ISRCTN03484127 https://doi.org/10.1186/ISRCTN03484127

Cystic fibrosis: a hereditary inflammatory process

Submission date	Recruitment status	[ ] Prospectively registered
12/09/2005	No longer recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
12/09/2005	Completed	[ ] Results
Last Edited	**Condition category**	[ ] Individual participant data
17/09/2008	Nutritional, Metabolic, Endocrine	[ ] Record updated in last year

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
NTR91

Study information

Scientific Title

Study objectives
One out of 3600 new-born children in the Netherlands has cystic fibrosis (CF). It is an autosomal recessive disease and about 70% of the Dutch CF-patients are homozygous for the delta-F508 mutation. Although the genetic mutation is identical in this group of patients, the pulmonary disease is very diverse. Causative factors are environmental and also co-genetic ones. Morbidity is caused by chronic inflammation and infection of the lungs, which leads to irreversible lung damage.

Neutrophils play a key role in the inflammatory cascade. It is assumed that parts of the acute inflammatory response of the neutrophil (chemotaxis/IL8 ± adhesion/selectines ± activation /TNFa ± production of e.g. superoxides or myeloperoxidase ±tissue destruction) play an important role in the inflammatory process in CF. There is a higher concentration of mediators (IL-8, sICAM1, sE-Selectin, TNFa) in patients with CF than in other patients with airway infections. The CFTR protein acts not only as a Cl channel but also as a Na/H antiport and influences the intracellular pH. This might affect the functional activity of the neutrophil. Recently, new activation markers (MoPhabs A17 and A27) located on leukocytes were described that may be an early sign of pulmonary inflammation. To be able to predict and intervene in the inflammatory process would improve the prognosis especially in young children before the process of irreversible lung damage.

The use of new and powerful inhaled corticosteroid medication enables us to give anti-inflammatory therapy to young children without the systemic side-effects of orally administered steroids.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics approval received from the local medical ethics committee

Study design
Randomised, double blind, placebo controlled, parallel group trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Not specified

Study type(s)
Treatment

Participant information sheet

Health condition(s) or problem(s) studied
Cystic fibrosis

Interventions
Inhaled HFA-Beclomethasone Diproprionate (Qvar®) 200 mcg twice daily by aerochamber or a placebo (also inhaled by aerochamber).

Intervention Type
Drug

Phase
Not Specified

Drug/device/biological/vaccine name(s)
Inhaled HFA-Beclomethasone Diproprionate

Primary outcome measure
Pulmonary
1. Forced expiratory volume in one second (FEV1), forced vital capacity (FVC), residual volume (RV)/total lung capacity (TLC) % after 3 years
2. Rint measurements

Secondary outcome measures
Immunological:
1. Neutrophil markers: MoPhabs A17 and A27, CD11b, CD11a
2. Interleukin-8 (IL-8), soluble intercellular adhesion molecule 1 (sICAM1), sE-Selectin, tumour necrotising factor alpha (TNFa)
3. End tidal carbon monoxide in exhaled breath

Microbiological:
1. Respiratory pathogens in culture

Serological:
1. Seroconversion to anti-pseudomonal antibodies

Clinical:
1. Adverse events
2. Clinical parameters (body weight, height, fat free mass)
3. Number of pulmonary exacerbations
4. Antimicrobial agent use
5. Quality of life questionnaire scores

Radiological:
1. Chest radiograph scored by CF chest radiograph scoring systems

Overall study start date
01/01/2002

Completion date

01/12/2005

Eligibility

Key inclusion criteria
For 3-years randomised controlled trial:
1. CF diagnosis as confirmed by sweat chloride test and/or genotyping
2. CF-patients 2 - 10 years old
3. Informed consent
4. Capable of using inhaled corticosteroids by aerochamber
5. Compliant to regular therapy

Participant type(s)
Patient

Age group
Child

Lower age limit
2 Years

Upper age limit
10 Years

Sex
Both

Target number of participants
60

Key exclusion criteria
For 3-years randomised controlled trial:
1. CF-patients less than 2 years
2. CF-patients greater than 10 years
3. Use of anti-inflammatory therapy in a period of 2 months before inclusion (orally administered steroids, inhaled corticosteroids and non-steroid anti-inflammatory drugs, non-steroidal anti-inflammatory drugs [NSAIDs])
4. Disease, other than CF, that affects growth
5. Participation in another study

Date of first enrolment
01/01/2002

Date of final enrolment
01/12/2005

Locations

Countries of recruitment
Netherlands

Study participating centre
Universitair Medisch Centrum, locatie AZU
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Sponsor information

Organisation
University Medical Centre Utrecht (UMCU) (The Netherlands)

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Sponsor type
University/education

ROR
https://ror.org/04pp8hn57

Funder(s)

Funder type
Government

Funder Name
The Netherlands Organization for Scientific Research (NWO) (The Netherlands)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not provided at time of registration