The BRIDGE study - Bronchiectasis Research Involving Databases, Genomics and Endotyping to match the right treatment to the right patient.

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This study aims to phenotype and endotype bronchiectasis during stable disease and exacerbations, to develop strategies for personalised medicine.3.1 Primary ObjectiveTo determine molecular endotypes of bronchiectasis which can guide response to...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Bronchial disorders (excl neoplasms)
Study type	Observational non invasive

Summary

ID

NL-OMON48313

Source
ToetsingOnline

Brief title
The BRIDGE Trial

Condition

- Bronchial disorders (excl neoplasms)

Synonym
bronchiectasis, dilated airways

Research involving
Human

Sponsors and support

Primary sponsor: University of Dundee - Ninewells Hospital

Source(s) of monetary or material Support: European Respiratory Society via EMBARC;British Lung Foundation;European Union Innovative Medicines Initiative

Intervention

Keyword: Bronchiectasis, Database, Endotyping, Genetics

Outcome measures

Primary outcome

- Medical history

- Height/ weight

- Spirometry outcome measures (FEV1, FVC, tiffenau)

- Results from the bronchiectasis quality of life questionnaire (Qol-B) and bronchiectasis health questionnaire (BHQ)

- Sputumcultures for microbiological examination and neutrophil elastase testing*

- Laboratory testing**

- alpha-1-antitrypsin levels and genotyping. Note that if the patient has previously been tested for alpha-1 antitrypsin levels and this is documented, there is no requirement to perform this further test.

- Urine and nasopharynx micribioma results

** Laboratory procedures may include the following*:

1. Protein proteomic analysis using liquid chromatography-mass spectrometry

2. qPCR to evaluate bacterial and viral load

3. Assays for inflammatory profiling such as ELISA for cytokine/ chemokine measurement, including neutrophil markers (elastase, resistin, OLF4), alpha 1

anti-trypsin, pH and other candidate markers.

4. Microbiome assessment by 16s rRNA amplicon sequencing on the Illumina MiSeq platform for bacteria and ITS sequencing for Fungi

5. Assessment of gene expression

6. Cell culture and subsequent sampling of culture supernatant for cell products

7. Challenge of cells with micro-organisms, environmental pollutants and pharmaceutical agents

8. Assessment of neutrophil function

9. Genotyping (including whole genome sequencing)

* Not all of the laboratory procedures will be conducted on all of the samples. Procedures will be performed centrally; no additional testing; materials will be shipped to the primary trial lab at the University of Dundee.

Secondary outcome

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Study description

Background summary

Bronchiectasis has been described as one of the most neglected diseases in respiratory medicine.(1,2) There are no licensed treatments, and the burden of disease is high and increasing. In the UK, bronchiectasis affects 485 per 100,000 men and 566 per 100,000 women and the prevalence has increased by approximately 40% in the past decade.(3) Traditional bronchiectasis guideline approaches to treatment are focussed on airway infection (long term oral/inhaled antibiotic treatments), mucus clearance (physiotherapy, devices, mucoactive drugs) and airway inflammation (inhaled corticosteroids, macrolides).(1) Clinical trials have failed to demonstrate clear benefit of inhaled antibiotics across multiple compounds.(4-6) Macrolides reduced the

frequency of exacerbations in 3 randomized trials, but up to 40% of patients do not respond to treatment in practice.(7-10) Mucoactive drugs are not widely used and clinical trials of mannitol have failed to meet their primary end-points, DNAse was found to be harmful in bronchiectasis despite benefits in cystic fibrosis, while hypertonic saline has not shown clear benefits over 0.9% saline.(11-14) A Cochrane review concluded that there is insufficient evidence to support the use of inhaled corticosteroids.(15) The failure of therapies to translate from cystic fibrosis to bronchiectasis is thought to be due to the greater inflammatory, microbiological, radiological and aetiological heterogeneity in bronchiectasis.(16)
Achieving success in developing new therapies for this disease requires detailed translational research to define patient phenotypes and endotypes. Personalised, stratified or precision medicine is increasing advocated across a range of conditions to improve targeting of therapies.(17-20).

Study objective

This study aims to phenotype and endotype bronchiectasis during stable disease and exacerbations, to develop strategies for personalised medicine.

3.1 Primary Objective
To determine molecular endotypes of bronchiectasis which can guide response to treatment.

3.2 Secondary Objectives
1. To determine molecular endotypes of stable bronchiectasis
2. To determine the causes and inflammatory profiles of bronchiectasis exacerbations
3. To validate candidate biomarkers of stable and exacerbation endotypes to use in stratified medicine
4. To perform in-vivo or in-vitro proof of concept studies using phenotypic data to identify patient populations likely to benefit in future randomized controlled trials

Study design

This is an observational, multi-centre study performed through the EMBARC consortium. Data and samples will be collected from approximately 8 European centres. Ethical approval of this protocol will be sought at country level.

The Dutch study site will aim to recruit 80 patients over the course of the study with 1000 recruited Europe-wide. These numbers are indicative and we reserve the right to recruit more or less patients in the Netherlands and elsewhere according to study need. Patients will be recruited whilst clinically stable and asked to attend an annual visit at a clinical research facility for the research procedures outlined below.

Study burden and risks

This study is observational and no interventional product or device will be adminstered. The majority of study procedures are part of the routine follow up of bronchiectasis patients in our hospital and thus will not provide additional risks and/ or burden for participants.

Therefore, the participant's burden consists of the extra time needed for:

- quality of life questionnaires
- blood/ urine sampling
- naso-pharyngeal swabs

The risks for participants are limited to the risks knowing to be involved in venapunction (hematoma, mild pijn, infection of puncture site).

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age

Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

A previous CT scan showing bronchiectasis along with compatible clinical syndrome of cough, sputum production and/or recurrent respiratory tract infections.
A primary diagnosis of bronchiectasis made by a respiratory physician
At the screening visit the individual will have been clinically stable for 4 weeks indicated by the lack of any treatment with antibiotics or corticosteroids for a pulmonary exacerbation in the previous 4 weeks.

Exclusion criteria

Inability to give informed consent
<18years of age
Patients with active tuberculosis
Treatment with antibiotics or corticosteroids for a pulmonary exacerbation in the previous 4 weeks

Study design

Design

Study type: Observational non invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	16-02-2021
Enrollment:	80
Type:	Actual

Ethics review

Approved WMO Date:	19-02-2020
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-03-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
ClinicalTrials.gov	NCT03791086
CCMO	NL69656.018.19