Changes in the respiratory and faecal microbial and biochemical environment after the initiation of a triple CFTR targeted treatment in patients with cystic fibrosis

Published: 28-08-2019
Last updated: 10-04-2024

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

Summary

ID

NL-OMON54939

Source
ToetsingOnline

Brief title
CF Triple Therapy Microbiome study

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: CFTR, Cystic fibrosis, Microbiome, Triple therapy

Outcome measures

Primary outcome

Four visits are planned per patient as part of standard care. Material will obtained during all visits. Lung function, microbial cultures of sputum and blood sampling will be performed as part of routine care. An oral wash, nasal wash, and exhaled breath, and faeces and DBS with a finger prick collection will be obtained as additional procedure. Functional metagenomics and metabolomics analysis will be performed on sputum samples, oral and nasal wash, and faeces samples. The primary endpoint is the change in bacterial diversity after the start of Elexacaftor/Tezacaftor/Ivacaftor.

Secondary outcome

NA

Study description

Background summary

The lungs of patients with CF are characterized by (1) impaired mucus clearance, (2) acidic milieu, (3) increased number of neutrophils and (4) increased bacterial loads. Novel therapies target the CF transmembrane conductance regulator (CFTR) and increase its activity. A novel triple CFTR targeted therapy is shown to have a major effect on pulmonary function, mucociliary clearance and reduction in sweat chloride test. 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 Achromobacter 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). Third we relate the changes of the respiratory and gut microbiome. Fourth, we will explore the differences in pre-medication respiratory microbiome / metabolome between patients that clinically respond and do not respond to treatment. Finally, we will clinically validate a dried blood spot (DBS) sampling method.

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 addition procedure is the exhaled breath sampling, and faeces and DBS collection, both non-invasive procedures. 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
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)

Inclusion criteria

Start with Elexa-/Teza-/Ivacaftor therapy on basis of compassionate use

Exclusion criteria

none

Study design

Design

Study type: Observational non invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	30-10-2019
Enrollment:	20

Type:	Actual

Ethics review

Approved WMO Date:	28-08-2019
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-10-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-03-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-07-2021
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
CCMO	NL70667.018.19