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Healthy feces to treat intestinal disease in transplant patients

Submission date	Recruitment status	[_] Prospectively registered
11/07/2018	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
23/07/2018	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
02/02/2021	Digestive System	

Plain English summary of protocol

Background and study aims
Cancers of the blood, such as acute leukemia, can be treated through transplantation of stem cells from healthy donors. Because stem cells can develop into different types of cells, transplantation leads to development of a new immune system derived from the donor stem cells, which can then respond to the tumor cells and clear the tumor.
However, the new, donor immune system can sometimes respond to healthy tissue in the patient, which causes 'graft versus host disease' (GvHD). This can often occur in the intestines. In healthy patients, the intestines have microbes that help to keep it healthy (gut microbiota). However, in patients with stem cell transplants, especially those who develop GvHD as a result, this damages that normal, healthy gut microbiota. Restoring a healthy gut microbiome could therefore cure GvHD.
One method of restoring a healthy gut microbiome is through fecal transplantation from people with healthy gut microbiota. We aimed to determine whether transplantation of healthy feces into the intestine of GvHD patients could cure GvHD and restore a healthy gut microbiome.

Who can participate?
Stem cell transplant patients aged 18 or older with intestinal GvHD that did not respond to corticosteroid treatment

What does the study involve?
Participants will receive a fecal microbiota transplant, donated from healthy volunteers on the same day, into the upper intestine using a nasogastric tube.

What are the possible benefits and risks of participating?
The possible benefit to participants of taking part is that FMT can result in a reduction in symptoms of GvHD. The possible risk to participants of taking part is that due to their intestinal inflammation, bacteria transplanted into the gut may be able to relocate into the blood stream, which could cause infection.

Where is the study run from?
Amsterdam University Medical Centers location AMC, Amsterdam, Netherlands

When is the study starting and how long is it expected to run for?
July 2015 to January 2019

Who is funding the study?
1. Netherlands Organisation for Scientific Research (Netherlands)
2. Landsteiner Foundation for Blood Research (Netherlands)
3. AMC Foundation (Netherlands)

Who is the main contact?
Dr M.D. Hazenburg
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Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
FARAH trial

Study information

Scientific Title
FARAH study: Fecal trAnsplantation to Reduce therapy-refractory graft versus host disease in Allogeneic Hematopoietic stem cell transplantation

Acronym
FARAH

Study objectives
Steroid-refractory or steroid-dependent GvHD can be treated by infusion of healthy feces via duodenal tube

Ethics approval required
Old ethics approval format

Ethics approval(s)
Medical ethics committee of the Academic Medical Center (AMC), 07/07/2016, NL55067.018.15, 2016_003#B2016460

Study design
Interventional single-armed non-randomised pilot study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Graft versus host disease of the intestine (GvHD)

Interventions
Healthy volunteers (male and female, aged less than 60 years, Western diet) were used as donors for FMT (fecal microbiota transplantation) and received a bowel lavage with 1 litre of macrogol solution (Klean-Prep/Moviprep/Norgine) at least two hours before FMT. Donor feces was collected on the day of transplantation and immediately processed by dilution with sterile saline (0.9%), stirring and filtration to obtain a fecal suspension of 300-500 ml. This solution was then administered to participants through a nasoduodenal tube within 6 hours after donor feces collection.
After FMT, patients are seen by their transplantation hematologist at a weekly interval during the first 4 weeks after FMT. During tapering of immunosuppressants, patients are seen weekly or biweekly, depending on the clinical situation. A significant number of patients will be admitted to the hospital during at least the first 4-6 weeks after FMT, where they will be taken care of by the ward hematologist.

Intervention Type
Biological/Vaccine

Primary outcome(s)
1. Response to treatment measured by stool frequency and volume at 7 days, 28 days, 3 months and 6 months after FMT
2. Complete response to treatment defined as complete resolution of GvHD symptoms 4 weeks after FMT. Participants were classified as CR/sf (complete responders with secondary failure) or NR (non-responders, if there was no improvement in clinical grade or follow-up time was too short to assess the effect of FMT). This is self-reported (participants keep a defecation diary) and is assessed by a physician.

Key secondary outcome(s))
1. Normalisation of gut microbiome diversity, measured by 16S sequencing of microbiome diversity in stool at 1, 4, 12 and 24 weeks after FMT
2. Changes in inflammatory markers in blood and affected tissues, measured using C-reactive protein, immune subsets (T cells, B cells, innate lymphoid cells), their activation status and pro-inflammatory cytokines in the blood at 1, 4, 12 and 24 weeks after FMT. At 3 and 6 months after FMT, colon biopsies will be taken to investigate immune subsets and infiltration of inflammatory cells to this region using immunohistochemistry
3. Total number and severity of infections will be assessed using patients' medical charts

4. Total duration of hospital stays and readmissions will be assessed using patient's medical charts

Completion date
15/01/2019

Eligibility

Key inclusion criteria
1. Steroid-refractory or steroid-dependent graft versus host disease of the intestine
2. Aged 18 years or older

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
Not Specified

Total final enrolment
15

Key exclusion criteria
1. Unable to provide informed consent

The use of immunosuppressive therapy and/or concurrent (systemic) infection does not exclude patients from participation in the study.

Date of first enrolment
06/09/2016

Date of final enrolment
17/05/2018

Locations

Countries of recruitment
Netherlands

Study participating centre

Amsterdam University Medical Centers location AMC
Meibergdreef 9
Amsterdam
Netherlands
1105 AZ

Sponsor information

Organisation
Amsterdam UMC Department of Hematology

ROR
https://ror.org/00q6h8f30

Funder(s)

Funder type
Not defined

Funder Name
Netherlands Organisation for Scientific Research (NWO)

Funder Name
Landsteiner Foundation for Blood Research

Funder Name
AMC Foundation

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from Dr MD Hazenberg (m.d.hazenberg@amc.nl), after the follow up of the last patient has been finalized (expected early January 2019). Data on safety and preliminary results are available any time, please contact Dr Hazenberg by email. There are no ethical or legal restrictions. Informed consent was obtained from all participants.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	12/08/2020	02/02/2021	Yes	No