ISRCTN34467677 https://doi.org/10.1186/ISRCTN34467677

Can restoring the balance of healthy bowel bacteria help to fight antibiotic resistance?

Submission date
08/10/2019

Recruitment status
No longer recruiting

Registration date
20/01/2020

Overall study status
Completed

Last Edited
09/06/2025

Condition category
Infections and Infestations

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

Plain English summary of protocol

Background and study aims
The human gut has trillions of bacteria (bugs) which are important to keep us healthy. In total these bugs are called the microbiota. The bugs are always evolving to beat antibiotics used to fight them (resistance). Resistance to antibiotics allows bugs to survive and spread. This is a growing and serious threat to worldwide health, and means that doctors may be limited in the types of treatments that they can offer to patients. Without effective antibiotics even simple infections could become deadly, making routine medical procedures too dangerous to perform. There is an urgent need to find new antibiotics, but this takes time and is very expensive. There is growing interest in non-antibiotic treatments like Faecal Microbiota Transplant (FMT) to deal with this problem. FMT is the transfer of bacteria from the guts of healthy donors (taken from their poo) into the gut of a patient. The aim is to restore a healthy balance of bacteria (reducing harmful ones and increasing good ones). It is currently used to treat patients with repeated Clostridium difficile infection. This is an infection causing severe diarrhoea and stomach pain, normally after having antibiotics which have harmed the microbiota. FMT is very effective and safe in treating this group of patients, with success rates of over 80%. Initial research shows that it may be helpful in other conditions. Especially for excluding antibiotic resistant bacteria (ARB) found in some patients' guts.

This study will look at whether giving FMT to patients with ARB is an achievable treatment and if it is both safe and acceptable to patients, without side effects. This will allow doctors to treat infections in these patients better. If the treatment works it could be rapidly brought into the NHS. This could help patients who have ARB and can't be treated with current antibiotics.

Who can participate?
Adult patients with ARB.

What does the study involve?
Patients and members of the public will be involved by inviting then to have a say in how the study is designed, performed and reported. 40 patients with ARB will be randomly chosen to receive FMT (swallowed as capsules). Another 40 patients will be randomly chosen to receive identical capsules without the bugs. This is known as a ‘placebo’. Patients will have stool (poo) samples collected before and after FMT. These will be taken at days 10, 40, 100 and 190.

Samples will be used to see what impact the treatment has on their gut bugs. Side effects like bad taste, burping, diarrhoea and infection will also be assessed.

What are the possible benefits and risks of participating?
Any risk and burdens are detailed in the patient information sheets and will be discussed with the patient during the informed consent process. Participants will be advised to speak to a member of the study team if they have any questions. In order to minimise the number of times participants will need to visit the hospital, follow up visits at 1 week, 3 months and 6 months will be conducted by telephone. Participants will be asked to post stool samples to the study team using the approved pre-paid collection kits provided. Participants will also be reimbursed for travel costs for all visits if required. Participants are asked to provide blood samples and may experience discomfort or some minor bruising. The samples will be taken by appropriately trained and qualified member of the study team. Participants are asked to provide five stool samples over the course of the study. he main risk of associated with FMT is transmission of infection from donor samples. The donor faecal transplant is robustly screened following a strict protocol, approved by… Donors provide fully informed consent to donate samples for the FERARO study, and serological testing is undertaken. All samples have full traceability to donors and recipient serum is saved prior to transplantation in the event that this needs to be tested for antibodies to an infectious agent at a later date. Donations are processed and stored in a medical laboratory accredited by the UK Accreditation Service (UKAS) to ISO 15189:2012 standards.
The rising trend in antimicrobial resistance and the bleak outlook for introduction of new classes of antimicrobial agents from the pharma industry mean that antimicrobial resistance is a significant problem that is likely to worsen. There is no standard of care treatment to decolonise gastrointestinal carriage of ARB, although previous research has suggested that FMT might be able to reduce ARB carriage.
There may be no direct benefit to participants, as FMT may or may not be able to reduce or eliminate ARB, and half of the participants will receive placebo. As a feasibility study, it will provide the data needed to determine if a larger clinical trial to test if FMT is effective and if it is possible, based on patient acceptability and the safety and tolerability of the treatment.

Where is the study run from?
Guy's and St Thomas' NHS Foundation Trust, UK

When is the study starting and how long is it expected to run for?
March 2020 to May 2023

Who is funding the study?
National Institute for Health Research (NIHR), UK

Who is the main contact?
Dr Simon Goldenberg
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Study website
https://www.fmt-trials.org/

Contact information

Type(s)
Scientific

Contact name
Dr Simon Goldenberg

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Additional identifiers

EudraCT/CTIS number
2019-001618-41

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
1.1, CPMS 44544

Study information

Scientific Title
A prospective, randomised placebo controlled feasibility trial of Faecal microbiota Transplant to ERadicate gastrointestinal carriage of Antibiotic Resistant Organisms (FERARO)

Acronym
FERARO

Study objectives
This is a feasibility trial to determine the likely success of a larger substantive trial

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 20/02/2020, London - City & East Research Ethics Committee (Bristol Research Ethics Committee Centre, Whitefriars, Level 3, Block B, Lewins Mead, Bristol, BS1 2NT, UK; +44 (02071048033; cityandeast.rec@hra.nhs.uk), ref: 20/LO/0117

Study design
Randomised controlled patient-blinded single-centre feasibility trial with two parallel groups

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

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

Health condition(s) or problem(s) studied
Antimicrobial resistance (carbapenem resistant Enetrobacteriales and/or extended spectrum beta-lactamase producing Enterobacteriales)

Interventions
For the active arm, participants will be dosed with lyophilised faecal microbiota derived from 100g of stool and encapsulated in five coloured delayed release methylcellulose. The dose is repeated for two further consecutive days. The placebo will be matched to the active and will comprise microcrystalline methylcellulose encapsulated with the same delayed release capsules. The number of capsules and dosing days are as per the active arm. The assignment to one of two possible treatment arms of the study (FMT or placebo capsules) will be performed. Participants will be evenly distributed to both groups in a 1:1 ratio. The randomisation schedule will be generated using a validated randomisation programme and verified for accuracy using strict quality control procedures.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Lyophilised faecal microbiota

Primary outcome measure
Consent rate (%) of eligible patients

Secondary outcome measures
Current secondary outcome measures as of 18/03/2020:
1. Proportion of patients fulfilling inclusion / exclusion criteria at endline
2. Proportion of patients receiving IMP / placebo (as a % of those consenting) at endline

3. Proportion of patients returning for follow up visits (face to face visit at Day 40)
4. Proportion of patients providing follow up stool samples (Days 10, 40, 100, 190)
5. Ability to recruit sufficient healthy donors to manufacture all FMT doses to meet demands of this and a future substantive RCT. Assessed by delay in dosing patients (measured in days) at end of study
6. Collection of data that may be used in estimating of costs/resources needed to provide FMT in the NHS at end of study
7. An embedded qualitative study to explore views and experiences of research participants.
8. Gastrointestinal carriage of CRE / ESBL (detected / not detected) by stool culture over time (days 10, 40, 100 and 190)
9. Gastrointestinal carriage of CRE / ESBL (detected / not detected) by multiplex PCR over time (days 10, 40, 100 and 190)
10. Proportion of patients experiencing reflux following administration of FMT at each dosing day (days 1,2,3) and follow up visit 1(day 10)
11. Proportion of patients suffering intolerable (resulting in withdrawal from the study) gastrointestinal side effects (including diarrhoea, constipation, abdominal pain, flatulence and bloating). This will be assessed by direct questioning and completion of a short patient questionnaire at each dosing day (days 1,2,3) and follow up visit 1(day 10)
12. Identification of unanticipated harms involved with administration of FMT at each dosing day (days 1,2,3) and follow up visits days 10, 40, 100 and 190
13. Occurrence of any adverse drug reaction at each dosing day (days 1,2,3) and follow up visits days 10, 40, 100 and 190
14. Occurrence of any adverse event/serious adverse event at each dosing day (days 1,2,3) and follow up visits days 10, 40, 100 and 190

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Previous secondary outcome measures:
1. Proportion of patients fulfilling inclusion / exclusion criteria at endline
2. Proportion of patients receiving IMP / placebo (as a % of those consenting) at endline
3. Proportion of patients returning for follow up visits (face to face visit at Day 40)
4. Proportion of patients providing completed diary card at follow up visit (face to face at Day 40)
5. Proportion of patients providing follow up stool samples (Days 10, 40, 100, 190)
6. Ability to recruit sufficient healthy donors to manufacture all FMT doses to meet demands of this and a future substantive RCT. Assessed by delay in dosing patients (measured in days) at end of study
7. Collection of data that may be used in estimating of costs/resources needed to provide FMT in the NHS at end of study
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14. Occurrence of any adverse drug reaction at each dosing day (days 1,2,3) and follow up visits days 10, 40, 100 and 190
15. Occurrence of any adverse event/serious adverse event at each dosing day (days 1,2,3) and

follow up visits days 10, 40, 100 and 190

Overall study start date
01/09/2019

Completion date
31/05/2023

Eligibility

Key inclusion criteria
Current participant inclusion criteria as of 20/07/2020:
1. Adult patients (age 18 years or older at time of consent)
2. Current or previous patient at Guy's and St Thomas' NHS Foundation Trust
3. Ability to understand the purpose, potential benefits, and risks of the study and capable of giving informed consent. The participant must be able to provide written informed consent.
4. Documented gastrointestinal carriage of ESBL or CPE (stool sample) in the 21 days prior to consent.
5. Symptomatic infection with the same target organism of interest in the preceding 6 months

Previous participant inclusion criteria:
1. Adult patients (age >18 years at time of randomisation)
2. Current or previous patient at Guy's and St Thomas' NHS Foundation Trust
3. Ability to understand the purpose, potential benefits and risks of the study and capable of giving informed consent. The participant must be able to provide written informed consent
4. Documented gastrointestinal carriage of ESBL or CPE (rectal swab or stool sample) within 21 days of randomisation
5. Symptomatic infection with the same target organism of interest in the preceding 6 months

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
80

Total final enrolment
44

Key exclusion criteria
Current participant exclusion criteria as of 20/07/2020:
1. Pregnancy or planned pregnancy. Urine testing will be performed at screening to rule out

pregnancy
2. Breastfeeding
3. Severe or life-threatening food allergy
4. Allergy or other contraindication to omeprazole, IMP or placebo ingredients
5. Treatment with systemic antibiotic on the day prior to 1st IMP/placebo dosing to the end of the dosing period
6. Treatment with pre or probiotics in the 4 weeks prior to randomisation and for the duration of the study
7. Severe immunodeficiency
7.1. Systemic chemotherapy <30 days from baseline or planned chemotherapy within the upcoming 6 months
7.2. Known HIV infection with CD4 count <250 cells/uL
7.3. Known neutropenia with absolute neutrophils <1.0x109
7.4. Prolonged treatment with corticosteroids (equivalent to prednisone >60 mg daily for > 30 days) within 8 weeks of randomisation
8. Life expectancy <6 months
9. Swallowing disorder, oral-motor dyscoordination or likely inability/unwillingness to ingest study medication
10. Patients who have received another investigational drug or device within 4 months prior to randomisation

Previous participant exclusion criteria:
1. Pregnancy or planned pregnancy. Urine testing will be performed at screening to rule out pregnancy in females
2. Breastfeeding
3. Severe or life-threatening food allergy
4. Allergy or other contraindication to any of the study drugs (omeprazole 20 mg)
5. Treatment with systemic antibiotic on the day prior to 1st IMP/placebo dosing to the end of the dosing period
6. Treatment with pre or probiotics in the 4 weeks prior to randomisation and for the duration of the study
7. Severe immunodeficiency;
7.1. Systemic chemotherapy <30 days from baseline or planned chemotherapy within the upcoming 6 months
7.2. Known HIV infection with CD4 count <250 cells/uL
7.3. Known neutropenia with absolute neutrophils <1.0x109
7.4. Prolonged treatment with corticosteroids (equivalent to prednisone >60 mg daily for > 30 days) within 8 weeks of randomisation
8. Life expectancy <6 months
9. Swallowing disorder, oral-motor dyscoordination or likely inability/unwillingness to ingest study medication
10. Patients who have received another investigational drug or device within 30 days prior to randomisation
11. Any condition or circumstance, in the opinion of the investigator, that would compromise the safety of the patient or the quality of the study data

Date of first enrolment
01/09/2020

Date of final enrolment
30/11/2022

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Guy's and St Thomas' NHS Foundation Trust
Westminster Bridge Road
London
United Kingdom
SE1 7EH

Sponsor information

Organisation
Guy's and St Thomas' NHS Foundation Trust

Sponsor details
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United Kingdom
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Sponsor type
Hospital/treatment centre

Funder(s)

Funder type
Government

Funder Name
National Institute for Health Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
The results will be published in an open access journal with peer review.

Intention to publish date
31/12/2023

Individual participant data (IPD) sharing plan
The current data sharing plans for this study are unknown and will be available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	25/05/2020	28/05/2020	Yes	No
HRA research summary			28/06/2023	No	No
Results article		16/05/2025	09/06/2025	Yes	No