CFTR microbiome analysis

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1) After the initiation of targeted CFTR therapy: a. Microbiome diversity increases (primary hypothesis, also used for sample size calculation) b. Well-adapted microbial species (e.g. Pseudomonas, Achromobacter) decrease in abundance c. The...

Ethische beoordeling	Positief advies
Status	Werving gestart
Type aandoening	-
Onderzoekstype	Observationeel onderzoek, zonder invasieve metingen

Samenvatting

ID

NL-OMON23453

Bron
Nationaal Trial Register

Aandoening

Cystic fibrosis

Ondersteuning

Primaire sponsor: University of Amsterdam
Overige ondersteuning: Longfonds (Dutch lung foundation)

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

• Bacterial sequences in sputum, broncho-alveolar lavage fluid and oral and nasal wash.
• Metabolic profiles in broncho-alveolar lavage fluid and oral wash.
• Volatile metabolites in breath.

Toelichting onderzoek

Achtergrond van het onderzoek

Rationale: 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 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 Achromobacter and maintain a healthy respiratory flora.

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 population: 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. There are no exclusion criteria.

Main study parameters/endpoints: Five 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 will be obtained as additional procedure. A bronchoscopic bronchial wash of the central airways and both lungs will be performed in patients that (1) have no contra-indications for bronchoscopy and (2) provide informed consent for this procedure. During bronchoscopy, breath will be obtained from both lungs separately through the bronchoscope. Functional metagenomic and metabolomics analysis will be performed on sputum samples, broncho-alveolar lavage fluid and oral and nasal wash. The primary endpoint is the change in bacterial diversity after the start of Ivacaftor/Lumacaftor.

Nature and extent of the burden and risks associated with participation, benefit and group relatedness: 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.

Doel van het onderzoek

1) After the initiation of targeted CFTR therapy:

a. Microbiome diversity increases (primary hypothesis, also used for sample size calculation)

b. Well-adapted microbial species (e.g. Pseudomonas, Achromobacter) decrease in abundance

c. The biochemical environment moves towards normal (e.g. increased pH)

2) An improved lung function is associated with:

a. Increased diversity of the microbiome

b. Decreased abundance of well-adapted microbial species (e.g. Pseudomonas)

c. Increased pH and less inflammatory response

3) Patients with a microbiome that is less well-adapted to the CF lung environment tend to show less clinical improvement.

Onderzoeksopzet

Before start. After 3,6,9 and 12 months.

Onderzoeksproduct en/of interventie

Start of orkambi is part of routine care.

Contactpersonen

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

In order to be eligible to participate in this study, a subject must meet all of the following criteria:

• Patients with a (predominant) class II mutation (almost exclusively homozygous Phe508del) for cystic fibrosis.

• Start with Ivacaftor/Lumacaftor (Orkambi) therapy

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

A potential subject who meets any of the following criteria will be excluded from participation in this study:

• None

For bronchoscopy the following patients will be excluded:

• Pre-lung transplant trajectory

• No informed consent for the procedure

• Deemed inappropriate by the treating physician.

Onderzoeksopzet

Opzet

Type:	Observationeel onderzoek, zonder invasieve metingen
Onderzoeksmodel:	Anders
Toewijzing:	N.v.t. / één studie arm
Blindering:	Open / niet geblindeerd
Controle:	N.v.t. / onbekend

Deelname

Nederland

Status:	Werving gestart
(Verwachte) startdatum:	13-11-2017
Aantal proefpersonen:	20
Type:	Verwachte startdatum

Ethische beoordeling

Positief advies

Datum:	13-11-2017
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL6643
NTR-old	NTR6829
Ander register	: 2016_336

Resultaten