MONITOR CF: Monocytes In TiMaSCAN for monitoring respiratory infections in Cystic Fibrosis

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Our main aim is to validate the TiMaSCAN as both a diagnostic and monitoring tool in the treatment of pulmonary exacerbations in CF patients.

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

Summary

ID

NL-OMON51190

Source
ToetsingOnline

Brief title
MONITOR CF study

Condition

- Respiratory disorders congenital
- Bacterial infectious disorders
- Congenital respiratory tract disorders

Synonym
Cystic Fibrosis

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Stichting Sophia Fonds

Intervention

Keyword: Bacterial infection, Cystic fibrosis, Monocytes, Pulmonary exacerbation

Outcome measures

Primary outcome

OBJECTIVE 1 - Validate qualitative TiMaSCAN results as diagnostic tool

Hypothesis 1A. TiMaSCAN results, expressed as positive or negative for CF-specific pathogens, will correlate with results from (lower) airway cultures.

Primary endpoint: percentage of concordance of positive TiMaSCAN result for a CF specific pathogen with result of sputum or BAL cultures

Secondary outcome

OBJECTIVE 2 - Validate quantitative TiMaSCAN results as monitoring tool of treatment efficacy.

Hypothesis 2A. The number of pathogen-positive TiMas in peripheral blood will go down over the course of antibiotic treatment.

Hypothesis 2B. A decreasing number of pathogen-positive TiMas correlates with lung function improvement.

Hypothesis 2C. A decreasing number of pathogen-positive TiMas correlates with improvement of clinical symptoms.

Hypothesis 2D. Persistent presence of pathogen-positive TiMas at the end of treatment correlates with shorter time to next exacerbation.

Primary endpoint: Change in number of pathogen-positive TiMas over the course of antibiotic treatment.

Other outcome parameters:

- percentage of disconcordance of positive TiMaSCAN result for a CF specific

pathogen with the result of sputum or cough swab cultures.

- Correlation pathogen-positive TiMas with lung function.

- Correlation pathogen-positive TiMas with mean change in CFRSD/CRISS score and

CFQ-R.

- Correlation number of pathogen-positive TiMas at end of treatment with time

to next exacerbation, with either oral or iv treatment (follow up of maximum

one year).

Study description

Background summary

In cystic fibrosis (CF), fast and effective treatment of acute lung attacks, so-called pulmonary exacerbations, is important to limit deterioration and damage to the lungs. These acute lung attacks are caused by infections. Antibiotics are given as treatment, the choice being based on results of previous airway cultures and empirically on previous good response. Bacteria are identified by culture of sputum or swabs of the upper airways. However, these methods are a) insensitive, since bacteria residing deep in the lungs are not always present in the sputum; b) insufficiently specific, as asymptomatic colonization in the upper respiratory tract may occur. To obtain more accurate information, bronchoalveolar lavage fluid (BALF) can be used for culture. However, BAL by bronchoscopy is an invasive procedure which must be done under anesthesia in children and therefore cannot be obtained often. The current treatment of pulmonary exacerbations is therefore based on symptoms and suboptimal knowledge about the microorganisms that play a role at that specific moment. Treatment of a lung attack can be improved if an accurate and rapid assessment of a specific infection can be made before antibiotics are administered.

We have developed a new diagnostic method called TiMaSCAN that can distinguish infection in the lungs from colonization of the upper airways. TiMaSCAN is based on the scanning of monocyte content in peripheral blood using flow cytometry and pathogen-specific antibodies.

The optimal duration of antibiotic treatment for pulmonary exacerbations is a matter of debate. The duration of an IV course is determined by improved lung function and symptoms. In young children, however, lung function assessment is difficult, requiring clinicians to rely on symptoms to guide treatment success, which may not be accurate enough. Thus, there is an urgent need for a quick, easy-to-perform test that is specific for CF bacteria and can measure whether the treatment is effective.

Our hypothesis is that TiMaSCAN results will correlate with airway cultures and that the amount of pathogen-positive TiMas will decrease over the course of antibiotic treatment.

Study objective

Our main aim is to validate the TiMaSCAN as both a diagnostic and monitoring tool in the treatment of pulmonary exacerbations in CF patients.

Study design

Observational study, ex-vivo analysis of peripheral blood monocytes from children with CF, correlations with results from airway cultures and clinical data such as respiratory symptoms and spirometry.

Study burden and risks

In most patients a minor burden is associated with this study, with no additional risks or benefits. No additional study visits are required. For this study we plan to collect peripheral blood and sputum. The blood sample is taken from the i.v. canula or central line at the time of insertion, during treatment, and immediately after the course of antibiotics, just before it is removed. Usually no additional puncture is required. Obtaining an extra tube of blood does not place an additional burden on the patient.
Sputum is collected at the same time points as peripheral blood. If no sputum can be coughed up, we will collect a cough swab. This method is also widely used in routine care and does not pose a risk to the patient.
If a bronchoscopy with BAL is performed at the start of treatment, these cultures will also be included in analysis. However, no bronchoscopy is performed for research purposes only. Rest material is used for research purposes.
Lung function is analysed by standard spirometry according to routine care

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)

Inclusion criteria

• Diagnosed with CF, either by abnormal sweat test and/or confirmed with 2 mutations found by genetic analysis, either from heel-prick screening or diagnosed later in life;
• Aged 5 - 18 years at time of hospitalization;
• Able to perform lung function test;
• Having an indication to receive intravenous antibiotic treatment because of a pulmonary exacerbation
• Authorized by a written informed consent from parents (and patient, if aged > 12) to collect a vial of EDTA blood from i.v. canula, to undergo a sputum induction (if sputum collection is not possible, a cough swab is collected) and to assess lung function, and permission to use excess biomaterials and coded clinical data for research.

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:
• Diagnosed with allergic bronchopulmonary Aspergillosis
• Use of prednisone
• Antibiotic iv treatment has already been started more than 12 hours before collection of first blood and/or sputum cultures
• Use of inhaled antibiotics during antibiotic iv course.

Study design

Design

Study type: Observational non invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	23-09-2021
Enrollment:	20
Type:	Actual

Ethics review

Approved WMO

Date:	20-08-2021
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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: 25786
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
CCMO	NL77646.078.21
Other	NL9423
OMON	NL-OMON25786