

# A prospective randomised controlled trial of thiopurine methyltransferase (TPMT) genotyping in the management of patients, prior to commencement of azathioprine

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|----------------------------------------|---------------------------------------------------|---------------------------------------------------------------------------------------------------|
| <b>Submission date</b><br>07/03/2005   | <b>Recruitment status</b><br>No longer recruiting | <input checked="" type="checkbox"/> Prospectively registered<br><input type="checkbox"/> Protocol |
| <b>Registration date</b><br>29/06/2005 | <b>Overall study status</b><br>Completed          | <input type="checkbox"/> Statistical analysis plan<br><input checked="" type="checkbox"/> Results |
| <b>Last Edited</b><br>04/08/2011       | <b>Condition category</b><br>Other                | <input type="checkbox"/> Individual participant data                                              |

**Plain English summary of protocol**  
Not provided at time of registration

## Contact information

**Type(s)**  
Scientific

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## Additional identifiers

**Protocol serial number**  
PHGX09A

## Study information

## **Scientific Title**

### **Acronym**

TARGET (TPMT: Azathioprine Response to Genotyping and Enzyme Testing)

### **Study objectives**

This study uses a prospective randomised controlled trial (PRCT) design, to assess the clinical utility and relative cost effectiveness of a pharmacogenetic test (PGx) (TPMT: Thiopurine Methyltransferase) for use in patients treated with azathioprine (AZA) for inflammatory conditions. The objectives are to:

- a. Assess the relative clinical outcomes of using a PGx test in patients eligible for treatment with AZA as part of their routine care compared with standard care
- b. Assess the relative impact on health-related quality of life of using a PGx test in patients eligible for treatment with AZA as part of their routine care compared with standard care
- c. Identify the relative amounts of resource use and associated costs incurred by the NHS during the clinical consultation, associated laboratory tests and subsequent treatments in patients eligible for treatment with AZA as part of their routine care compared with standard care
- d. Use clinical, cost and quality of life data collected in this study to assess the relative cost effectiveness (value for money) of a PGx test compared to standard care in treatment with AZA
- e. Value service providers and users preferences for the outcome and process components of a PGx test

The project comprises a number of discrete studies that will each be used to address the stated research questions:

1. A national survey of prescribing practice in AZA
2. A PRCT of the clinical and relative cost effectiveness of a PGx test compared to standard care for a patient population who are eligible for treatment with AZA
3. A preference study to identify service users and providers views about introducing a PGx test
4. A phenotyping study investigating genotype-phenotype interactions and the potential role of other genes in the disease/treatment pathways
5. A study that examines the influences of various genetic variants on response to other immunosuppressive drugs including steroids and the new biologic agents

### **Ethics approval required**

Old ethics approval format

### **Ethics approval(s)**

Not provided at time of registration

### **Primary study design**

Interventional

### **Study design**

Randomised controlled trial

### **Study type(s)**

Treatment

### **Health condition(s) or problem(s) studied**

Inflammatory bowel disease, arthritides and atopic dermatitis

## **Interventions**

Intervention: Genotyping for TPMT + standard care

Control: Standard care with no TPMT genotyping

## **Intervention Type**

Drug

## **Phase**

Not Specified

## **Drug/device/biological/vaccine name(s)**

Azathioprine

## **Primary outcome(s)**

Neutropaenia (defined as a neutrophil count falling below  $1 \times 10^9/l$ ) in the first four months of maintenance AZA treatment.

## **Key secondary outcome(s)**

1. Reduction of AZA dose or stopping AZA because of intolerance in the first four months of maintenance AZA treatment.
2. Moderate neutropaenia (defined as a neutrophil count falling below  $1.5 \times 10^9/l$ ) in the first four months of maintenance AZA treatment.
3. No reduction in drug efficacy in each of the three conditions (IBD, arthritides and atopic dermatitis) under study because of changes in the dose prescribed. This will be measured using standard tools to value improvement in clinical status for each condition, which will be collected on day 0 and month 4.
4. Patients who stop AZA therapy because of non-haematological toxicity within 4 months (e.g. nausea, hepatotoxicity, pancreatitis). This will be measured by recording all side effects attributed to AZA throughout the study period.
5. Health related quality of life status. A standardised generic health status measurement tool, the EQ-5D (EuroQoL), will be used to assess the impact on health related quality of life. The EQ-5D (EuroQoL) will be completed by all study participants on two occasions (day 0 and month 4).

## **Completion date**

31/12/2007

## **Eligibility**

### **Key inclusion criteria**

Adult patients assessed as eligible for treatment with oral azathioprine in the management of selected conditions in gastroenterology, rheumatology or dermatology.

Selected conditions in gastroenterology (ulcerative colitis, Crohn's disease, indeterminate colitis, autoimmune hepatitis), rheumatology (rheumatoid arthritis, systemic lupus erythematosus, vasculitis, Wegener's granulomatosis, dermatomyositis) or dermatology (atopic dermatitis, contact dermatitis, chronic actinic dermatitis).

### **Participant type(s)**

Patient

**Healthy volunteers allowed**

No

**Age group**

Adult

**Sex**

All

**Key exclusion criteria**

Not provided at time of registration

**Date of first enrolment**

01/10/2005

**Date of final enrolment**

31/12/2007

**Locations****Countries of recruitment**

United Kingdom

England

**Study participating centre**

**Centre for Integrated Genomic Medical Research (CIGMR)**

Manchester

United Kingdom

M13 9PL

**Sponsor information****Organisation**

Laboratory of the Government Chemist (LGC) on behalf of the UK Department of Health

**ROR**

<https://ror.org/03sbpja79>

**Funder(s)****Funder type**

Government

**Funder Name**

Department of Health, Pharmacogenetics Research Programme PHGX09A, UK

## Results and Publications

**Individual participant data (IPD) sharing plan****IPD sharing plan summary**

Not provided at time of registration

**Study outputs**

| Output type                     | Details | Date created | Date added | Peer reviewed? | Patient-facing? |
|---------------------------------|---------|--------------|------------|----------------|-----------------|
| <a href="#">Results article</a> | results | 01/06/2011   |            | Yes            | No              |