International IBD Genetics Consortium

PRED4

Thiopurine Hypersensitivity Reaction

Case Report Form

Study Code

Please stick study label here

On completion, please return to:

Exeter IBD Pharmacogenetics Research Office
The Research, Innovation, Learning and Development Centre (RILD)
Barrack Road
Exeter
EX2 5DW

Thiopurine Hypersensitivity Reaction
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 Hypersensitivity Reaction

Section 1 - Inclusion Criteria

Study code ☐

1.1 Inclusion criteria (all must be met)

- ☐ Aged 6 years or over
- ☐ History of inflammatory bowel disease
- ☐ History of thiopurine exposure in the previous 7 days before the onset of adverse event
- ☐ Flu-like symptoms severe enough to lead to drug withdrawal even if temporary (symptoms should include one of the following: fever, muscle ache, joint pain)
- ☐ Onset of hypersensitivity reaction within 4 weeks of starting thiopurine
- ☐ Symptoms of hypersensitivity reaction resolved within 14 days of drug withdrawal (for historical cases, please use clinical judgement when defining this inclusion)

1.2 Exclusion criteria

- ☐ Patient tolerated re-challenge with the same thiopurine regardless of dose
- ☐ Drug withdrawn due to nausea and/or diarrhoea without any other symptoms
- ☐ Objective evidence of infection at the time of the onset of hypersensitivity reaction

1.3 Participant's eligibility

Is the participant eligible to take part in the research project based on the above criteria?

☐ Yes ☐ No

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

1.
2.
3.

Investigator's name (print) ☐ Date dd / mm / yyyy

Section 2 - Patient Details

Study code

2.1 Patient details

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

Weight at time of hypersensitivity reaction 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

Hospital name

Section 3 - Medical History

Study code

3.1 Other significant medical history

☐ Yes ☐ No

If yes, please give details here

3.2 Smoking history

☐ Never smoked ☐ Ex-smoker ☐ Current smoker

3.2.1 Start date dd / mm / yyyy

3.2.2 End date dd / mm / yyyy

3.2.3 Maximum number of cigarettes per day

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
- ☐ E2 Left sided UC (distal UC)
- ☐ E3 Extensive UC (pancolitis)
- ☐ Ex Unknown

4.2.2 Disease severity in 2 years prior to development of hypersensitivity reaction

- ☐ DS0 Clinical remission
- ☐ DS1 Mild relapses
- ☐ DS2 Moderate relapse
- ☐ DS3 Severe or refractory disease requiring inpatient admission or colectomy

4.3 Crohn's disease

4.3.1 Location

- ☐ L1 Ileal
- ☐ L2 Colonic
- ☐ L3 Ileocolonic
- ☐ 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
- ☐ B2 Stricturing
- ☐ B3 Internal penetrating
- ☐ p Perianal disease modifier

Section 5 - Hypersensitivity Reaction History

Study code

5.1 Which thiopurine was suspected of causing the hypersensitivity reaction?

☐ Azathioprine ☐ Mercaptopurine

5.2 Date thiopurine first commenced

dd / mm / yyyy

5.3 Maximum dose of thiopurine in 1 month prior to the hypersensitivity reaction

5.3.1 Date when this maximum dose was started

dd / mm / yyyy

5.4 Presentation

5.4.1 Symptoms

Date of onset of symptoms dd / mm / yyyy

Please tick all symptoms that apply:

☐ Fever
☐ Joint pain
☐ Muscle ache or pain
☐ Headache
☐ Fatigue
☐ General malaise
☐ Rash
☐ Nausea
☐ Vomiting
☐ Diarrhoea
☐ Other (please indicate)

Approximate duration of symptoms ☐ days

5.5 Blood test results

	Date	ALT	Date	Bilirubin	Date	WCC	Date	CRP
Normal range for your lab	dd/mm/yyyy		dd/mm/yyyy		dd/mm/yyyy		dd/mm/yyyy	
Baseline (last blood test before starting thiopurine)	dd/mm/yyyy		dd/mm/yyyy		dd/mm/yyyy		dd/mm/yyyy	
Worst blood test during presentation of symptoms	dd/mm/yyyy		dd/mm/yyyy		dd/mm/yyyy		dd/mm/yyyy	
Blood test >2 weeks after drug withdrawal	dd/mm/yyyy		dd/mm/yyyy		dd/mm/yyyy		dd/mm/yyyy	

5.6 Did the patient require hospital admission at any stage due to the hypersensitivity reaction?

☐ Yes ☐ No ☐ Unknown

If yes, date of admission dd / mm / yyyy

Date of discharge dd / mm / yyyy

Details

5.7 Tests conducted for investigation of hypersensitivity reaction

	Date	Please specify further details if positive or abnormal finding
None	dd/mm/yyyy	
Blood cultures	dd/mm/yyyy	
Urine culture	dd/mm/yyyy	
X-ray	dd/mm/yyyy	
CT	dd/mm/yyyy	
MRI	dd/mm/yyyy	
Ultrasound	dd/mm/yyyy	

Section 6 - Supplementary Information

Study code

6.1 Was the patient ever re-challenged with a thiopurine?

☐ Yes ☐ No ☐ Unknown

If yes:

Date of recommencement dd / mm / yyyy

Thiopurine used: ☐ Azathioprine ☐ Mercaptopurine ☐ Not known

Outcome:

☐ Tolerated (no adverse reaction)

Dose tolerated

☐ Not tolerated

Adverse reaction (please give details)

Was this similar to the previous reaction?

Date drug withdrawn dd / mm / yyyy

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

Genotype Level (u/ml)

Activity:
☐ Absent
☐ Low (carrier)
☐ Normal
☐ High

☐ Not done

Section 6 - Supplementary Information

Study code

6.3 Has the individual ever experienced any other adverse effects attributed to azathioprine/mercaptopurine?

☐ Yes ☐ No ☐ Unknown

If yes, please record below

6.3.1 Leucopenia - please give lowest WCC with dates

6.3.2 Pancreatitis - please give peak serum amylase/lipase and laboratory reference and dates

6.3.3 Liver injury - please give peak ALT/Bilirubin

6.4 Other comments

If you have any other comments regarding this patient, please give them here.

Section 7 - Other Drug History

Study code

7.1 Please record below the concomitant medication taken in the 7 days prior to the commencement of the hypersensitivity reaction.

Drug name	Dose, route and frequency	Start date	Stop date
		dd / mm / yyyy	dd / mm / yyyy
		dd / mm / yyyy	dd / mm / yyyy
		dd / mm / yyyy	dd / mm / yyyy
		dd / mm / yyyy	dd / mm / yyyy
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Thiopurine Hypersensitivity Reaction

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 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