A B2-agonist as a CFTR activator in CF Part II

No registrations found.

Ethical review	Not applicable
Status	Pending
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON24538

Source
NTR

Brief title
ABBA-2

Health condition

Cystic Fibrosis

Sponsors and support

Primary sponsor: University Medical Center Utrecht
Source(s) of monetary or material Support: ZonMw, NCFS

Intervention

Outcome measures

Primary outcome

Pulmonary function (spirometry and airway resistance measured with the bodybox and Rint)

Secondary outcome

• Fraction exhaled Nitric Oxide (FeNO) and Nasal Nitric Oxide (nNO) before and after the use

of salbutamol;

• BMI (=weight (in Kg)/Length2 (in cm)) before and after the use of salbutamol;

• Quality of life (measured with Cystic Fibrosis Questionnaire (CFQ)) before and after the use of salbutamol;

• Bile salt measurements in plasma and the feces before and after the use of salbutamol;

• Elastase measurements in the feces before and after the use of salbutamol;

• SCC measurements before and after the use of salbutamol;

• Upper and lower airway microbial profiles (microbiome) before and after treatment of the use of Salbutamol (conventional culturing, high throughout pyrosequencing (16S rRNA) for bacterial diversity and relative abundance).

• Correlation between individual salbutamol induced CFTR function in vitro (organoid-based measurements) and the in vivo treatment effect;

• The CFTR stimulating ability of the concentration of salbutamol in the patient's blood samples, examined by in vitro testing (in the organoid model);

Study description

Background summary

Objective: Primary objective of this study is to evaluate the clinical effect of a long term treatment (8 weeks) with oral B2-agonists in CF patients with residual CFTR function, especially on lung function (spirometry and airway resistance).

Secondary objectives are to:

1. Evaluate the correlations between individual B2-agonist-induced CFTR function in vitro (organoid-based measurements) and the long term clinical treatment effect (eg. lung function and airway resistance).

2. Assess the effect of the salbutamol concentration in the blood on CFTR function in the background of patient specific parameters. We will do this by examining the CFTR-stimulating potential of the patients' blood in vitro (in the organoid model).

Study design: A multicentre open label intervention study.

Study population: Adults with Cystic Fibrosis with a compound/A455E or compound/ R117H

mutation and proven residual CFTR function in vitro. We aim to include 20 patients.

Intervention: After baseline measurements all patients will receive oral Salbutamol during 8 weeks.

Main study parameters/endpoints: Pulmonary function (spirometry and airway resistance measured with the bodybox and Rint)

• Before and after treatment with salbutamol

Nature and extent of the burden and risks associated with participation, benefit and group relatedness: Patients participating in this study will be treated at home and will visit the hospital for two study visits. Salbutamol has been used in clinical practice for over decades in patients with asthma and no serious side effects have been reported. Therefore we do not expect serious problems or side effects during this study. We expect to see a clear clinical effect of long term treatment with oral salbutamol. When our hypothesis is confirmed, this is a major benefit for the patient. Not only during the study period but also for their further treatment. When this study confirms our hypothesis that organoids can predict clinical responders, this is a major benefit not only for the CF population but also for the individual patient. With the use of organoids we will then be able to generate optimal treatment strategies for individuals based on (combinations of) current and future drugs with only limited patient discomfort.

Study objective

Long term use (8 weeks) of oral B2-agonists increases CFTR function and improves disease parameters in patients with CF with a residual CFTR function.

Study design

Before and after treatment with oral salbutamol

Intervention

4dd4mg salbutamol oral

Contacts

Public
Wilhelmina Kinderziekenhuis
Huispostnummer KH 01.419.0
Postbus 85090
S. Michel
Utrecht 3508 AB

The Netherlands
+31 (0)88 75 537 25
Scientific
Wilhelmina Kinderziekenhuis
Huispostnummer KH 01.419.0
Postbus 85090
S. Michel
Utrecht 3508 AB
The Netherlands
+31 (0)88 75 537 25

Eligibility criteria

Inclusion criteria

- CFTR genotype compound/A455E or compound/R117H

- Already had a rectal biopsy to produce an organoid

- Males and females, aged 18 years or older on the date of informed consent

- Signed informed consent form (ICF)

Exclusion criteria

- Severe acute exacerbation or pulmonary infection during last four weeks (needing intravenous treatment and/or systemic corticosteroids)

- Known cardiovascular medical history like cardiac failure, arrhythmias, ischemic cardiac disease, long QT interval syndrome and hypertension

- Known hyperthyroidism, thyrotoxicosis, galactose intolerance, lactase deficiency or glucose-galactose malabsorption

- Haemoglobin A1C (HBA1C) > 45 mmol/mol

- Use of oral B2-agonist one week prior to the start of the study (V1)

- Use of: heart glycoside, high dose sympathomimetics, theophylline, thiazide diuretics or non-selective beta-blockers

- Pregnancy or breastfeeding

- Participation in another drug-investigating clinical study at the start

- Inability to follow instructions of the investigator

Study design

Design

Study type:	Interventional
Intervention model:	Factorial
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-07-2015
Enrollment:	20
Type:	Anticipated

Ethics review

Not applicable

Application type:	Not applicable

Study registrations

Followed up by the following (possibly more current) registration

ID: 43663
Bron: ToetsingOnline
Titel:

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

No registrations found.

In other registers

Register	ID
NTR-new	NL5108
NTR-old	NTR5240
CCMO	NL53059.041.15
OMON	NL-OMON43663

Study results

Summary results
Not applicable