

International IBD Genetics Consortium

PRED4

Thiopurine Induced Pancreatitis

Case Report Form

Please stick study label here

On completion, please return to:
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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 furosemide, 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- Medical opinion implicates thiopurine as the mostly likely cause of pancreatitis, and drug withdrawn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 (sum number of 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)

Thiopurine Induced Pancreatitis

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

Thiopurine Induced Pancreatitis

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

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 Pancreatitis

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 Did the patient require hospital admission

Yes

No

If yes date of admission

dd / mm / yyyy

Date of discharge

dd / mm / yyyy

5.7 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

5.8 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)

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Section 5 - Pancreatitis History

Study code

5.9 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 μmol/l or ≤2 mg/dl after rehydration)
 - Disseminated intravascular coagulation (Platelets ≤100, 000/mm³, fibrinogen <1.0 g/l and fibrin-split products >80 μg/l)
 - Severe metabolic disturbances (Calcium ≤1.87 mmol/l)
 - Death

5.10 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)

5.11 Did the patient have a rash?

Yes No Unknown

Was a skin biopsy carried out? Yes No

Histology

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

Yes No Unknown

If yes, did the individual tolerate the re-challenge?

Yes No – recurrent pancreatitis (defined as severe abdominal pain +/- rise in amylase)

No – other (please specify) Unknown

Thiopurine Induced Pancreatitis

Section 6 - Supplementary Information

Study code

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

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

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Section 6 - Supplementary Information

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6.3 What is the individual's thiopurine methyltransferase (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)

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

WCC ($\times 10^9/L$): Neutrophils ($\times 10^9/L$):

6.4.3 Other (please state):

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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

Principal Investigator's name (print)

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