International IBD Genetics Consortium

PRED4

Thiopurine Induced Pancreatitis

Case Report Form

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 Pancreatitis
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.

*** Other risk factors or potential causes for pancreatitis**

Gallstones, alcohol, hyperlipidaemia (in particular hypertriglyceridaemia), other drugs (metronidazole, tetracycline, frusemide, thiazides, sulphasalazine, 5-ASA), infection (e.g. Viruses-mumps, coxsackie, hepatitis B, CMV, varicella-zoster, HSV), post-ERCP, ischaemia, trauma

Thiopurine Induced Pancreatitis

Section 1 - Inclusion Criteria

Study code

1.1 Major criteria (all must be met)

- ☐ History of inflammatory bowel disease
- ☐ Acute severe abdominal pain
- ☐ History of thiopurine exposure in the previous 7 days
- ☐ Rise in serum pancreatic enzymes (amylase/lipase) (≥2 times upper limit of normal)
- ☐ Episode of acute pancreatitis within 3 months of starting thiopurine
- ☐ Medical opinion implicates thiopurine as the mostly likely cause of pancreatitis, and drug withdrawn

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

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

If yes, please specify

1.3 Minor criteria

- ☐ Imaging supports diagnosis of acute pancreatitis
- ☐ Recurrence of symptoms on re-challenge with either Azathioprine or Mercaptopurine
- ☐ Symptoms resolved rapidly on drug withdrawal (within 7 days)

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 when diagnosed with IBD (or nearest estimate) ☐ kg

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

Hospital

Hospital address

Consultant telephone

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 pancreatitis

- ☐ 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 - Pancreatitis History

Study code

5.1 Which thiopurine was suspected of causing pancreatitis?

☐ Azathioprine ☐ Mercaptopurine

5.2 Date thiopurine first commenced dd / mm / yyyy

5.3 Date of onset of acute pancreatitis episode dd / mm / yyyy

5.4 Maximum dose of thiopurine in 8 weeks prior to episode of acute pancreatitis

5.5 Peak serum amylase or lipase (and laboratory normal range) + date

Peak serum amylase or lipase

Normal range Date dd / mm / yyyy

5.6 Date drug withdrawn dd / mm / yyyy

5.7 Did the patient require hospital admission

☐ Yes ☐ No

If yes date of admission dd / mm / yyyy

Date of discharge dd / mm / yyyy

5.8 Did the individual have imaging evidence of pancreatitis (e.g. CT or Ultrasound) consistent with the timing of the symptoms?

☐ Yes ☐ No ☐ Unknown

If yes, please state modality and brief radiological findings

5.9 Severity – according to the modified Atlanta classification

- ☐ Mild acute pancreatitis (Associated with minimal organ dysfunction and an uneventful recovery; lacks the features of severe acute pancreatitis. Usually normal enhancement of pancreatic parenchyma on contrast-enhanced computed tomography)
- ☐ Severe acute pancreatitis (Associated with organ failure and/or local complications such as necrosis, abscess or pseudocyst)

5.10 Any organ failure and systemic complications?

☐ Yes ☐ No ☐ Unknown

If yes:
- ☐ Shock (Systolic blood pressure <90 mmHg)
- ☐ Pulmonary insufficiency (PaO2 ≤ 60 mmHg)
- ☐ Renal failure (Creatinine ≥177 umol/l or ≤2 mg/dl after rehydration)
- ☐ Disseminated intravascular coagulation (Platelets ≤100,000/mm3, fibrinogen <1·0 g/l and fibrin-split products >80 mg/l)
- ☐ Severe metabolic disturbances (Calcium ≤1·87 mmol/l)
- ☐ Death

5.11 Any local complications?

☐ Yes ☐ No ☐ Unknown

If yes:
- ☐ Acute fluid collections (Occur early in the course of acute pancreatitis, are located in or near the pancreas)
- ☐ Pancreatic necrosis (Diffuse or focal area(s) of non-viable pancreatic parenchyma, typically associated with peripancreatic fat necrosis)
- ☐ Acute pseudocyst (Collection of pancreatic juice enclosed by a wall of fibrous or granulation tissue, which arises as a result of acute pancreatitis, pancreatic trauma or chronic pancreatitis, occurring at least 4 weeks after onset of symptoms)
- ☐ Pancreatic abscess (Circumscribed, intra-abdominal collection of pus, usually in proximity to the pancreas, containing little or no pancreatic necrosis, which arises as a consequence of acute pancreatitis or pancreatic trauma; Often 4 weeks or more after onset)

Section 5 - Pancreatitis History

Study code

5.12 Did the patient have a rash?

☐ Yes ☐ No ☐ Unknown

Was a skin biopsy carried out? ☐ Yes ☐ No

Histology

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

☐ Yes ☐ No ☐ Unknown

If yes:

Date of recommencement dd / mm / yyyy

Thiopurine used ☐ Azathiopurine ☐ Mercaptopurine ☐ Not known

Outcome ☐ Tolerated (no adverse reaction)

Dose tolerated

☐ Not tolerated

Adverse reaction

Peak Amylase/lipase Date dd / mm / yyyy

Date drug withdrawn dd / mm / yyyy

Section 6 - Supplementary Information

6.1 Evidence that might suggest an alternative cause of pancreatitis?

6.1.1 Did the individual have a history of alcohol use that is more than the current recommended amount (i.e. 14 standard drinks/week for females and 21 standard drinks/week for males)?

☐ Yes ☐ No ☐ Unknown

If yes, please state amount (Units/week)

6.1.2 Did the individual have evidence of gallstones on imaging?

☐ Yes ☐ No ☐ Not done ☐ Unknown

6.1.3 Did the individual have a history of previous acute or chronic pancreatitis, unrelated to thiopurines?

☐ Yes ☐ No ☐ Unknown

Section 6 - Supplementary Information

Study code

6.1.4 Family history

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

If yes, give details

6.1.5 If any other potential causes of pancreatitis were identified (e.g. other drugs including 5-ASAs) please specify (see page 2)*:

6.2 Other causes of a rise in serum amylase**

☐ Yes ☐ No ☐ Unknown

*** Causes of elevated amylase or lipase*

Surgery, ERCP, Ductal obstruction, Pancreatic carcinoma, Cystic fibrosis, Infection, Trauma, Peptic ulcer, Perforated bowel, Liver disease, Severe gastroenteritis, Ruptured ectopic pregnancy, Ovarian or fallopian cysts, Neoplasms, Renal failure, Alcoholism, Pregnancy, Anorexia nervosa, Bulimia, Cholecystitis

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

Genotype Level (U/ml)

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

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

☐ Yes ☐ No ☐ Unknown

If yes:

6.4.1 Abnormal LFTs (please give peak ALT/AST)

Section 6 - Supplementary Information

Study code

6.4.2 Leucopaenia (please give lowest total white cell count/neutrophil count)

WCC (x10^9/L):

Neutrophils (x10^9/L):

6.4.3 Other (please state):

Section 7 - Other Drug History

7.1 Other drugs in 3 months prior to developing pancreatitis

Drug name	Dose and Route	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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		dd / mm / yyyy	dd / mm / yyyy

Thiopurine Induced Pancreatitis

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