International IBD Genetics Consortium

PRED4

Sulphasalazine Induced Neutropaenia

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

Sulphasalazine Induced Neutropaenia
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.

*Drug causes of neutropaenia

- Antithyroid drugs (thionamides – Methimazole, Carbimazole, Propylthiouracil)
- Anti-inflammatory drugs (Nonsteroidal anti-inflammatory drugs [NSAIDs], Penicillamine, Gold, Hydroxychloroquinine)
- 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

Section 1 - Inclusion Criteria

Study code

1.1 Major criteria (all must be met)

- ☐ History of inflammatory bowel disease or rheumatoid arthritis
- ☐ History of sulphasalazine exposure in the 30 days prior to developing neutropaenia
- ☐ Normal total white cell count and/or neutrophil count at baseline
- ☐ Fall in neutrophil count to $\leq 0.5 \times 10^9$/L
- ☐ Medical opinion implicating sulphasalazine leads to dose reduction or drug withdrawal (even if temporary)

1.2 Other risk factor(s) or potential causes for neutropaenia

- ☐ No
- ☐ Yes

If yes:

- ☐ Drugs, please specify (*see page 2)
- ☐ Lab data suggestive of recent viral infection, e.g. CMV, EBV

If yes, please provide details

- ☐ Myeloproliferative diseases
- ☐ SLE
- ☐ Hypersplenism
- ☐ Other, please specify

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 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 neutropaenia (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

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 4a - Diagnosis & Classification of IBD Study code

Please fill the appropriate disease section (4a for individuals with IBD and 4b for individuals with rheumatological disorders). If the individual has both, please complete both section 4a and 4b.

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 neutropaenia

- ☐ 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
- ☐ 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

4.4 Rheumatoid Arthritis

Date of diagnosis dd / mm / yyyy

4.4.1 Behaviour

Erosive Disease ☐ Yes ☐ No ☐ Unknown

4.4.2 Type

☐ Seropositive RA ☐ Seronegative RA ☐ Inflammatory polyarthritis

4.4.3 Antibody profile

ANA	☐ Yes	☐ No	☐ Unknown
Rheumatoid factor	☐ Yes	☐ No	☐ Unknown
Anti-CCP	☐ Yes	☐ No	☐ Unknown

4.4.4 Extra-articular manifestations

☐ Rheumatoid nodules
☐ Pyoderma gangreosum
☐ Interstitial lung disease
☐ Pleural effusion
☐ Scleritis
☐ Episcleritis
☐ Keratitis
☐ Cutaneous vasculitis
☐ Raynaud's phenomenon
☐ Pulmonary nodules
☐ Pulmonary vasculitis
☐ Pericarditis
☐ Mononeurritis multiplex
☐ Felty's syndrome

4.5 Seronegative Spondyloarthropathy

(please select on or more of the following diagnoses)

☐ Psoriatic arthritis
☐ Ankylosing spondylitis
☐ Enteropathic arthritis
☐ Reactive arthritis
☐ Undiffrentiated spondyloarthropathy

Date of diagnosis dd / mm / yyyy

Section 5 - Neutropaenia History

Study code

5.1 Date sulphasalazine first commenced

dd / mm / yyyy

5.2 Maximum dose of sulphasalazine in 1 month prior to episode of neutropaenia

5.2.1 Date when this maximum dose of sulphasalazine started

dd / mm / yyyy

5.3 Presentation

Did the patient present because of:

- ☐ Routine monitoring
- ☐ Sepsis
- ☐ Opportunistic blood test
- ☐ Unknown
- ☐ Other

5.4 Neutropaenia

	Date	Total white cell count	Neutrophil count	Haemoglobin	Platelet count
Normal range for lab	dd/mm/yyyy				
Baseline (last blood test prior to commencing sulphasalazine)	dd/mm/yyyy				
First blood test showing neutropaenia (below normal range for your lab)	dd/mm/yyyy				
Blood test demonstrating lowest total neutrophil count	dd/mm/yyyy				
First recovered neutrophil count (within normal range)	dd/mm/yyyy				

Section 5 - Neutropaenia History

Study code

5.5 Action taken

☐ Dose decreased Date dd / mm / yyyy

Reduced dose

☐ Tolerated (normal ALT/bilirubin on the dose) ☐ Not tolerated ☐ Not known

☐ Drug withdrawn Date dd / mm / yyyy

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

☐ Yes ☐ No ☐ Unknown

If yes, date of admission dd / mm / yyyy

Date of discharge dd / mm / yyyy

Details

5.7 Complications

Any infections during the neutopaenic episode? ☐ Yes ☐ No

If yes, please give details (infective condition, organism)

5.8 Was the individual ever re-challenged with sulphasalazine?

☐ Yes ☐ No ☐ Unknown

Outcome:

☐ Tolerated Dose tolerated

☐ Not tolerated Adverse reaction

Date of drug withdrawal dd / mm / yyyy

5.9 Was a bone marrow biopsy done?

☐ Yes ☐ No ☐ Unknown

If yes, please give results

5.10 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 neutropaenia?

Section 6 - Supplementary Information

Study code

6.1 Has the individual experienced any other adverse effects attributable to sulphasalazine?

☐ Yes ☐ No ☐ Unknown

If yes:

☐ Gastrointestinal

☐ Rash

☐ Pancreatitis (please provide peak amylase levels with normal range and date of test)

☐ Abnormal LFTs (please provide abnormal LFTs and date)

☐ Other

6.2 Other comments

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

Section 7 - Other Drug History

Study code

7.1 Other drugs in 3 months prior to development of neutropaenia

Drug name	Dose and frequency	Start date	Stop date
		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

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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 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