Genistein as an add-on treatment for CF?

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

Summary

ID

NL-OMON45929

Source
ToetsingOnline

Brief title
TRIO 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, Genistein, Ivacaftor, Organoid

Outcome measures

Primary outcome

The main study parameter is pulmonary function (Forced Expiratory volume in 1 second; FEV1) measured before and after the use of genistein and before and after the use of placebo.

Secondary outcome

Secondary endpoints to evaluate in vivo effect are:

* Sweat chloride concentration (SCC)

* Airway resistance (Rint and bodybox)

* Body Mass Index (BMI)

* Quality of life (measured with the Cystic Fibrosis Questionnnaire; (CFQ))

* Elastase measurements in the feces

* The CFTR stimulating ability of the concentration of genistein in the patient*s blood samples. We will also determine the plasma levels of genistein; Assessment of ß-adrenergic sweat secretion by evaporimetry is included as an exploratory endpoint.

Study description

Background summary

The cystic fibrosis trans membrane conductance regulator (CFTR), a chloride and bicarbonate channel encoded by the CFTR 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). Recently the first CFTR potentiator-drug Ivacaftor was approved for the treatment of CF patients with a (class III) gating mutation.

Using various primary cell models from CF patients (organoids), we found that adding the natural food supplement genistein to the approved CFTR potentiator Ivacaftor, might increase the function of the CFTR protein, thereby enhancing function of these mutants significantly.

Study objective

Our primary objective is to investigate whether a further gain in efficacy of oral Ivacaftor treatment can be reached by co-supplementation of genistein, as suggested by their highly synergistic action in intestinal organoids
Our secondary objectives are:
1: to evaluate the correlations between individual Ivacaftor genistein induced CFTR function in vitro (organoid-based measurements) and the in vivo treatment effect.
2: to evaluate the correlation between serum levels of Ivacaftor and genistein and the in vivo treatment effect.

Study design

A multicentre randomized double-blind placebo controlled trial.

Intervention

Patients will be randomized to receive genistein or placebo during a period of 8 weeks (treatment period 1). After an 4-week washout, patients will be crossed over to receive the opposite treatment (Treatment period 2).

Study burden and risks

Patients participating in this study will be treated at home and will visit the hospital for four study visits. During each visit several tests will be performed.
The patients will receive genistein and placebo during eight weeks. Genistein is a registered natural widely used food components. In a previously conducted study (the TICTAC I study) a total of 13 subjects received genistein in a maximum dose of 5,0 mg/Kg/day. There were no serious adverse events reported during this study. The dose of genistein that patients will receive in this study will not exceed the previously tested dose of 10mg/Kg/day. 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 in which the same dose was used (also see Investigator brochure).
When our hypothesis is confirmed and a further gain in efficacy of oral Ivacaftor treatment can be reached by co-supplementation of genistein this is a major benefit not only for the individual patient but for the entire CF-population. 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.

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

*CFTR genotype associated with residual CFTR function;
*Already had a rectal biopsy to produce an organoid;
*Use of Ivacaftor;
*Male and female patients, aged 6 years or older on the date of informed consent;
*Signed informed consent form (IC).

Exclusion criteria

*Use of genistein or curcumin at start or within four weeks prior to start of the study;
*Severe acute exacerbation or pulmonary infection during last four weeks (needing intravenous treatment and/or systemic corticosteroids);
*(History of) hypothyroidism;
*Women who are trying to become pregnant or are pregnant or breastfeeding;
*Women with estrogen receptor-positive tumors;
*Postmenopausal women on tamoxifen therapy for estrogen-responsive breast cancer;
*Participation in another drug-investigating clinical study at the start or within four weeks prior to the start;
*Inability to follow instructions of the investigator.

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	02-06-2017
Enrollment:	20
Type:	Actual

Ethics review

Approved WMO

Date:	15-03-2017

Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	27-03-2017
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	03-07-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	15-11-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	01-12-2017
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: 24579
Source: NTR
Title:

In other registers

Register	ID
EudraCT	EUCTR2016-001619-19-NL
CCMO	NL57585.041.16
OMON	NL-OMON24579

Study results

Date completed:	18-10-2018
Actual enrolment:	14