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The Colitis Once Daily Asacol® study: efficacy and safety of dosing mesalazine in the maintenance of remission of ulcerative colitis

Submission date 23/03/2007	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 10/05/2007	**Overall study status** Completed	
Last Edited 12/08/2016	**Condition category** Digestive System	

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
NCT00708656

Secondary identifying numbers
HAW0105

Study information

Scientific Title
A randomised, multicentre, parallel group single-blind study to assess the efficacy and safety of dosing mesalazine 800 mg tablets (Asacol®) at 2.4 g once daily versus divided doses three times daily for 12 months in the maintenance of remission of ulcerative colitis

Acronym
CODA

Study objectives
Does Asacol® 2.4 g taken daily as a single morning dose prevent relapses of ulcerative colitis as effectively and safely as 800 mg taken three times a day, over a one year period?

Ethics approval required
Old ethics approval format

Ethics approval(s)
Leicestershire, Northamptonshire & Rutland Research Ethics Committee 2, 31/01/2006, ref: 05 /Q2502/156

Study design
Randomised single-blind multi-centre study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
See additional files

Health condition(s) or problem(s) studied
Ulcerative colitis

Interventions
This is a randomised, single-blind, multicentre study in patients with ulcerative colitis who have been in remission for more than four weeks, but no longer than two years, and who are already taking 5-ASA therapy. It will involve approximately 40 to 50 study sites in the UK.

Asacol® 2.4 g daily, taken orally as a single morning dose versu 800 mg taken three times a day, over one-year period.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Asacol®

Primary outcome measure
Proportion in each treatment group who have relapsed by one year, based on an intention to treat. All available follow-up data will be utilised. A per protocol analysis will also be performed restricted to those complying fully with the protocol (who complete the study regardless of treatment outcome, meet inclusion and exclusion criteria, and who take study medication as prescribed, with compliance more than 75%).

Non-inferiority will be concluded if the upper limit of the 95% confidence interval (one sided) for the difference in the proportion of patients relapsing at one year between intervention and control is less than 10%, based on an intention to treat analysis.

Secondary analyses with the primary outcome will repeat the primary analysis, but on a per protocol basis. Where non-inferiority has been shown, a superiority analysis will be conducted. Additional exploratory analysis will assess whether other factors such as time since last relapse prior to study entry, concomitant therapies, extent of disease, disease duration, smoking status, age at diagnosis, and baseline measures act as effect modifiers using logistic regression.

Secondary outcome measures
Secondary analysis will be conducted on both an intention to treat and per protocol basis. The two groups will be compared in terms of the proportion of patients experiencing adverse reactions in each group. It is estimated that this rate will be 2 - 4%. This low rate is likely because all patients entering the study will have already been using mesalazine-containing products. Non-inferiority in terms of safety will be concluded if the limit of 95% one-sided confidence interval for the difference in rate of adverse reactions is less than 4% (with 80% power, assuming an event rate of 4%) . Time until relapse will be compared between the two groups using Kaplan Meier curves.

Mayo scores will be analysed by comparing changes at relapse or 12 months, in comparison to baseline. Individual components of the Mayo score, particularly sigmoidoscopy score, but also rectal bleeding and diarrhoea will be analysed independently.

For each participant, tablet counts will be carried out to estimate a daily dosage in order to check his/her compliance throughout the period of study. The mean daily dosage will be compared between the two groups using a t-test.

Overall study start date
10/07/2005

Completion date
14/07/2011

Eligibility

Key inclusion criteria
1. Male and female patients aged over 18 with ulcerative colitis confirmed by histology who are in remission (no symptoms of active disease, and modified Baron sigmoidoscopic score of 0 or 1)
2. If female, must be (as documented in patient notes) one of the following:
2.1. Post-menopausal (at least 1 year without spontaneous menses)
2.2. Surgically sterile (tubal ligation or hysterectomy at least 6 months prior to enrolment)
2.3. Using acceptable contraception (e.g. oral, intramuscular, or implanted hormonal contraception) at least 3 months prior to enrolment
2.4. Have a sexual partner with non-reversed vasectomy (with confirmed azoospermia)
2.5. Using 1 barrier method (e.g. condom, diaphragm, spermicide, or intra-uterine device)
3. Patients whose ulcerative colitis has been in clinical remission for 4 weeks or longer, and who have had a symptomatic relapse within the past two years
4. Patients taking mesalazine, sulfasalazine or other drug containing 5-aminosalicylic acid (5-ASA) for 4 weeks or longer
5. Patients capable of giving written informed consent

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
250 (previously 660 prior to 26/06/2009)

Key exclusion criteria
1. Patients with Crohns disease
2. Patients with symptoms of active colitis
3. Modified Baron sigmoidoscopy score of 2 or 3
4. Patients who have used oral, enema, intravenous or suppository preparations of corticosteroids, oral or intravenous ciclosporin, mesalazine enemas or suppositories within the past four weeks
5. Patients taking azathioprine or 6-mercaptopurine who have altered the dose or started treatment within the past three months (these drugs are permitted in stable dose during the study)
6. Patients with intolerance to Asacol® 400 mg or mesalazine
7. Women who are pregnant or lactating
8. Patients with known human immunodeficiency virus (HIV) infection
9. Patients with hepatic disease
10. Patients with renal impairment (creatinine above local reference range), or with positive urine dipstick test to blood or protein
11. Other serious medical or psychiatric illness that in the opinion of the investigator would possibly comprise the study
12. Patients with problem alcohol excess or drug abuse

Date of first enrolment
16/10/2006

Date of final enrolment
30/06/2009

Locations

Countries of recruitment
England

Scotland

United Kingdom

Wales

Study participating centre
Good Hope Hospital
Rectory Road
Sutton Coldfield
United Kingdom
B75 7RR

Study participating centre
Rotheram District General Hospital
Morrgate Road
Rotherham
United Kingdom
S60 2UD

Study participating centre
Hull Royal Infirmary
Anlaby Road
Hull
United Kingdom
HU3 2JZ

Study participating centre
Derby City General Hospital
Uttoxeter Road
Derby

United Kingdom
DE22 3NE

Study participating centre
Yeovil District Hospital
Higher Kingston
Yeovil
United Kingdom
BA21 4AT

Study participating centre
Russells Hall Hospital
Pensnett Road
Dudley
United Kingdom
DY1 2HQ

Study participating centre
Barnsley District General Hospital
Pogmoor Road
Barnsley
United Kingdom
S75 2EP

Study participating centre
York District Hospital
Wigginton Road
York
United Kingdom
YO31 8HE

Study participating centre
St Luke's Hospital
Little Horton Lane
Bradford
United Kingdom
BD5 0NA

Study participating centre

Queen Elizabeth II Hospital
Howlands
Welwyn Garden City
United Kingdom
AL7 4HQ

Study participating centre
Royal Berkshire Hospital
London Road
Reading
United Kingdom
RG1 5AN

Study participating centre
Royal Cornwall Hospital
2 Penventinnie Lane
Treliske
Truro
United Kingdom
TR1 3LQ

Study participating centre
University Hospital Birmingham
Selly Oak Hospital
Birmingham
United Kingdom
B29 6JD

Study participating centre
Glan Clwyd Hospital
Rhuddlan Road
Bodelwyddan
Rhyl
United Kingdom
LL18 5UJ

Study participating centre
New Cross Hospital
Wednesfield Road

Wolverhampton
United Kingdom
WV10 0QP

Study participating centre
Queen Alexandra Hospital
Cosham
Portsmouth
United Kingdom
PO6 3LY

Study participating centre
University Hospital of Hartlepool
Holdforth Road
Hartlepool
United Kingdom
TS24 9AH

Study participating centre
Glasgow Royal Infirmary
84 Castle Street
Glasgow
United Kingdom
G4 0SF

Study participating centre
Darlington Memorial Hospital
Hollyhurst Road
Darlington
United Kingdom
DL3 6HX

Study participating centre
Walsgrave General Hospital
Clifford Bridge Road
Walsgrave
Coventry
CV2 2DX

Study participating centre
Macclesfield District General Hospital
Victoria Road
Macclesfield
United Kingdom
SK10 3BL

Study participating centre
Birmingham Heartlands
Bordesley Green
Birmingham
United Kingdom
B9 5ST

Study participating centre
Llandough Hospital
Longcross Street
Cardiff
United Kingdom
CF24 0SZ

Study participating centre
University Hospital of Wales
Heath Park
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CF14 4XW

Study participating centre
Worcester Royal Hospital
Charles Hastings Way
Worcester
United Kingdom
WR5 1DD

Study participating centre
Royal Sussex County Hospital
Eastern Road
Brighton
United Kingdom
BN2 5BE

Study participating centre
Worthing Hospital
Lyndhurst Road
Worthing
United Kingdom
BN11 2DH

Study participating centre
Bristol Royal Infirmary
Upper Maudlin Street
Bristol
United Kingdom
BS2 8HW

Study participating centre
University Hospital of North Tees
Hardwick Road
Hardwick
Stockton-on-Tees
United Kingdom
TS19 8PE

Study participating centre
Louth County Hospital
High Holme Road
Louth
United Kingdom
LN11 0EU

Study participating centre
The L&D Hospital NHS Foundation Trust
Lowsey Road
Luton
United Kingdom
LU4 0DZ

Sponsor information

Organisation
Cardiff and Vale NHS Trust (UK)

Sponsor details
Research and Development Department
Ground floor, Radnor House
University Hospital of Wales
Heath Park
Cardiff
Wales
United Kingdom
CF14 4XW

Sponsor type
Hospital/treatment centre

Website
http://www.cardiffandvale.wales.nhs.uk/

ROR
https://ror.org/0489f6q08

Funder(s)

Funder type
Industry

Funder Name
Procter and Gamble Pharmaceuticals (USA) - provided a donation, managed by the study Sponsor (Cardiff and Vale NHS Trust) (UK)

Results and Publications

Publication and dissemination plan
Planned publication in a peer reviewed journal.

Intention to publish date
31/10/2012

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/10/2012		Yes	No
Participant information sheet		01/07/2005	12/08/2016	No	Yes