A search for novel therapeutic targets and biomarkers in patients with Systemic Lupus Erythematosus

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Ethical review	Approved WMO
Status	Will not start
Health condition type	Autoimmune disorders
Study type	Observational invasive

Summary

ID

NL-OMON36575

Source
ToetsingOnline

Brief title
New biomarkers for disease activity and treatment in SLE

Condition

- Autoimmune disorders

Synonym
SLE, systemic lupus erythematosus

Research involving
Human

Sponsors and support

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

Intervention

Keyword: disease activity, Lupus, SLE

Outcome measures

Primary outcome

The expression of IL-7, TSLP, CD30L and their receptors in peripheral blood and urine of patients with SLE as compared to healthy controls.

Secondary outcome

The longitudinal approach will be used to assess the correlation between the changes in IL-7, TSLP and CD30L and their receptor with the changes in disease activity and immunologic parameters.
Identify biomarkers different from healthy controls that reflect disease activity and can be play a role in the pathogenesis of SLE. The results of the proposed studies may contribute to a future treatment strategy by blockade of some of the investigated inflammatory mediators.

Third objective: Leucocytes will also be stored for DNA isolation, which will be used for analyses of polymorphic sites that might be involved in regulation of transcription of the investigated molecules

Study description

Background summary

Systemic lupus erythematosus (SLE) is an auto-immune disease in which the interplay between dendritic cells and T and B cells plays an important role in the immunopathology. IL-7 and IL-7-related cytokine TSLP (thymic stromal lymphopoeitin) are members of the IL-2 family that are able to promote

autoimmunity by activation effector T cells and dendritic cells. Activated T cells cause activation of B cells by upregulated expression of costimulatory molecules such as CD30L. This latter molecule is crucially involved in the generation of pathogenic autoantibodies in animal models for SLE.
Despite all this we do not completely understand the pathogenesis of this disease. In relation with that, a biomarker found in pathogenesis that correlates with disease activity is still lacking

Study objective

Our aim of the study is to investigate IL-7, TSLP and CD30(L) expression in SLE patients en healthy controls to better understand pathogenesis and to find a biomarker that is related to disease activity. With this potential new therapeutic targets can be developed.

Study design

It*s a prospective observational cohort study of SLE-patients, with longitudinal and cross-sectional analysis.
After providing informed consent, clinical data will be gathered including information regarding previous history of lupus activity and involvement, past concomitant medical diseases, past medical history, concomitant medications and a disease acitivty measurement (SLEDAI and BILAG). Additionally 80cc*s of blood will be sampled from which serum and cells for DNA and Phosflow will be isolated and from which miRNA and mRNA will be isolated from the T-cell, monocyte and remaining cell-populations. After that flow-cytometry data from whole blood will be provided to Amgen.
Clinical data, urine collection and sampled blood will be five times in 1 year (timepoint 0, 3, 6, 9 and-12 months) in the active patients (n=20). For the inactive patients clinical data en blood en urine will be sampled only once. In case of active disease during follow-up, these patients will be followed every 3 months with samples en clinical data at entry (inactive), active fase, 3 months, 6 months and 12 months (somewhat like the active patients at inclusion). The same biomaterials will be collected from 25 healthy controls at five timepoints for 10 persons en only once for 13 persons

Study burden and risks

There will be no additional risks for the subject. Blood is already taken three monthly in the standard follow-up of SLE patients. Now there will be taken extra blood (80cc) for research in the same setting, so basically no extra venapuncture is needed in the patient group. The healthy controles need a venapuncture but the underlying risks can be neglected. No other invasive procedures will be done.

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

Patients full-filling the ACR criteria for systemic lupus erythematosus
Controles: 18 years or older

Exclusion criteria

Patients: patients with proven other auto-immune disorders, pregnancy and malignancy
Controls: a history or presence of auto-immune disease and current use of immunosupressants or pregnancy

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:	Will not start
Enrollment:	75
Type:	Anticipated

Ethics review

Approved WMO

Date:	29-03-2012
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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	NL34374.041.11