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Randomised controlled trial of 6-Mercaptopurine (6MP) versus placebo to prevent recurrence of Crohn's disease following surgical resection

Submission date
22/02/2007

Registration date
15/06/2007

Last Edited
18/04/2017

Recruitment status
No longer recruiting

Overall study status
Completed

Condition category
Digestive System

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol
http://www.clinicaltrials.ed.ac.uk/TrialsPortfolio.aspx

Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
G0600329

Study information

Scientific Title
Randomised controlled trial of 6-Mercaptopurine (6MP) versus placebo to prevent recurrence of Crohn's disease following surgical resection

Acronym
TOPPIC (Trial Of Prevention of Post-operative Crohn's disease)

Study objectives
Therapy with 6 MP prevents or delays post-operative recurrence of Crohn's disease.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Scotland A Research Ethics Committee, NHS Scotland, 14/08/2007, ref: 07/MRE00/74

Study design
Multi-centre double-blind randomised placebo-controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Crohn's disease

Interventions
Patients randomised to treatment with 6MP or matching placebo. 6MP will be given at a dose of 1 mg per kg body weight per day, rounded to the nearest 25 mg, for 3 years or until study drug is permanently discontinued. Safety monitoring of 6MP will be performed continuously throughout the trial, involving full blood count and liver function tests at appropriate intervals

Intervention Type
Drug

Phase
Not Applicable

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

Primary outcome(s)
Post-operative recurrence of Crohns disease requiring anti-inflammatory rescue therapy and time of recurrence

Key secondary outcome(s))
1. The need for a second operation to remove recurrent Crohns disease from the anastomotic site

2. Changes in quality of life scores (assessed at 4 weeks [baseline/randomisation], 17 weeks, 1 year, 2 and 3 years using Inflammatory Bowel Disease Questionnaire [IBDQ], Medical Outcome Survey Short Form 36 [SF-36] and EQ-5D)
3. Endoscopic recurrence of Crohns disease (assessed at 1 year and 3 years)
4. Relation of faecal calprotectin to time of disease recurrence
5. Relation of drug metabolite levels to time of disease recurrence
6. Exploratory analyses of clinical, genetic and serological markers for predicting disease recurrence

Completion date
30/09/2015

Eligibility

Key inclusion criteria
Current inclusion criteria as of 15/03/2011:
1. At least 16 years of age in Scotland and 18 years of age in England and Wales
2. Established diagnosis of Crohn's disease confirmed at recent resection
3. Ileocolonic or small bowel resection within 3 months before screening
4. No more than 100 cm of fixed small bowel resected in total. Previous ileocolonic resection is acceptable
5. Able to start oral nutrition within the first 2 postoperative weeks
6. Normal or heterozygous TPMT (activity present or reduced consistent with carrier status)
7. Able to provide written informed consent prior to screening and to comply with the requirements of the study protocol
8. Off antibiotics 2 weeks prior to randomisation

Previous inclusion criteria:
1. Male or female, at least 16 years of age in Scotland and 18 years of age in England and Wales
2. Established diagnosis of Crohns disease
3. Ileocolonic resection within 3 months
4. Able to start oral nutrition and medication within the first 2 postoperative weeks
5. Normal or heterozygous Thio Purine Methyl-Transferase (TPMT) genotype
6. No more than 100 cm of fixed small bowel resected in total. Previous ileocolonic resection is acceptable
7. Able to provide written informed consent prior to screening and to comply with the requirements of the study protocol

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex

All

Key exclusion criteria

Current exclusion criteria as of 15/03/2011:
1. Pregnancy at baseline or breastfeeding
2. A known hypersensitivity or intolerance to 6MP
3. Pancreatitis associated with azathioprine
4. Receiving an experimental treatment for Crohn's disease in the 4 weeks prior to study entry
5. Known to require further surgery at study entry i.e. for the removal of an abscess developing from the primary surgery
6. Strictureplasty procedure alone
(Please note that strictureplasty and resection procedure together will not be considered an exclusion)
7. Presence of stoma
8. Significant haematological, renal or hepatic dysfunction or clinically important lung disease (i. e. liver function tests [except GGT] >x2 upper limit of normal, haemoglobin ¡Ü10, total white blood cell count <3.5, neutrophils <1.5, platelets <100x106/l)
9. Systemic infection including hepatitis B, hepatitis C, HIV and active TB
10. A diagnosis of indeterminate colitis or ulcerative colitis
11. A history of illicit drug or alcohol abuse in the 1 year prior to study entry
12. Active or untreated malignancy (excluding basal cell carcinoma and in situ tumours).
(Patients who have had successful treatment for malignancy and have been in remission for more than 5 years may be considered for inclusion only after detailed discussion with, and written approval, from the patient's medical oncologist)
13. Presence of a medical or psychiatric condition, disease or laboratory abnormality that in the opinion of the PI may place the subject at unacceptable risk during the study
14. Homozygous deficient for TPMT (absent activity)
15. Evidence of untreated post-operative infection e.g. clostridium difficile, urinary tract infection or chest infection. If these have been appropriately treated in the opinion of the PI, and inclusion criteria 8 is met, this will not be considered an exclusion
16. Taking any medication for Crohn's disease

Previous exclusion criteria:
1. Pregnancy or breastfeeding
2. Hypersensitivity or intolerance to 6MP or pancreatitis associated with azathioprine
3. Receiving an experimental treatment for Crohns disease in the 4 weeks prior to study entry
4. Known to require further surgery at study entry
5. Presence of stoma
6. Significant renal or hepatic dysfunction, clinically important lung disease
7. Systemic infection including hepatitis C, HIV and active tuberculosis (TB)
8. A diagnosis of indeterminate colitis or ulcerative colitis
9. A history of illicit drug or alcohol abuse in the 1 year prior to study entry
10. History of cancer - excluding basal cell carcinoma treated more than 5 years previously and in situ tumours
11. Presence of a medical or psychiatric condition, disease or laboratory abnormality that in the opinion of the PI may place the subject at unacceptable risk during the study
12. Homozygous deficient for TPMT
13. Initiation of the following drugs during the study is not allowed: corticosteroids (it is expected that patients may be on corticosteroids at entry. Doses will be tapered according to local protocols), anti-tumour necrosis factor, azathioprine, methotrexate, antibiotics (for a duration of >10 days), non-steroidal anti-inflammatory drugs

Date of first enrolment
01/10/2007

Date of final enrolment
31/03/2015

Locations

Countries of recruitment
United Kingdom

Scotland

Study participating centre
Western General Hospital
Edinburgh
United Kingdom
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Sponsor information

Organisation
University of Edinburgh, Lothian Health Board, University Hospitals Division (UK)

ROR
https://ror.org/01nrxwf90

Funder(s)

Funder type
Government

Funder Name
Medical Research Council (UK) (Grant No: G0600329)

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, Medical Research Committee and Advisory Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

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?
Results article	results	01/12/2016		Yes	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes