Validation of *in vitro counterpart* models to enable personalized care in CF

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The specific objectives are:1. What is the difference of in vitro CFTR function in CF patients with either mild (compound heterozygote A455E) mutations or severe (homozygote F508del) mutations with mild or severe clinical disease? 2. What is the...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Respiratory disorders congenital
Study type	Observational invasive

Summary

ID

NL-OMON40312

Source
ToetsingOnline

Brief title
VICI CF study

Condition

- Respiratory disorders congenital
- Lower respiratory tract disorders (excl obstruction and infection)

Synonym
cystic fibrosis

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: Christinafonds (NCFS);WKZ fonds

Intervention

Keyword: cftr rescue, cure, cystic fibrosis, personalized medicine

Outcome measures

Primary outcome

Primary endpoint: CFTR activity (expressed as absolute swelling of organoids, and % apical CFTR-expressing nasal epithelial cells) measured in intestinal organoids and nasal epithelial cells.

Secondary outcome

Secondary endpoints: Clinical correlates: Intestinal current measurement (ICM) in rectal biopsies; Current lung function and at age 12; Slope of lung function decline; Exacerbation rate; Current nutritional status and at age 12; Current chronic infection with Pseudomonas and Staphylococci and at age 12; Current Chest X-ray Chrispin Norman score and at age 12; current Chest CT Brodi score.

Study description

Background summary

Cystic Fibrosis is a lethal disease for which only symptomatic treatment is available. Emerging knowledge on upcoming drugs targeting the basic defect of CF announces new opportunities for curative treatment. Proper targeting of these drugs to responsive patients will be very important to demonstrate their clinical efficacy, and to achieve maximal cost-effectiveness of care. We recently developed two novel unique patient derived in vitro models that are very promising for prediction of clinical effects of CF basic defect-restoring compounds in single patients. In this project we will validate the predictive capacity of these 'in vitro counterparts' for clinical outcome in CF patients with different clinical and genetic expressions of the disease. In vitro measurements will be related to clinical outcomes in homozygous F508del patients with severe and mild phenotype and in F508del/A455E compound heterozygous patients that display a mild phenotype. This study is a crucial

intermediate for development of personalized care in CF.

Study objective

The specific objectives are:
1. What is the difference of in vitro CFTR function in CF patients with either mild (compound heterozygote A455E) mutations or severe (homozygote F508del) mutations with mild or severe clinical disease?
2. What is the association of in vitro CFTR function with clinical correlates of heterozygote A455E CF patients or F508del/F508del CF patients that display mild or severe clinical disease?
3. What is the association of novel in vitro CFTR function measurements with existing ex vivo intestinal current measurements (ICM) in rectal biopsies?

Study design

This study will be a multicenter, observational study.

Study burden and risks

The study will be performed in adults aged 18 years or older depending on the mutation, which enables proper documentation of the patients' clinical phenotype over a long time-span.
Since there is a broad diversity in clinical phenotype depending on the CFTR mutation, but also in patients carrying the same mutation (dF508), three groups will need to be included.
The study will lead to one extra visit besides the scheduled follow-up visits. Nasal brushes can cause some irritation of the nasal mucosa for several hours and/or some self-limiting light bleeding in case of damaged mucosa prior to the study. Rectal biopsies are painless because of the insensitivity of the upper layer of the rectal mucosa. The risk of complications is very low, the patient can encounter some slight loss of rectal blood. This is benign and in almost all cases self-limiting.
A rectal biopsy might be a psychological loaden procedure, when patients agree to participate the risks in this study can be considered low, whereas the benefits might be substantial.
Direct benefits for the individual patient lie in the value of the in vitro model in directing individual patient tailored care. We can use the patients* unique material to predict individual responses to CFTR-restoring drugs in follow up studies. After validation of this model we plan to set up a follow-up study to use the in vitro models of all study patients to assess the most effective individualized treatment strategy.

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

- Being able to sign informed consent form (ICF).
- Males and females aged 18 to 40 years on the date of informed consent and homozygous for the
F508del-CFTR mutation (as documented in the subject's medical record)
or:
- Males and females aged 18 years or older on the date of informed consent and hetrozygous for
the compound/A455E mutation (as documented in the subject's medical record)

Exclusion criteria

CF patients with:
Instabile CF-related diabetes
Active ABPA (allergic bronchopulmonary aspergillosis)
Other major CF related complications (CF related liver disease with abnormal coagulation).

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	12-12-2013
Enrollment:	60
Type:	Actual

Ethics review

Approved WMO Date:	10-09-2013
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	16-06-2014
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	19-11-2014
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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	NL44524.041.13