Assessing the role of local inflammatory, fibroproliferative, and osteogenic biomarkers in Systemic Sclerosis related Interstitial Lung Disease.

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1. To compare the proinflammatory, profibrotic and osteogenic cytokine profile in BAL fluid between SSc patients without ILD, with limited ILD, and with extensive ILD.2. To compare the proinflammatory, profibrotic and osteogenic differentiation of...

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

Summary

ID

NL-OMON49016

Source
ToetsingOnline

Brief title
ILD-SSc study

Condition

- Autoimmune disorders
- Lower respiratory tract disorders (excl obstruction and infection)
- Skin vascular abnormalities

Synonym
CREST, lung fibrosis, scleroderma

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: 4de geldstroom (Sanofi Genzyyme) + PPP allowence,Sanofi-aventis

Intervention

Keyword: inflammation, interstitial lung disease, raynaud, systemic sclerose

Outcome measures

Primary outcome

1. Level of IL-6 in BAL fluid

2. Inflammatory, fibroproliferative and osteogenic cytokines in BAL fluids

3. Degree of proinflammatory, profibrotic and osteogenic differentiation of fibroblasts isolated from lung BAL and bronchial biopsies

4. Degree of tissue markers involved in the calcification process and SSc progression in bronchial biopsies

5. Degree of other serum markers of the calcification process: T50, calcium, phosphorus, parathormone, fetuin-A, Fibroblast Growth Factor-23 (FGF23), αKlotho;

6. Degree and extent of pulmonary involvement of ILD and pulmonary ossifications by lung function (FVC, FEV1, DLCO), and HRCT

7. Degree of vasculopathy by: noninvasive nailfold capillary microscopy; arterial stiffness; digital artery involvement as assessed with ultrasound;

8. Clinical parameters on SSc organ and degree of skin and additional organ involvement, SSc-antibody profile, medication use, and comorbidities.

Secondary outcome

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Study description

Background summary

Systemic sclerosis (SSc) is a rare progressive autoimmune disease hallmarked by severe vasculopathy, leading to skin and internal organ complications and premature mortality. A considerable proportion of SSc patients develop Systemic Sclerosis related Interstitial Lung Disease (SSc-ILD), for which treatment options are limited. Although extensive SSc-ILD has been shown to be associated with large fibroproliferative changes, early phases of limited SSc-ILD seem to be characterized by local inflammation. Pre-clinical and early clinical studies indicate that interleukin-6 may play a central role during the early phase of SSc-ILD. Additionally, patients with SSc are prone to enhanced calcification of skin (calcinosis cutis) and vasculature. This calcification process is strongly associated with local inflammation in the skin, which is a process that may very well also occur in internal organs and serve as an early proxy for long-term SSc-related complications. In fact, in patients with SSc, diffuse pulmonary ossifications are frequently observed, which may indicate a common pathway of systemic inflammation, fibrosis, and calcification in interstitial lung disease (ILD) in SSc.

Hypothesis: Assessment of the proinflammatory, profibrotic and osteogenic profile of the lungs in patients with SSc could serve as early markers of disease, and could potentially facilitate upfront treatment in patients with limited SSc-ILD.

Study objective

1. To compare the proinflammatory, profibrotic and osteogenic cytokine profile in BAL fluid between SSc patients without ILD, with limited ILD, and with extensive ILD.
2. To compare the proinflammatory, profibrotic and osteogenic differentiation of fibroblasts isolated from lung BAL fluid and lung biopsies between SSc patients without ILD, with limited ILD, and with extensive ILD.
3. To compare the expression of markers involved in the calcification process in lung biopsies assessed by immunohistochemistry between SSc patients without ILD, with limited ILD, and with extensive ILD.
4. To assess the association of diffuse pulmonary ossifications on HRCT with the cytokine profile in BAL fluid, the fibroblast differentiation in lung fibroblasts, and calcification process in lung tissue in patients with SSc

Study design

This is an explorative substudy of the CALC-SSc study (NL65651.042.18, METC

2018.373), with a case-control and prospective longitudinal design.

Study burden and risks

Attempts will be made to have patients and healthy controls visit our center only once for assessment of all study parameters. Blood drawing will be combined with routine clinical practice assessments to minimize the venipuncture burden. Bronchoscopy may result in minor discomfort (not needing medical attention) in <10%, and in <1% it may result in more severe complications (pneumonia and bleeding) needing medical attention and intervention. By excluding participants using anticoagulants or anti-platelet drugs, the risk of bleeding is limited as much as possible.

Contacts

Public
Universitair Medisch Centrum Groningen

Hanzeplein 1
Groningen 9713GZ
NL
Scientific
Universitair Medisch Centrum Groningen

Hanzeplein 1
Groningen 9713GZ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

• Age 18-70 years
• Written informed consent
• Formal diagnosis of Systemic Sclerosis based on ACR/EULAR criteria
• Formal diagnosis of interstitial lung disease (for 15 of 20 included patients)

Exclusion criteria

• Patients who are mentally incompetent
• Vascular event or chemotherapy in the preceding 3 months
• Inflammation of unknown origin
• Other lung disease present
• Use of anti-inflammatory medication or antibiotics

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	21-09-2020
Enrollment:	20
Type:	Actual

Ethics review

Approved WMO

Date:	09-09-2020

Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	NL68835.042.20