A B2-agonist as a CFTR activator in CF

No registrations found.

Ethical review	Not applicable
Status	Recruitment stopped
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON21450

Source
Nationaal Trial Register

Brief title
ABBA-study

Health condition

CFTR residual function, Salbutamol, CFTR activation, personalized medicine

Sponsors and support

Primary sponsor: UMCU Utrecht, Prof. dr. C.K. van der Ent
Source(s) of monetary or material Support: Application at ZON-MW The Netherlands

Intervention

Outcome measures

Primary outcome

Difference in nasal potential difference (NPD) and sweat chloride concentration (SCC) before and after treatment with B2-agonists (per inhalation or oral)

Secondary outcome

- Difference between change in NPD and SCC when treated with B2-agonist per inhalation and oral B2-agonist

- Correlation between individual B2-agonist-induced CFTR function (organoid-based measurements) and in vivo treatment effect (NPD, SCC)

- The CFTR stimulating effect of patients' blood samples in vitro, on autologous organoid cultures

Study description

Background summary

We hypothesized that CF subjects with significant CFTR residual function benefit from therapeutic interventions that activate signal transduction pathways that increase CFTR function. In vitro (with the use of organoids) we found beta-2 adrenergic receptor agonists (B2-agonists) as potent activators of CFTR in patients with residual CTFR function. Restoration of the CF phenotype in vitro by a B2-agonist is variable between patients.

Primary objective of this pilot study is to evaluate the in vivo response to B2-agonists treatment in CF patients with residual CFTR function, using dosages which are clinically used in patients with asthma.
Secondary objectives are: to evaluate the difference between B2-agonist treatment per inhalation and oral B2-agonist treatment, to evaluate the correlations between individual B2-agonist-induced CFTR function in vitro and the in vivo treatment response and to assess whether the dosage of Salbutamol used in the clinical study is sufficient to stimulate CFTR function. To reach these objectives, adults with Cystic Fibrosis with a compound/A455E or compound/ R117H mutation and proven residual CFTR function in vitro will receive Salbutamol per inhalation and Salbutamol per os. Main study parameters will be the nasal potential difference (NPD) and sweat chloride concentration (SCC) before and after both treatments with Salbutamol. These treatment effects will be compared with in vitro effects.

Study objective

B2-agonists can increase CFTR function and improve disease parameters in patients with CF with a residual CFTR function. Multiple patient-specific parameters are important for the amount of B2-agonist induced CFTR function, measurements in organoids can predict individual treatment efficacy.

Study design

Before and after treatment with the oral B2-agonists and B2-agonist per inhalation.

Intervention

All patients will receive an oral B2-agonist and a B2-agonist per inhalation. Measurements will be done before and after both treatments. The results will be compared with the results seen

in the organoids.

Contacts

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Eligibility criteria

Inclusion criteria

- CFTR genotype compound/A455E or compound/R117H

- CFTR measurement available in intestinal biopsies

- 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 (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

- HBA1C > 45 mmol/mol

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

- Use of: heart glycoside, sympathomimetic drugs, theophylline, thiazide diuretics or non-selective beta-blockers

- Pregnancy or breastfeeding

- Participation in another drug-investigating clinical study at the start or within 1 month prior to the start

- Inability to follow instructions of the investigator

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-05-2014
Enrollment:	10
Type:	Actual

Ethics review

Not applicable

Application type:	Not applicable

Study registrations

Followed up by the following (possibly more current) registration

ID: 40957
Bron: ToetsingOnline
Titel:

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

No registrations found.

In other registers

Register	ID
NTR-new	NL4382
NTR-old	NTR4513
CCMO	NL47622.041.14
OMON	NL-OMON40957

Study results