

# International IBD Genetics Consortium

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**PRED4**

**Thiopurine Induced Leucopaenia**

**Case Report Form**

Please stick study label here

**On completion, please return to:**  
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Barrack Road, Exeter, EX2 5SQ, UK

# Thiopurine Induced Leucopaenia

## Introduction

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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)

# Thiopurine Induced Leucopaenia

## 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

# Thiopurine Induced Leucopaenia

## Section 3 - Medical History

Study code

### 3.1 Hospital Details

#### 3.1.1 Consultant Gastroenterologist

Hospital

Hospital address

Consultant telephone

Consultant email

#### 3.1.2 Consultant Haematologist

Hospital

Hospital address

Consultant telephone

Consultant email

### 3.2 Other significant medical history

Yes

No

If yes, please give details here


# Thiopurine Induced Leucopaenia

## 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

L3 Ileocolonic

L2 Colonic

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

B3 Internal penetrating

B2 Stricturing

p Perianal disease modifier

# Thiopurine Induced Leucopaenia

## 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<sup>8</sup> 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				

# Thiopurine Induced Leucopaenia

## 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?



# Thiopurine Induced Leucopaenia

Section 6 - Supplementary Information

Study code

## 6.1 What is the individual's thiopurine methyltransferase (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 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.

Principal 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**