Childhood Lupus cohort study

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To initiate a Dutch cohort with standardized follow-up measures and investigating blood, liquor, urine samples and videocapillaroscopy findings (nailfold and under the tongue) for prognostic factors during disease quiescence and at times of disease...

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

Summary

ID

NL-OMON52716

Source
ToetsingOnline

Brief title
CHILL-NL cohort

Condition

- Autoimmune disorders

Synonym
Autoimmunity, systemic lupus erythematosus

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Stichting Vrienden van het Sophia;bedrag toegekend voor volledige project

Intervention

Keyword: Autoimmunity, Biomarker, Lupus, Pediatric rheumatology

Outcome measures

Primary outcome

This is a non-interventional, observational cohort study, in which we aim to standardize the assessment of disease activity in all cSLE patients at baseline visit, during regular outpatient visits and disease flares.

For the NP-SLE part of the study: clinical phenotype, MRI abnormalities, EEG patterns, autoantibodies in serum and CSF.

Secondary outcome

- To determine response to treatment

- To register adverse events during treatment

- To develop prognostic factors by RNA-, DNA-, protein profiling and videocapillaroscopy of the small vessels in the nailfold and under the tongue for monitoring and predicting disease activity, response to treatment and disease flares

Study description

Background summary

Systemic Lupus Erythematosus (SLE) is a chronic auto-immune disease with a highly heterogeneous presentation that may involve almost any organ system. Disease onset during childhood occurs in 10 - 20% of SLE patients. Childhood onset SLE (cSLE) follows a more aggressive course: disease activity is higher both at onset and during life. Immunosuppressive medication is used in order to manage the disease. However, despite aggressive drug regimes, cumulative damage over time is higher and develops faster in these patients, and drug-free remission is rarely achieved. Additionally, quality of life in cSLE patients is gravely influenced by the effects of the disease and medication.

cSLE is a rare disease (incidence 0.3 - 0.9, prevalence of 3.3 - 8.8 per 100.000 children), which means that medical specialists do not see these

patients often. Standards of care and treatment guidelines are lacking, which leads to differences in management and quality of care.

Nationally combining knowledge on the clinical presentation, management and possible prognostic factors of cSLE in the Netherlands and analyzing the impact of the disease on quality of life and other related issues will help to improve care in the future.

In addition the care for SLE patients with involvement of the nervous system has to be improved. We call this neuro-psychiatric SLE (NP-SLE). This is the most severe presentation of SLE and more common in children than in adults. In NP-SLE, the brain or peripheral nervous system are involved, leading to symptoms like (severe) headaches, impaired cognitive functioning, epilepsy, hallucinations and brain infarctions. Unfortunately, the diagnosis of NP-SLE in children is difficult to make because symptoms are non-specific and current diagnostic tools are not accurate enough. Unfortunately, patients and doctors are left in doubt about the correct diagnosis leading to (unintended) inadequate treatment. This has great clinical implications because NP-SLE patients have a more severe course of the disease, develop more damage and die more often than non-NP-SLE patients. Therefore, better recognition of NP-SLE is essential to improve the outcome of these severely ill children.

Study objective

To initiate a Dutch cohort with standardized follow-up measures and investigating blood, liquor, urine samples and videocapillaroscopy findings (nailfold and under the tongue) for prognostic factors during disease quiescence and at times of disease flare. This will provide valuable insights in the clinical presentation, disease outcome and will lead to the development of new biomarkers.

In addition, the aim of this project is to find new diagnostic tools to improve diagnosing children with NP-SLE.
The objectives for this are:
1. better identification of clinical symptomatology of NP-SLE using structured and detailed analysis of patient histories and physical examination, neuropsychological testing and detailed questionnaires for patients on clinical neuropsychiatric symptoms;
2. using innovative Brain MR-Imaging techniques to detect NP-SLE;
3. using new electrophysiological brain testing to identify brain networks and patterns characteristic of NP-SLE;
4. detecting novel and existing neuronal surface auto-antibodies in both serum and cerebrospinal fluid by using immunohistochemistry techniques, immunocytochemistry (live hippocampal neurons) and existing or newly developed cell-based assays;
5. developing a diagnostic algorithm for the diagnosis of NP-SLE and form this into an evidence-based diagnostic guideline that can

easily be used in clinical practice.

Study design

Multicentre longitudinal observational cohort study

Study burden and risks

Principally, all investigations and procedures listed in the study protocol and intended to be executed and collected in our study patients, are part of normal clinical practice and considered *standard of care*. These procedures hence do not oppose an increased risk or burden for included patients. Only with respect to health analysis we aim to collect data from short validated questionnaires not directly related to standard care of our patients (i.e. quality of life and fatigue). Standard of care laboratory examinations are carried out at each visit. In addition, for a maximum of 6 times/year, and only if routine care laboratory investigations are already warranted, a limited amount of extra blood and, if applicable, urine samples will be collected for research intentions. The frequency of sampling, the total volume per sampling time and the total cumulative volume sampled per year will remain well within the limits of the WHO guidelines on peripheral blood sampling for minors of 2015 (~0,8 ml/kg/sampling time with a maximum of 50 ml/draw, not exceeding 6 times a year).

If a lumbar puncture is performed for diagnostic purposes an extra amount of liquor (maximum of 3ml) will be collected for the study.

Videocapillaroscopy of the blood vessels in the nailfold and under the tongue is a non-invasive, non-painful method to visualize the smallest blood vessels in the nailfold area of the fingertips and under the tongue. These procedures are painless and do not cause any harm to the patient.

For the NP-SLE part of the study, patients will visit the Sophia Children's hospital once for a study visit, MRI and EEG. Performing those investigations does not oppose any health risk or burden, but some patients may find it time consuming (on average, 4 hours). The travel and lunch costs will be compensated.

The risks associated with participation in this study for our patients are estimated to be negligible and the burden minimal. There are no direct benefits for the participants. There is a group benefit for future patients with cSLE.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Children (2-11 years)

Inclusion criteria

All children from 0-18 years old, with the diagnosis of SLE, fulfilling Systemic Lupus International Collaborating Clinics (SLICC) criteria

Exclusion criteria

- Refusal to participate in the study
- Insufficient knowledge of the Dutch language

Study design

Design

Study type: Observational non invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	14-10-2019
Enrollment:	250
Type:	Actual

Ethics review

Approved WMO

Date:	20-09-2019
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO

Date:	11-02-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Not approved

Date:	29-06-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO

Date:	03-05-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO

Date:	18-02-2025
Application type:	Amendment
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	NL68778.078.19