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

Submission date 07/03/2005	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol
Registration date 29/06/2005	**Overall study status** Completed	[_] Statistical analysis plan [X] Results
Last Edited 04/08/2011	**Condition category** Other	[_] 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

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
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

Study design
Randomised controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Not specified

Study type(s)
Treatment

Participant information sheet

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 TMPT genotyping

Intervention Type
Drug

Phase
Not Specified

Drug/device/biological/vaccine name(s)
Azathioprine

Primary outcome measure
Neutropaenia (defined as a neutrophil count falling below 1 x 10^9/l) in the first four months of maintenance AZA treatment.

Secondary outcome measures
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 x 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).

Overall study start date
01/10/2005

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

Age group
Adult

Sex
Both

Target number of participants
1000

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
England

United Kingdom

Study participating centre
Centre for Integrated Genomic Medical Research (CIGMR)
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Sponsor information

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

Sponsor details
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Sponsor type
Government

ROR
https://ror.org/03sbpja79

Funder(s)

Funder type
Government

Funder Name
Department of Health, Pharmacogenetics Research Programme PHGX09A, UK

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

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?
Results article	results	01/06/2011		Yes	No