

International IBD Genetics Consortium

PRED4

Thiopurine Induced Liver Injury

Case Report Form

Study Code

Please stick study label here

On completion, please return to:
IBD Pharmacogenetics Research Office
The Research, Innovation, Learning and Development Centre (RILD)
Barrack Road
Exeter
EX2 5DW

Thiopurine Induced Liver Injury

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.

Thiopurine Induced Liver Injury

Section 1 - Inclusion Criteria

Study code

1.1 Major criteria (all must be met)

- History of inflammatory bowel disease
- Normal ALT and bilirubin at baseline
- No pre-existing liver disease
- Elevation of ALT and/or bilirubin to ≥ 5 times upper limit of normal (defined by local lab)
- History of thiopurine exposure in the previous 30 days prior to this abnormal blood test
- Medical opinion implicating thiopurine in development of hepatotoxicity leads to dose reduction or drug withdrawal (even if temporary)

1.2 Other risk factor(s) or potential causes for elevated liver enzymes

Drugs: Yes No Unknown

If yes, please specify

Was this drug withdrawn?

 Yes No

If yes, date

Alcohol use: Yes No Unknown

If yes, please provide estimated daily intake

Tests done to rule out other causes (provide results if done)

Hepatitis A IgM antibody	
HbsAg	
HCV antibody	
Hepatitis E IgM antibody	
Anti-smooth muscle antibody or anti-LKM antibody	
Immunoglobulin G (IgG) level	
Anti-mitochondrial antibody	
Serum copper/caeruloplasmin	
Haemochromatosis genotyping	
Alpha-1 antitrypsin	
Imaging (U/S or MRI showing no biliary dilatation or other biliary abnormality)	
Other	

1.3 Participant's eligibility

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 name (print)

Date

Thiopurine Induced Liver Injury

Section 2 - Patient Details

Study code

2.1 Patient details

Date of Birth

dd / mm / yyyy

Sex: M

F

Weight at time of liver injury (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

Name of person taking consent (print)

Designation

Thiopurine Induced Liver Injury

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 Ulcerative colitis

4.2.1 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

4.2.2 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

4.3 Crohn's disease

4.3.1 Location

L1 Ileal

L3 Ileocolonic

L2 Colonic

L4 Isolated upper disease

4.3.2 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 Liver Injury

Section 5 - Liver Injury History

Study code

5.1 Which thiopurine was suspected of causing liver injury?

Azathioprine

Mercaptopurine

5.2 Date thiopurine first commenced

dd / mm / yyyy

5.3 Maximum dose of thiopurine in 1 month prior to episode of abnormal LFTs

5.3.1 Date when this maximum dose of thiopurine started

dd / mm / yyyy

5.4 Presentation

Did the patient present because of:

Routine monitoring

Opportunistic blood test

Symptoms (give details)

Other

5.5 Blood test results

	Date	ALT	Bilirubin	AST	GGT	ALP	Albumin	WCC	Hb	INR	Platelets
Normal range for your lab	dd/mm/yyyy										
Baseline (last blood test before starting thiopurine)	dd/mm/yyyy										
First blood test showing elevated ALT/ bilirubin (above reference range for your lab)	dd/mm/yyyy										
Blood test showing worst ALT	dd/mm/yyyy										
Blood test showing worst bilirubin	dd/mm/yyyy										
First recovered ALT (within normal range)	dd/mm/yyyy										
First recovered bilirubin (within normal range)	dd/mm/yyyy										

Thiopurine Induced Liver Injury

Section 5 - Liver Injury History

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5.6 Were thiopurine metabolites measured within 2 months of hepatotoxicity?

Yes No

If yes, please give details

Date

6-TGN

6-MMP

5.7 Action taken

Drug withdrawn Date

Dose decreased Date

Reduced dose

Tolerated (normal LFTs on this dose) Not tolerated Not known

Allopurinol started Date

Decreased thiopurine dose

Tolerated (normal LFTs on this dose) Not tolerated Not known

5.8 Was a liver biopsy done?

Yes No Unknown

If yes, please give results

5.9 Did the patient require hospital admission at any stage due to liver toxicity?

Yes No Unknown

If yes, date of admission

Date of discharge

Details

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

Yes No Unknown

If yes:

Date of recommencement

Thiopurine used Azathiopurine Mercaptopurine Not known

Outcome Tolerated (no adverse reaction)

Dose tolerated

Not tolerated

Adverse reaction

Date drug withdrawn

Thiopurine Induced Liver Injury

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