ISRCTN76612274 https://doi.org/10.1186/ISRCTN76612274

Mesalazine for the treatment of diarrhoea-predominant irritable bowel syndrome (IBS-D)

Submission date
19/02/2010

Recruitment status
No longer recruiting

Registration date
28/05/2010

Overall study status
Completed

Last Edited
30/08/2018

Condition category
Digestive System

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

Plain English summary of protocol

Background and study aims.
Irritable bowel syndrome with diarrhoea (IBS-D) affects around 3% of the population and is characterised by abdominal pain and frequent loose bowel movements. There are few treatments for these symptoms that work and this study aims to see whether an anti-inflammatory drug called Mesalazine might help those with IBS-D. Previous studies have suggested benefit but this needs confirmation.

Who can participate?
Patients diagnosed by their doctors as having irritable bowel syndrome with diarrhoea.

What does the study involve?
Patients will be required to take either Mesalazine or a dummy drug (placebo) twice daily for 3 months. At the beginning of the study, an examination of the lower bowel will be made and a small specimen taken from the lining (biopsy). This procedure is routinely performed to identify the different causes of diarrhoea. The biopsy will be repeated at the end of the study to look at the effect of Mesalazine on the gut lining.

What are the possible benefits and risks of participating?
We are hoping that towards the end of the 3 month period diarrhoea and abdominal pain will improve. The drug has been used for many years and the side effects are well recognised. About 1 in 10 of the patients will not tolerate the drug because of nausea or abdominal discomfort and only rarely (less and one in a thousand) will there be any serious adverse effects.

Where is the study run from?
The Nottingham Digestive Diseases Biomedical Research Unit

When is the study starting and how long is it expected to run for?
The study started in October 2010 and is planned to end in May 2013.

Who is funding the study?
The National Institute for Health Research (NIHR) and the Medical Research Council (MRC)

Who is the main contact?
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Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

ClinicalTrials.gov (NCT)
NCT01316718

Protocol serial number
EME 09/20/16; Final Version 1.0

Study information

Scientific Title
Efficacy and mode of action of mesalazine in the treatment of diarrhoea-predominant irritable bowel syndrome (IBS-D): a multicentre parallel group randomised controlled trial

Acronym
MIBS

Study objectives
The purpose of the trial is to define the clinical benefit and possible mediators of the benefit of mesalazine in irritable bowel syndrome (IBS) with diarrhoea. The primary endpoint is to assess the effect of mesalazine on stool frequency.

We will therefore evaluate symptoms (primarily bowel frequency) and markers reflecting mast cell activation and small bowel tone.

Link to EME project website: http://www.eme.ac.uk/projectfiles/092016info.pdf

Please note that as of 13/01/2011 the anticipated start and end dates of this trial have been updated. The previous dates were as follows:
Previous anticipated start date: 01/05/2010
Previous anticipated end date: 30/04/2013

Ethics approval required
Old ethics approval format

Ethics approval(s)
Not provided at time of registration

Study design
Multicentre two-arm parallel group double-blind randomised placebo-controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Diarrhoea-predominant irritable bowel syndrome (IBS-D)

Interventions
Current Interventions as of 13/01/2011:
Mesalazine granules or matching placebo for 12 weeks, with the week 1 of treatment at 2g, once a day, then a step increase to 2g, twice a day for the remainder of the 12 weeks.

Previous Interventions:
Mesalazine versus placebo treatment for 12 weeks. 2 week run-in, 12 weeks treatment, no follow up. Oral (granules) - dose to be confirmed

Intervention Type
Drug

Phase
Phase IV

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

Primary outcome(s)
Average stool frequency during weeks 11 - 12 of the treatment period.

Key secondary outcome(s))
Current secondary outcome measures as of 13/01/2011:
Clinical secondary endpoints:
1. Average daily severity of abdominal pain on a 0 - 10 scale
2. Days with urgency during weeks 11 - 12 post-randomisation
3. Mean stool consistency using Bristol Stool Form Score

4. Global satisfaction with control of IBS symptoms as assessed from the answer to the question "Have you had satisfactory relief of your IBS symptoms? Yes/No"

Mechanistic secondary endpoints:
1) Mast cell tryptase release during 6 hour biopsy incubation
2) IL-1β, TNF-a, histamine and serotonin secretion during same incubation
3) Small bowel tone assessed by volume of fasting small bowel water
4) Faecal Tryptases
5) Difference in primary outcome measure between those with different TNFSF15 polymorphism will be assessed using ANOVA

Ancillary secondary endpoints:
1) EQ-5D
2) CDC HRQOL4
3) HADS
4) PHQ-15

Previous secondary outcome measures:
Clinical secondary endpoints:
1. Average daily severity of abdominal pain on a 0 - 10 scale
2. Days with urgency during weeks 11 - 12 post-randomisation
3. Mean stool consistency using Bristol Stool Form Score
4. Global satisfaction with control of IBS symptoms as assessed from the answer to the question "Have you had satisfactory relief of your IBS symptoms? Yes/No"

Mechanistic secondary endpoints:
5. Mast cell tryptase release during 6-hour biopsy incubation
6. Interleukin-1 (IL-1), tumour necrosis factor-alpha (TNF-a), histamine and serotonin secretion during same incubation
7. Small bowel tone assessed by volume of fasting small bowel water

Ancillary secondary endpoints, measured at time 0 and 12 weeks (before and after treatment):
8. EQ-5D (standardised instrument for use as a measure of health outcome)
9. Centers for Disease Control and Prevention Health-Related Quality-of-Life, 4-item set of Healthy Days core questions (CDC HRQOL4)

Completion date
30/09/2013

Eligibility

Key inclusion criteria
Current inclusion criteria as of 13/01/2011:
1) Male or Female patients aged 18-75 years able to give informed consent.
2) Patients should all have had a colonoscopy within the last 12 months to exclude microscopic or any inflammatory colitis. (If not, but they have had a negative colonoscopy within 5 years and symptoms are unchanged, then a sigmoidoscopy and mucosal biopsy of the left colon would be sufficient to exclude microscopic or any inflammatory colitis).
3) IBS-D Patients meeting Rome III criteria prior to screening phase.
4) Patients with ≥25% soft (score >4) and <25% hard (score 1 or 2) stools during the screening phase, as scored by the daily symptom and stool diary*.

5) Patients with an average stool frequency of 3 or more per day during the screening phase*.
6) Satisfactory completion of the daily stool and symptom diary during the screening phase at the discretion of the investigator.
7) Women of child bearing potential willing and able to use at least one highly effective contraceptive method throughout the study. In the context of this study, an effective method is defined as those which result in low failure rate (i.e. less than 1% per year) when used consistently and correctly such as: implants, injectables, combined oral contraceptives, sexual abstinence or vasectomised partner.

*If inclusion criterion 4 and/or 5 is/are not met but the results are considered atypical (as observed from medical history and patient recall) then the patient can be re-screen on 1 occasion only.

Previous inclusion criteria:
1. IBS-D patients meeting Rome III criteria
2. Male or female patients aged 18 - 75 years
3. Able to give informed consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
75 years

Sex
All

Key exclusion criteria
Current exclusion criteria as of 13/01/2011:
1) Women who are pregnant or breast feeding
2) Prior abdominal surgery which may cause bowel symptoms similar to IBS (note appendectomy and cholecystectomy will not be an exclusion)
3) Patients unable to stop anti-muscarinics, anti-spasmodics, high dose tricyclic antidepressants (i.e. above 50 mg/day), opiates / anti-diarrhoeal drugs*, NSAIDs (occasional over the counter use and topical formulations are allowed), long-term antibiotics, other anti-inflammatory drugs or 5-ASA containing drugs.
4) Patients on selective serotonin re-uptake inhibitors and low dose tricyclic antidepressants (i.e. up to 50 mg/day) for at least 3 months previous unwilling to remain on a stable dose for the duration of the trial.
5) Patients with other gastro-intestinal diseases including colitis and Crohns disease.
6) Patients with the following conditions: Renal impairment, severe hepatic impairment or salicylate hypersensitivity.

7) Patients currently participating in another trial or have been in a trial within the previous 3 months
8) Patients who in the opinion of the investigator are considered unsuitable due to inability to comply with instructions
9) Patients with serious concomitant diseases e.g. cardiovascular, respiratory, neurological etc.

*Loperamide is allowed as rescue medication through-out the trial, however if >2 doses / week are taken during the screening phase then they are not eligible, though they can be re-screened on 1 occasion only.

Previous exclusion criteria:
1. Women who are pregnancy or breast feeding or women of child bearing potential who are not willing to use medically acceptable forms of contraception during the study, (e.g. implants, injectables, combined oral contraceptives, sexual abstinence or vasectomised partners)
2. Prior abdominal surgery which may cause bowel symptoms similar to IBS (note appendectomy and cholecystectomy will not be an exclusion)
3. Patients unable to stop anti-diarrhoeal drugs, non-steriodal anti-inflammatory drugs (NSAIDs) (occasional over the counter use is allowed), other anti-inflammatory drugs (azathioprine or related drugs) or already taking 5-aminosalicylic acid (5-ASA) containing drugs.
4. Patients with other gastro-intestinal diseases including colitis and Crohn's disease
5. Patients with the following conditions: renal impairment, severe hepatic impairment or salicylate hypersensitivity
6. Patients currently participating in another trial or have been in a trial within the previous 3 months
7. Patients who in the opinion of the investigator are considered unsuitable due to inability to comply with instructions

Date of first enrolment
01/10/2010

Date of final enrolment
30/09/2013

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Nottingham Digestive Diseases Biomedical Research Unit
Nottingham
United Kingdom
NG7 2UH

Sponsor information

Organisation
University of Nottingham (UK)

ROR
https://ror.org/01ee9ar58

Funder(s)

Funder type
Government

Funder Name
Medical Research Council (MRC)/National Institutes of Health Research (NIHR) (UK) - Efficacy and Mechanism Evaluation (EME) Programme (ref: 09/20/16)

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	01/01/2016		Yes	No
Protocol article	protocol	09/01/2013		Yes	No