxes where indicated and in black ball point pen.

If you make a mistake please put a line through the box, initial and date and write answer to the side.

Complete dates in format dd/mm/yyyy

The patient identification number is the bar code on the front of the CRF. Please transcribe this on to the top of the page in each relevant section.

For study inclusion participants must meet all the major criteria and any number of the additional minor criteria.

*Drug causes of leucopaenia

- Allopurinol
- Antithyroid drugs (thionamides – Methimazole, Carbimazole, Propylthiouracil)
- Anti-inflammatory drugs (Sulfasalazine, Nonsteroidal anti-inflammatory drugs [NSAIDs], Penicillamine)
- Psychotropic drugs (Clozapine, Phenothiazines, Tricyclic and tetracyclic antidepressant)
- Gastrointestinal drugs (Sulfasalazine, Histamine H2- receptor antagonists)
- Cardiovascular drugs (Antiarrhythmic agents (tocainide, procainamide, flecainide), ACE inhibitors (enalapril, captopril), Propranolol, Dipyridamole, Digoxin)
- Dermatologic drugs (Dapsone, Isotretinoin)
- Antibacterial drugs (Macrolides including minocycline, Trimethoprim-sulfamethoxazole, Chloramphenicol, Sulfonamides, Vancomycin, Cephalosporin)
- Antimalarial drugs
- Antifungal agents (Amphotericin B, Flucytosine)
- Anticonvulsants (Carbamazepine, Phenytoin, Ethosuximide, Valproate, lamotrigine)
- Diuretics (Thiazides, Acetazolamide, Frusemide, Spironolactone)
- Chlorpropamide
- Bupropion
- Immunosuppressive drugs

Thiopurine Induced Leucopaenia

Section 1 - Inclusion Criteria

Study code

1.1 Major criteria (all must be met)

- ☐ History of inflammatory bowel disease
- ☐ History of thiopurine exposure in the previous 7 days
- ☐ Normal total white cell count and/or neutrophil count at baseline
- ☐ Fall in total white cell count to $\leq 2.5 \times 10^9$/L, or reduction in neutrophil count to $\leq 1.0 \times 10^9$/L
- ☐ Medical opinion implicating thiopurine leads to dose reduction or drug withdrawal (even if temporary)

1.2 Other risk factor(s) or potential causes for leucopaenia (see page 2)*

- ☐ No - Category A
- ☐ Yes - Category B

If yes:

- ☐ Drugs, please specify (* See page 2)
- ☐ Symptoms suggestive of recent viral infection
- ☐ Myeloproliferative diseases
- ☐ Rheumatoid arthritis, SLE
- ☐ B12 or folate deficiency
- ☐ Hypersplenism
- ☐ Other, please specify

1.3 Minor criteria (sum number of criteria):

- ☐ Fall in total white cell count or neutrophil count within 12 months of introduction of thiopurines
- ☐ White cell count and neutrophil count returns to normal range after dose reduction or drug withdrawal
- ☐ Recurrence (defined as total white cell count $\leq 3.5 \times 10^9$/L or neutrophil count $\leq 2.0 \times 10^9$/L) on re-challenge with either Azathioprine or Mercaptopurine

1.4 Number of minor criteria

1.5 Participant's eligibility Investigator sign-off

Is the participant eligible to take part in the clinical trial? ☐ Yes ☐ No

If no, please give reason(s) for screen failure:

1.

2.

3.

Investigator's signature

Date dd / mm / yyyy

Investigator's name (print)

Section 2 - Patient Details

Study code

2.1 Patient details

Date of Birth dd / mm / yyyy Sex: M ☐ F ☐

Weight at time of leucopaenia (or nearest estimate) ☐ kg

Date of weight dd / mm / yyyy Height ☐ cm

2.2 Ethnicity - *Please tick as appropriate*

White

- ☐ British
- ☐ Irish
- ☐ Any other White background

Black or Black British

- ☐ Caribbean
- ☐ African
- ☐ Any other Black background

Mixed

- ☐ White and Black Caribbean
- ☐ White and Black African
- ☐ White and Asian
- ☐ Any other Mixed background

Chinese or Other Ethnic Group

- ☐ Chinese
- ☐ Any other ethnic group (*please specify*)

☐

- ☐ Not stated

Asian or Asian background

- ☐ Indian
- ☐ Pakistani
- ☐ Bangladeshi
- ☐ Any other Asian background

2.3 Participant informed consent

Date participant signed written consent form dd / mm / yyyy

Date of blood sample taken dd / mm / yyyy

Section 3 - Medical History

Study code

3.1 Hospital Details

3.1.1 Consultant Gastroenterologist

3.1.2 Consultant Haematologist

Hospital

Hospital

Hospital address

Hospital address

Consultant telephone

Consultant telephone

Consultant email

Consultant email

3.2 Other significant medical history

☐ Yes ☐ No

If yes, please give details here

Section 4 - Diagnosis & Classification of IBD

Study code

4.1 Diagnosis and classification of IBD

- ☐ Crohn's disease — Date of diagnosis: dd / mm / yyyy
- ☐ Ulcerative Colitis — Date of diagnosis: dd / mm / yyyy
- ☐ IBD unclassified — Date of diagnosis: dd / mm / yyyy

4.2 Smoking history

4.2.1 Start date: dd / mm / yyyy

4.2.2 End date: dd / mm / yyyy

4.2.3 Maximum number of cigarettes per day

4.3 Ulcerative colitis

4.3.1 The extent of ulcerative colitis can be classified as:

- ☐ E1 Ulcerative proctitis - inflammation is limited to the rectum (proximal extent of inflammation is distal to the rectosigmoid junction)
- ☐ E2 Left sided UC (distal UC) - inflammation limited to a proportion of the colorectum up to the splenic flexure
- ☐ E3 Extensive UC (pancolitis) - inflammation extends beyond the splenic flexure
- ☐ Ex Unknown

4.3.2 Disease severity in 2 years prior to development of leucopaenia

- ☐ DS0 Clinical remission. Asymptomatic; no escalation of treatment
- ☐ DS1 Mild relapses – managed with oral or rectal aminosalicylates and/or rectal steroids: **no oral steroids** required
- ☐ DS2 Moderate relapses requiring oral steroids and/or addition of immunomodulator
- ☐ DS3 Severe or refractory disease requiring inpatient admission or colectomy

4.4 Crohn's disease

4.4.1 Location

- ☐ L1 Ileal
- ☐ L2 Colonic
- ☐ L3 Ileocolonic
- ☐ L4 Isolated upper disease

4.4.2 Behaviour - the behaviour can be defined by looking at reports from Barium enema, colonoscopy, MRI, CT

- ☐ B1 Non stricturing, non-penetrating
- ☐ B2 Stricturing
- ☐ B3 Internal penetrating
- ☐ p Perianal disease modifier

Section 5 - Leucopaenia History

Study code

5.1 Which thiopurine was suspected of causing leucopaenia?

☐ Azathioprine ☐ Mercaptopurine

5.2 Date thiopurine first commenced

dd / mm / yyyy

5.3 Maximum dose of thiopurine in 8 weeks prior to episode of leucopaenia

5.3.1 Date when this maximum dose of thiopurine started

dd / mm / yyyy

5.4 Were TGN levels measured within 2 months of detecting the leucopaenia

☐ Yes ☐ No ☐ Unknown

If yes, what was the level (pmol/8 x 10^8 RBC)?

5.5 Presentation

Did the patient present because of:

☐ Routine monitoring ☐ Sepsis

☐ Opportunistic blood test ☐ Other

5.6 Leucopaenia

	Date	Total white cell count	Neutrophil count	Haemoglobin	Platelet count
Normal range for lab	dd/mm/yyyy				
Last blood test prior to commencing thiopurine	dd/mm/yyyy				
First blood test demonstrating leucopaenia (below normal range for your lab)	dd/mm/yyyy				
Blood test demonstrating lowest total white cell count	dd/mm/yyyy				
Blood test demonstrating lowest neutrophil count	dd/mm/yyyy				

Section 5 - Leucopaenia History

Study code

5.7 Recovered cell counts

	Date	Cell count
Best recovered total white cell count within 8 weeks of dose reduction/withdrwal	dd / mm / yyyy	
Best recovered neutrophil count within 8 weeks of dose reduction/withdrawal	dd / mm / yyyy	

Time to best recovered total white cell count/neutrophil count (days)

5.8 Did the patient require hospital admission at any stage due to leucopaenia

☐ Yes ☐ No

If yes, date of admission dd / mm / yyyy

Date of discharge dd / mm / yyyy

5.9 Complications

Any infections? ☐ Yes ☐ No

If yes, please give details

5.10 Was the individual ever re-challenged with a thiopurine?

☐ Yes ☐ No ☐ Unknown

If yes, what was the outcome of the re-challenge?

5.11 Was a bone marrow biopsy done?

☐ Yes ☐ No ☐ Unknown

If yes, please give results

5.12 Was the patient ever treated with G-CSF?

☐ Yes ☐ No ☐ Unknown

If yes, what was the start date? dd / mm / yyyy

What was the end date? dd / mm / yyyy

Did the patient respond?

Did the patient receive any other treatment for leucopaenia?

Section 6 - Supplementary Information

Study code

6.1 What is the individual's thiopurine methytransferase (TPMT) genotype/ activity ?

Genotype

Activity: ☐ Absent Level (U/ml)

☐ Low (carrier)

☐ Normal

☐ High

6.2 Has the individual experienced any other adverse effects attributable to azathioprine/mercaptopurine?

☐ Yes ☐ No ☐ Unknown

If yes:

6.2.1 Abnormal LFTs (please give peak ALT/AST and laboratory reference range)

6.2.2 Pancreatitis (please state peak serum amylase/lipase and laboratory reference)

6.2.3 Other (please state):

6.3 Family history

Family history of thiopurine induced leucopaenia ☐ Yes ☐ No ☐ Unknown

If yes, give details

Thiopurine Induced Leucopaenia

Section 7 - Other Drug History

Study code

7.1 Did the patient receive steroids in the 3 months prior to recognition of leucopaenia?

☐ Yes ☐ No ☐ Unknown

If yes, type of steroid

Dose

Date commenced dd / mm / yyyy

Date ceased dd / mm / yyyy

7.2 Other drugs in 3 months prior to development of leucopaenia

Thiopurine Induced Leucopaenia

Section 8 - Principal Investigator Statement Study code

I have reviewed this CRF and confirm that, to the best of my knowledge, it accurately reflects the study information obtained for this participant. All entries were made either by myself or by a person under my supervision who has signed the Delegation and Signature Log.

Prinicpal Investigator's signature

Date dd / mm / yyyy

Principal Investigator's name (print)

ONCE SIGNED, NO FURTHER CHANGES CAN BE MADE TO THIS CRF WITHOUT A SIGNED DATA QUERY FORM