Changes in the respiratory microbial and biochemical environment after the start of CFTR targeted treatment in patients with cystic fibrosis

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

Summary

ID

NL-OMON45428

Source
ToetsingOnline

Brief title
Microbiome changes after CFTR targeted therapy

Condition

- Bronchial disorders (excl neoplasms)

Synonym
Cystic fibrosis

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum

Source(s) of monetary or material Support: Longfonds

Intervention

Keyword: Cystic fibrosis, Metabolomics, Microbiome, Respiratory colonization

Outcome measures

Primary outcome

* Bacterial sequences in sputum, broncho-alveolar lavage fluid and oral and nasal wash.

* Metabolic profiles in broncho-alveolar lavage fluid and oral wash by mass spectrometry.

* Volatile metabolites in breath.

Secondary outcome

* Bacterial culture result from sputum and broncho-alveolar lavage fluid.

* Lung function test results (FEV1/FVC, etc).

* Routine plasma parameters of (chronic) inflammation (IgG, CRP, leukocyte count) and inflammatory profiles of sputum and broncho-alveolar lavage fluid measured by luminex.

* Quality of life and fatigue assessments.

Study description

Background summary

The lungs of patients with CF are characterized by (1) impaired mucus clearance, (2) acidic milieu, (3) increased neutrophils but impaired function and (4) increased bacterial loads. Novel therapies target the CF transport receptor (CFTR) and increase it*s activity. They improve lung function in patients with a specific mutation. However, very little is known about the influence of the targeted CFTR therapies on the respiratory microbiome. One of

the major challenges in CF is to limit the colonization of the respiratory tract by well-adapted microbes such as Pseudomonas and maintain a healthy respiratory flora.

Study objective

We aim to evaluate the changes in the composition and the function of the respiratory microbiome after the initiation of targeted CFTR therapy. Second we want to relate the change in respiratory biochemical and microbial environment to clinical changes (for example lung function). Finally, we will explore the differences in pre-medication respiratory microbiome / metabolome between patients that clinically respond and do not respond to treatment.

Study design

Longitudinal observational cohort study.

Study burden and risks

All assessment will be performed in conjunction with routine visits to the outpatient clinic as much as possible. The most important additional procedure for the patient are two additional bronchoscopies in a selected group of patients. This procedure is unpleasant but is of low risk in the patients that are included for bronchoscopy. The patient will not have benefit from participation in the study. We aim for improved treatment of bacterial dysbalance in the respiratory tract of all patients with CF and in that respect the results of the study may improve treatment in the future for the patients participating in the study or any patient with similar characteristics.

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

Patients with a (predominant) class II mutation (almost exclusively homozygous Phe508del) for cystic fibrosis (N<=20) who will be started on Ivacaftor/Lumacaftor (CFTR targeted therapy; Orkambi) therapy will be included in this longitudinal observational study.

Exclusion criteria

For the bronchoscopy (part of the research protocol) the following patients will be excluded:
* Pre-lung transplant trajectory
* No informed consent for the procedure
* Deemed inappropriate by the treating physician.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	13-11-2017
Enrollment:	20
Type:	Actual

Ethics review

Approved WMO Date:	23-03-2017
Application type:	First submission
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
CCMO	NL60220.018.16