ISRCTN65163992 https://doi.org/10.1186/ISRCTN65163992

# RAPID study: Rifaximin for preventing relapse of Clostridium associated diarrhoea

**Submission date**
25/10/2012

**Recruitment status**
No longer recruiting

**Registration date**
26/10/2012

**Overall study status**
Completed

**Last Edited**
30/07/2019

**Condition category**
Infections and Infestations

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

## Plain English summary of protocol

Background and study aims
Clostridium difficile associated diarrhoea is a serious health problem with over 14,139 cases reported in 2015-16 in England and Wales. There are lots of beneficial gut bacteria which help suppress the growth of Clostridium difficile bacteria. However, taking antibiotics can kill these beneficial bacteria, allowing C. difficile to grow and causing inflammation of the bowel. Standard antibiotics used to treat C. difficile are vancomycin or metronidazole which kill C. difficile but also suppress the beneficial bacteria, meaning relapse of C. difficile occurs in around 1 in 3 patients. Rifaximin is an antibiotic which prevents C. difficile growth but only partly inhibits the growth of beneficial gut bacteria, allowing them to recover. A recent small study found that for patients successfully treated for C. difficile, relapse could be reduced from 31% to 15% by taking a course of Rifaximin. The aim of this study is to evaluate the effectiveness of Rifaximin for preventing relapse of C. difficile in a large study.

Who can participate?
Patients aged 18 or over who have been diagnosed with C. difficile infection and are currently being or have recently been successfully treated with a course of Metronidazole and/or Vancomycin. Adults who lack mental capacity who have a legal representative are also included.

What does the study involve?
Participants are randomly allocated to be treated with 2 weeks of Rifaximin 400mg three times daily, followed by 2 more weeks of 200mg three times daily or identical looking tablets which have no active ingredient (placebo). Blood and stool samples (serum to assess antibody response to C. difficile toxins, apart from participants with legal representative consent) are collected for those patients who have consented to provide these. Neither the doctors or the nurses or the patient know which treatment the patient received. Patients are interviewed at 12 weeks to see if they have had a relapse.

What are the possible benefits and risks of participating?
One in four patients completing a successful course of Metronidazole and Vancomycin may experience a return of their infection. It is anticipated that this will be lower in the group receiving Rifaximin but this cannot be guaranteed. Rifaximin works differently from other antibiotics because it passes through the stomach and into the intestines without being

absorbed into the blood stream, so it is very safe. Most people have no side effects though rarely nausea and headache have been reported and there is a very low risk of an allergic reaction developing. Giving a blood sample may cause discomfort or bruising though this usually resolves within a few days. Adults who lack mental capacity are not required to provide a blood sample.

Where is the study run from?
The NIHR Nottingham Digestive Diseases Biomedical research unit at Nottingham University Hospitals is organising the research; trial coordination takes place at the Nottingham Clinical Trials Unit, University of Nottingham (UK).

When is the study starting and how long is it expected to run for?
December 2012 to July 2016

Who is funding the study?
NIHR Research for Patient Benefit Programme (UK)

Who is the main contact?
Kirsty Sprange
rapid@nottingham.ac.uk

# Contact information

### Type(s)
Scientific

### Contact name
Ms Kirsty Sprange

### Contact details
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# Additional identifiers

### EudraCT/CTIS number
2012-003205-10

### IRAS number

### ClinicalTrials.gov number

### Secondary identifying numbers
12990

# Study information

### Scientific Title
A randomised placebo controlled trial of "follow on" Rifaximin for the prevention of relapse of Clostridium associated diarrhoea

### Acronym
RAPID

### Study objectives
Rifaximin is a poorly absorbed antibiotic which has been used for many years in Italy and the USA for the treatment of traveller's diarrhoea and IBS. It has an excellent safety record and has been shown to achieve high concentrations in the bowel. It has been used effectively to treat Clostridium difficile infection and has a low rate of antibiotic-resistance development. It has also been suggested as beneficial when used after an effective course of the antibiotic, metronidazole since it is said to disturb the normal gut bacteria less than metronidazole and vancomycin and hence might be predicted to reduce the incidence of relapse. This hypothesis is tested in this study. A reduction in recurrence rate of C. difficile from 30% to 10% would significantly reduce the burden of this disease in hospitals and the community and provide an inexpensive solution to this serious illness.

### Ethics approval required
Old ethics approval format

### Ethics approval(s)
NRES Committee East Midlands - Leicester, First MREC approval date 31/08/2012, ref:12/EM /0292

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

### Primary study design
Interventional

### Secondary study design
Randomised parallel trial

### Study setting(s)
Hospital

### Study type(s)
Prevention

### Participant information sheet
Not available in web format, please use the contact details to request a patient information sheet

### Health condition(s) or problem(s) studied
Clostridium difficile-associated diarrhoea

### Interventions
Patients randomised to receive either Rifaximin (200mg tablets) or placebo.

Dosage: Treatment is for 4 weeks. The initial trial daily dose will be 2 x 200mg tablets three times a day for first 2 weeks then, 1 x 200mg tablet three times a day for the final 2 weeks.

### Intervention Type
Other

### Phase
Not Applicable

### Primary outcome measure
The difference in % relapse between Rifaximin and placebo at week 12

### Secondary outcome measures
Current secondary outcome measures as of 30/04/2015:
Clinical:
1. Proportion with relapse of CDAD within 6 months
2. Proportion rehospitalised for CDAD within 6 months
3. Length of in-hospital stay following start of treatment

Exploratory:
1. Stool frequency and consistency during 12 weeks after start of treatment
2. Microbiological assessments

Previous secondary outcome measures:
1. Bowel symptoms measured at weeks 1-4 and weeks 11-12
2. Length of stay on active versus placebo measured at week 12
3. Microbiological exploratory assessments measured at week 12
4. Safety/Adverse events measured at 6 months
5. The difference in relapse of CDAD within 6 months of start of therapy

### Overall study start date
11/12/2012

### Completion date
14/07/2016

## Eligibility

### Key inclusion criteria
Current inclusion criteria as of 30/04/2015:
1. Men/women aged 18 and over (adults who lack mental capacity for whom there is a legal representative are included)
2. Successful treatment of clinically diagnosed CDAD using standard therapy (metronidazole or vancomycin given according to standard local hospital guidelines)

Previous inclusion criteria:
1. Men/women aged 18 and over (adults who lack mental capacity for whom there is a legal representative are included)
2. Successful treatment of clinically diagnosed C. difficile-associated diarrhea (CDAD) using standard therapy (metronidazole or vancomycin given according to standard local hospital guidelines
3. Able to swallow tablets
4. Able to stop chronic antibiotic use
5. Women of child bearing potential willing and able to use at least one highly effective contraceptive method throughout the study. Acceptable contraceptive methods include: established use of oral, injected or implanted hormonal methods; placement of an intrauterine device (IUD) or intrauterine system (IUS); condom or occlusive cap (diaphragm or cervical/vault caps) with spermicide; true abstinence (when this is in line with the preferred and usual lifestyle of the participant); or vasectomised partner.

## Participant type(s)
Patient

## Age group
Adult

## Lower age limit
18 Years

## Sex
Both

## Target number of participants
Planned Sample Size: 180; UK Sample Size: 180

## Total final enrolment
151

## Key exclusion criteria
Current exclusion criteria as of 24/02/2016:
1. Woman of childbearing potential and not willing to use at least one highly effective contraceptive method throughout the study*
2. Male with spouse/partner of childbearing potential and not willing to use condoms
3. Pregnant or breastfeeding
4. Unable to swallow tablets
5. Life expectancy of <4 weeks
6. Hypersensitivity to the active substance, to any rifamycin (e.g. rifampicin or rifabutin) or to any of its excipients (tablet core: sodium starch glycolate type A, glycerol distearate, colloidal anhydrous, silica, talc and microcrystalline cellulose. Tablet coating: hypromellose, titanium dioxide (E171), disodium edentate, propylene glycol and red iron oxide E172)
7. >5 days post standard therapy (metronidazole or vancomycin) for clinically diagnosed CDAD
8. Taking ciclosporin

* Acceptable contraceptive methods include: established use of oral, injected or implanted hormonal methods; placement of an intrauterine device (IUD) or intrauterine system (IUS); condom or occlusive cap (diaphragm or cervical/vault caps) with spermicide; true abstinence

(when this is in line with the preferred and usual lifestyle of the participant); or vasectomised partner.

Exclusion criteria from 30/04/2015 to 24/02/2016:
1. Woman of childbearing potential and not willing to use at least one highly effective contraceptive method throughout the study*
2. Male with spouse/partner of childbearing potential and not willing to use condoms
3. Pregnant or breastfeeding
4. Unable to swallow tablets
5. Life expectancy of <4 weeks
6. Hypersensitivity to the active substance, to any rifamycin (e.g. rifampicin or rifabutin) or to any of its excipients (tablet core: sodium starch glycolate type A, glycerol distearate, colloidal anhydrous, silica, talc and microcrystalline cellulose. Tablet coating: hypromellose, titanium dioxide (E171), disodium edentate, propylene glycol and red iron oxide E172)
7. >5 days post standard therapy (metronidazole or vancomycin) for clinically diagnosed CDAD

* Acceptable contraceptive methods include: established use of oral, injected or implanted hormonal methods; placement of an intrauterine device (IUD) or intrauterine system (IUS); condom or occlusive cap (diaphragm or cervical/vault caps) with spermicide; true abstinence (when this is in line with the preferred and usual lifestyle of the participant); or vasectomised partner.

Original exclusion criteria:
1. Pregnant or breast feeding
2. Hypersensitivity to the active substance, to any rifamycin (e.g. rifampicin or rifabutin) or to any of its excipients (Tablet core: Sodium starch glycolate type A, glycerol distearate, colloidal anhydrous, silica, talc and microcrystalline cellulose. Tablet coating: hypromellose, titanium dioxide (E171), disodium edentate, propylene glycol and red iron oxide E172)
3. >5 days post standard therapy (metronidazole or vancomycin) for clinically diagnosed CDAD

### Date of first enrolment
11/12/2012

### Date of final enrolment
10/03/2016

## Locations

### Countries of recruitment
England

United Kingdom

### Study participating centre
**Nottingham University Hospitals**
Nottingham
United Kingdom
NG7 2UH

**Study participating centre**
**King's Mill Hospital**
Sutton-in-Ashfield
United Kingdom
NG17 4JL

**Study participating centre**
**Royal Derby Hospital**
Derby
United Kingdom
DE22 3NE

**Study participating centre**
**Northern General Hospital**
Sheffield
United Kingdom
S5 7AU

**Study participating centre**
**Chesterfield Royal Hospital**
Chesterfield
United Kingdom
S44 5BL

**Study participating centre**
**Royal Shrewsbury Hospital**
Shrewsbury
United Kingdom
SY3 8XQ

**Study participating centre**
**County Durham and Darlington NHS Foundation Trust**
Darlington
United Kingdom
DL3 6HX

**Study participating centre**

**Sunderland Royal Hospital**
Sunderland
United Kingdom
SR4 7TP

**Study participating centre**
**Kettering General Hospital**
Kettering
United Kingdom
NN16 8UZ

**Study participating centre**
**Dorset County Hospital**
Dorchester
United Kingdom
DT1 2JY

**Study participating centre**
**James Cook Hospital**
Middlesbrough
United Kingdom
TS4 3BW

**Study participating centre**
**North Cumbria University Hospitals**
Carlisle
United Kingdom
CA2 7HY

**Study participating centre**
**Hampshire Hospitals NHS Foundation Trust**
Basingstoke
United Kingdom
RG24 9NA

**Study participating centre**

**University Hospitals Southampton**
Southampton,
United Kingdom
SO16 6YD

**Study participating centre**
**New Cross Hospital**
Wolverhampton
United Kingdom
WV10 0QP

**Study participating centre**
**Doncaster Royal Infirmary**
Doncaster
United Kingdom
DN2 5LT

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

**Study participating centre**
**Stepping Hill Hospital**
Stockport
United Kingdom
SK2 7JE

**Study participating centre**
**Queens Hospital**
Romford
United Kingdom
RM7 0AG

**Study participating centre**

**King's College Hospital**
London
United Kingdom
SE5 9RS

# Sponsor information

**Organisation**
University of Nottingham (UK)

**Sponsor details**
Research Innovation Services
Kings Meadow Campus
Lenton Lane
Nottingham
England
United Kingdom
NG7 2NR

**Sponsor type**
University/education

**ROR**
https://ror.org/01ee9ar58

# Funder(s)

**Funder type**
Government

**Funder Name**
National Institute of Health Research (NIHR) (UK) - Research for Patient Benefit (RfPB) Grant Codes: PB-PG-1010-23257

# Results and Publications

**Publication and dissemination plan**
Planned publication in a high impact peer reviewed journal, and dissemination of study results at scientific congresses.

**Intention to publish date**
31/07/2018

## Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are/will be available upon request from the Nottingham Clinical Trials Unit (NCTU) (ctu@nottingham.ac.uk) once the results of the trial have been published.

## IPD sharing plan summary

Available on request

## Study outputs

| Output type | Details | Date created | Date added | Peer reviewed? | Patient-facing? |
|---|---|---|---|---|---|
| Results article | results | 01/07/2019 | | Yes | No |
| Results article | results | 01/07/2019 | 30/07/2019 | Yes | No |
| HRA research summary | | | 28/06/2023 | No | No |