# Peripheral targeting of inhaled rhDNase in stable CF patients.

Gepubliceerd: 19-02-2007 Laatst bijgewerkt: 18-08-2022

rhDNase targeted to the peripheral airways improves lung function in children with CF and a stable clinical condition.

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|---|---|
| **Ethische beoordeling** | Niet van toepassing |
| **Status** | Werving gestopt |
| **Type aandoening** | - |
| **Onderzoekstype** | Interventie onderzoek |

## Samenvatting

### ID

NL-OMON23855

**Bron**
NTR

**Aandoening**

Cystic Fibrosis, rhDNase (Pulmozyme), inhalation, airways.

### Ondersteuning

**Primaire sponsor:** Investigator initiated study.
Initiator: Harm Tiddens, M.D. PhD.
ErasmusMC - Sophia Children's Hospital
**Overige ondersteuning:** partially:
Roche B.V. financially supports this research by means of a grant

and partially:
fund = initiator = sponsor

### Onderzoeksproduct en/of interventie

### Uitkomstmaten

**Primaire uitkomstmaten**

Primary endpoint will be the change in FEF75 as a result of treatment. FEF75 is the most suitable endpoint since it is sensitive to peripheral airways obstruction.

# Toelichting onderzoek

### Achtergrond van het onderzoek

SUMMARY
Rationale: Respiratory disease in patients with cystic fibrosis (CF) is characterized by an abnormal composition of the epithelial lining fluid. As a result patients develop chronic airway infection and inflammation which start early in life[1-3]. The sputum in CF is rich in leukocyte-derived DNA which greatly contributes to abnormal viscoelasticity of the CF sputum [4]. This purulent, infected sputum can obstruct the airways. RhDNase is an identical copy of the native human DNase. RhDNase cleaves extracellular DNA through hydrolyses and reduces the viscoelasticity of CF sputum in vitro [5]. RhDNase has been shown to reduce sputum viscosity, improve pulmonary function, and reduce the number of pulmonary exacerbations in patients with moderate lung disease [6-8]. Similar effects have been demonstrated in patients with mild disease, making rhDNase currently the only mucolytic in CF with proven efficacy [8, 9].
Lung damage In CF is thought to begin by mucus impaction predominantly localized in the peripheral airways. Chronic infection and chronic airway inflammation lead to structural damage [10]. To prevent this damage from occurring sputum mobilization using physiotherapy techniques is important in the treatment of CF pulmonary disease. Daily nebulization of rhDNase facilitates the mobilisation of mucus from the airways. However, relatively little of the inhaled drug is deposited in the peripheral airways. Hence this compartment of the lung is thought to be relatively under treated. Mucus clearance from peripheral airways can probably be improved by targeting rhDNase selectively to these airways. Therefore we hypothesize that rhDNase targeted to the peripheral airways can improve lung function in children with CF.
Objective: Primary Objective: To investigate the effect of treatment with nebulized rhDNase targeted to the peripheral airways compared to rhDNase targeted to the central airways on FEF75 (a lung function parameter for peripheral airflow limitation) in children with CF who are on maintenance treatment with rhDNase.
Study design: This study will be a multi centre, randomized controlled clinical trial.
Study population: Children with CF aged 6-18 years, who are on maintenance treatment with rhDNase and who are in a stable clinical condition. A total of 50 children will be included, 25 children in each group.
Intervention (if applicable): One group receives nebulized rhDNase targeted to the peripheral airways once daily, the other group receives nebulized rhDNase targeted to the central airways once daily. Duration of study treatment will be 4 weeks.
Main study parameters/endpoints: Primary endpoint will be the change in FEF75 compared to baseline after one month of treatment. FEF75 is the most suitable endpoint since it is sensitive to peripheral airways obstruction.

### Doel van het onderzoek

rhDNase targeted to the peripheral airways improves lung function in children with CF and a stable clinical condition.

### Onderzoeksproduct en/of interventie

25 patients will receive four weeks of treatment with inhaled rhDNase targeted to the peripheral airways and 25 patients will receive four weeks of treatment with inhaled rhDNase targeted to the central airways. The central airways regimen is aimed to simulate equal deposition pattern as compared to conventional maintenance therapy. The peripheral airway regimen deposits a greater percentage of the medication in the peripheral airways.

## Contactpersonen

### Publiek

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### Wetenschappelijk

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## Deelname eisen

## Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. Age between 6 and 18 years old;
2. Diagnosis of CF confirmed by sweat-test and/or DNA analysis and/or electro physiology testing (nasal potential difference measurement);
3. Routine treatment with rhDNase once daily, started at least one month before enrolment in the study;
4. Stable condition, in this study defined as: no i.v antibiotics (hospital or at home) in the previous month and constant medication regime during the previous 2 weeks (for example: no additional oral antibiotics course, no newly started inhaled or systemic corticosteroids etc).
5. Ability to perform lung function tests (assessed by trained lung function technician);
6. Lung function: FVC > 40% predicted;
7. Signed written informed consent.

## Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. Inability to follow instructions of the investigator;
2. Inability to inhale rhDNase;
3. Clinical condition not stable, as assessed by the patient’s paediatrician;
4. Concomitant medical conditions that effect inhaled treatment (e.g. cleft palate, severe malacia);
5. Current respiratory tract infection;
6. Pulmonary complications that might put the patient at risk to participate in the study;
7. Neuromuscular disease;
8. Poor compliance with treatment as assessed by the patient’s paediatrician;
9. Active ABPA (allergic bronchopulmonary aspergillosis) defined as an oral course of prednisone for ABPA within the last three months.

# Onderzoeksopzet

## Opzet

| | |
|---|---|
| Type: | Interventie onderzoek |
| Onderzoeksmodel: | Parallel |
| Blindering: | Dubbelblind |
| Controle: | Geneesmiddel |

## Deelname

Nederland

| | |
|---|---|
| Status: | Werving gestopt |
| (Verwachte) startdatum: | 01-05-2007 |
| Aantal proefpersonen: | 50 |
| Type: | Werkelijke startdatum |

# Ethische beoordeling

Niet van toepassing

| | |
|---|---|
| Soort: | Niet van toepassing |

# Registraties

## Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

## Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

## In overige registers

| Register | ID |
|---|---|
| NTR-new | NL661 |
| NTR-old | NTR912 |
| Ander register | : 2412325-3 |
| ISRCTN | ISRCTN64225851 |

# Resultaten

**Samenvatting resultaten**

Earlier publications have shown that:
- patients develop chronic airway infection and inflammation which start early in life

[1. Dakin, C.J., et al., Inflammation, infection, and pulmonary function in infants and young children with cystic fibrosis. Am J Respir Crit Care Med, 2002. 165(7): p. 904-10.
2. Armstrong, D.S., et al., Lower airway inflammation in infants and young children with cystic fibrosis. Am J Respir Crit Care Med, 1997. 156(4 Pt 1): p. 1197-204.
3. Nixon, G.M., et al., Early airway infection, inflammation, and lung function in cystic fibrosis. Arch Dis Child, 2002. 87(4): p. 306-11].
And that:
- Predominantly the peripheral airways are damaged and filled with sputum in CF
[Tiddens, H.A., et al., Cartilaginous airway wall dimensions and airway resistance in cystic fibrosis lungs. Eur Respir J, 2000. 15(4): p. 735-42].

Therefore we hypothesize that rhDNase targeted to the peripheral airways can improve lung function in children with CF.