The Role of Type I Interferon in Interstitial Lung Disease

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Ethical review	Approved WMO
Status	Pending
Health condition type	Autoimmune disorders
Study type	Observational invasive

Summary

ID

NL-OMON56690

Source
ToetsingOnline

Brief title
INITIALISE

Condition

- Autoimmune disorders

Synonym
Connective TIssue Diseases, rheumatic diseases

Research involving
Human

Sponsors and support

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

Intervention

Keyword: 1.Systemic autoimmune diseases, 2.Interstitial Lung Disease, 3.Type I Interferon, 4.Fibrosis

Outcome measures

Primary outcome

Our main study parameters will be IFN-I activation at baseline and after

standard care immunosuppressants and relation between IFN-I and fibrosis in an

in vitro model.

Secondary outcome

Not applicable.

Study description

Background summary

A shared feature of all systemic autoimmune diseases (SADs) is interstitial lung disease (ILD), which is a leading cause of death. Type I Interferon (IFN-I) plays a key role in the pathogenesis of SADs. However, much is still unknown and one of the unanswered questions is whether IFN-I also plays a role in the development of ILD in SADs. New treatments blocking the IFN-I pathway activation are emerging and IFN-I might be a potential treatment target for ILDs as well. Moreover, there are patients who do not meet criteria for a certain SAD, but have a combination of ILD and autoimmune features. These are patients with IPAF (Interstitial Pneumonia with Autoimmune Features). It would be valuable to study whether these patients also have increased IFN-I activity, so that they too can be considered for anti-IFN therapies.

Study objective

The overall aim of this project is to unravel the role of IFN-I in ILD in the known/classified SADs and in ILD with autoimmune features but without a specific SAD diagnosis (IPAF), with as ultimate goal better treatment. Since 13-40% of ILD patients will develop a progressive fibrosing form of ILD, we will also look into the relation between IFN-I and fibrosis. We will do this by assessing IFN-I activity in patients with a typically fibrotic ILD but without autoimmune features i.e. Idiopathic Pulmonary Fibrosis (IPF) and by performing

mechanistic studies in in vitro models for fibrosis. Furthermore, we want to explore whether IFN-I activity can be predictive for response of ILD to standard care immunosuppression and be used as a stratification tool for selection of ILD patients for immunosuppression or for anti-fibrotic agents.
The 5 objectives are:
1: To assess IFN-I activity in different SADs with and without ILD to determine possible differences in IFN-I activity
2: To assess IFN-I activity in patients with IPAF
3: To assess IFN-I activity in patients with IPF
4: To study whether baseline IFN-I activity predicts the response to standard care immunosuppressive therapy after 3 months of treatment defined as increase in pulmonary function test
5: To elucidate the relation between IFN-I and lung fibrosis in in vitro models for fibrosis

Study design

Blood samples will be collected from 30 SAD patients without ILD, 30 SAD patients with ILD, 30 IPAF and 30 IPF patients. To assess IFN-I activity, five IFN-I induced genes (i.e. IFN-I signature) will be assessed by PCR in whole blood and IFN-I protein will be measured by Simoa (single-molecule array) in serum. Blood tests for assessing IFN-I activity and pulmonary function tests will be performed in ILD SAD and IPAF patients before start of standard care immunosuppressants and 3 months after to evaluate whether IFN-I activity can predict the level of response to standard care immunosuppression. The relation between IFN-I and fibrosis will be studied in two in vitro models for fibrosis.

Study burden and risks

The burden on the patients in this study is negligible. Clinical data will be collected anonymized and extra study blood samples will only be taken in addition to blood samples drawn for clinical use. Pulmonary function tests will be performed as part of standard clinical care. In this way there are no extra risks for the participating patients.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

In order to be eligible to participate in this study as a patient, a subject must meet all of the
following criteria:
1.Established diagnosis of:
-SAD without ILD (according to the latest ACR-EULAR criteria)
-SAD with ILD (according to the latest ACR-EULAR criteria and ILD diagnostics)
-IPAF patients (according to latest consensus) [9]
-IPF patients (according to latest diagnostics) [11]
2.Age >= 18 years
3. Providing informed consent after reading patient information.

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:
1.No established diagnosis of SAD, IPAF or IPF.
2.Refusal to participate in the study.
3.Insufficient knowledge of the Dutch language.

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	04-02-2024
Enrollment:	120
Type:	Anticipated

Ethics review

Approved WMO Date:	24-04-2024
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

No registrations found.

In other registers

Register	ID
CCMO	NL85295.078.23