The effect of curcumin and genistein in CF patients with a class III mutation

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Primary objective:To investigate the clinical response to treatment with curcumin and genistein in CF-patients with a class III S1251N mutation.. Secondary objectives:1.To evaluate the correlations between individual curcumin+genistein induced CFTR...

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

Summary

ID

NL-OMON40933

Source
ToetsingOnline

Brief title
TICTAC I study

Condition

- Respiratory disorders congenital
- Congenital respiratory tract disorders

Synonym
Cystic Fibrosis, Mucoviscidosis

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: Ministerie van OC&W,NCFS

Intervention

Keyword: CFTR activation, Curcumin en genistein, Cystic Fibrosis, Treatment

Outcome measures

Primary outcome

Difference in sweat choline concentration before and after receiving curcumin+genistein.

Secondary outcome

Secondary endpoints will include:

• Difference in lung function (%FEV1) and airway resistance (Rint and bodybox) before and after the use of curcumin+genistein;

• Difference in BMI before and after the use of curcumin+genistein;

• Difference in quality of life (measured with CFQ-questionnaire) before and after the use of curcumin+genistein;

• Bile salt measurements in plasma and the feces before and after the use of curcumin+ and genistein;

• Elastase measurements in the feces before and after the use of curcumin+ and genistein;

• Correlation between individual curcumin+genistein induced CFTR function in vitro (organoid-based measurements) and in vivo effect (lung function, SCC);

• The CFTR stimulating ability of the concentration of curcumin+genistein in the patient*s blood samples, examined by in vitro testing (in the organoid model).

Study description

Background summary

The cystic fibrosis trans membrane conductance regulator (CFTR), a chloride and bicarbonate channel encoded by the CF gene, is essential for fluid and electrolyte homeostasis at the epithelial surfaces of many organs, including the lung, intestine, and sweat gland. Over 1900 CFTR mutations have been identified causing impaired protein production (class I), folding (class II), channel gating (class III), conductance (class IV), or reduced synthesis (class V).

Currently, several CF patients with gating mutations use curcumin and genistein because of anecdotally reported beneficial effects of these self-administered food supplements. Curcumin and genistein are freely available plant extracts which can be bought on the internet. Formal efficacy studies of these supplements have never been done. Recently, using various primary cell models from CF patients (organoids), we found the natural food components curcumin and genistein as potent correctors of the channel gating defect, capable of enhancing the activity of class III gating mutants (e.g. G551D; S1251N).

Study objective

Primary objective:
To investigate the clinical response to treatment with curcumin and genistein in CF-patients with a class III S1251N mutation..

Secondary objectives:
1.To evaluate the correlations between individual curcumin+genistein induced CFTR function in vitro (organoid-based
measurements) and the in vivo treatment effect (lungfunction, airway resistance and SCC);
2.To assess whether the dosage of curcumin+genistein used in the clinical study is sufficient to stimulate CFTR function. We will
evaluate the CFTR stimulating ability of the concentration of curcumin+genistein in the patient*s blood samples. We will examine this by in vitro testing (in the organoid model), evaluating the CFTR stimulating ability of the concentration of curcumin+genistein and Ivacaftor in the patient*s blood samples. we will also determine the serum levels of curcumin and genistein.

Study design

This study will be a multi centre pilot open label intervention-study.

Intervention

After baseline measurements all patients will receive curcumin and genistein during 8 weeks. Study measurements will be performed during two visits; before and after receiving curcumin+genistein.

Study burden and risks

In this study patients will receive the natural food components curcumin and genistein and the drug Ivacaftor. Curcumin and genistein are registered natural food supplements, widely and freely available on internet and in reform-shops and used by millions of people world-wide. Unless we will give these components in a higher dose, we do not expect serious problems or side effects during this study because of the limited side effects that have been described in earlier studies with higher doses (also see Investigator Brochures) and the positive experience of the four patients who are already being treated. In the context of this study, patients have to visit the hospital 2 times during 2,5 hours and at home they need to write down their use of curcumin+genistein in a diary and perform a FEV1 test every week.

A number of patients with a S1251N class III gating mutation use curcumin and genistein themselves as part of their regular care and they show a clear diminution of their CF symptoms, without detectable side-effects. When our hypothesis is confirmed and curcumin and genistein turn out to improve the CFTR function in patients with a class III gating mutation and therefore diminish CF symptoms, this is a major benefit not for these patients.

When this study also confirms our hypothesis that organoids can predict clinical responders, this is a major benefit not only for the individual patient but for the entire CF-population. With the use of organoids we will be able to generate optimal treatment strategies for individuals based on (combinations of) current and future drugs with only limited patient discomfort.

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)
Children (2-11 years)
Elderly (65 years and older)

Inclusion criteria

1. CFTR genotype compound/ S1251N
2. CFTR measurement available in intestinal biopsies
3. Males and females, aged 6 years or older on the date of informed consent or, where appropriate, date of assent
4. Signed informed consent form (IC), and where appropriate, signed assent form

Exclusion criteria

1. Severe acute exacerbation or pulmonary infection during last four weeks (needing intravenous
treatment);
2. Use of curcumin and or genistein at start or within four weeks prior to start of the study;
3. Participation in another drug-investigating clinical study at the start or within four weeks prior to the
start;
4. Known cholelithiasis;
5. Inability to follow instructions of the investigator.

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	18-09-2014
Enrollment:	10
Type:	Actual

Ethics review

Approved WMO Date:	22-05-2014
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	14-08-2014
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	05-11-2014
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	12-11-2014
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

Approved WMO Date:	05-12-2014
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	22-12-2014
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

ID: 23234
Source: NTR
Title:

In other registers

Register	ID
EudraCT	EUCTR2014-000817-30-NL
CCMO	NL48122.041.14
OMON	NL-OMON23234

Study results

Date completed:	08-05-2015
Actual enrolment:	13