Taxonomy, Treatment, Targets and Remission (3TR): Systemic Lupus Erythematosus study

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1. To determine biomarkers of response and non-response to treatment for active SLE in a prospective study where patients will be allocated to therapy according to current clinical practice and the EULAR guidelines (response biomarker study; 3TR SLE...

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

Summary

ID

NL-OMON52022

Source
ToetsingOnline

Brief title
3TR: SLE study

Condition

- Autoimmune disorders

Synonym
lupus, SLE, Systemic lupus erthematosus

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: This project has received funding from the Innovative Medicines Initiative 2 Joint Undertaking (JU) under grant agreement No 831434.

The JU receives support from the European Union's Horizon 2020 research and innovation programme and EFPIA.

Intervention

Keyword: Biomarkers, Systemic lupus erythematosus

Outcome measures

Primary outcome

- Flare biomarker study: Proportion of patients developing a flare within 24 months of follow-up, defined as a new BILAG A or B in any clinical domain. The impact of the presence of anti-SARS-CoV-2 antibodies of different isotypes (IgA, IgG, IgM) on this outcome will be addressed.

- Response biomarker study: BICLA response at week 52 from baseline.

Secondary outcome

- Flare biomarker study: Proportion of patients developing a flare within 24 months of follow-up, defined according to the SELENA-SLEDAI Flare Index (SFI). The impact of the presence of anti-SARS-CoV-2 antibodies of different isotypes (IgA, IgG, IgM) on this outcome will be addressed.

- Reponse biomarker study: SLE Responder Index (SRI)-4, SRI-5 and SRI-6 response (at all time points); Time to BICLA response and SRI response; failure to attain BICLA response or SRI-4, SRI-5 and SRI-6 response (at all time points); Change in SLEDAI-2K scores, Physician*s Global Assessment (PhGA, on a scale 0-3) and Patient*s Global Assessment (PGA, on a 0-10 VAS) (at all time points); LLDAS, and its individual components (at all time points); Remission according to DORIS, and its individual components (at all time points); Flare, based on BILAG (any new worsening in BILAG, or any new BILAG A or B) or

SELENA-SLEDAI Flare Index (SFI) (at all time points); Renal response/non-response, according to the 2019 EULAR/EDTA recommendations; Organ-specific outcome measures (e.g. CLASI for mucocutaneous involvement, 44 joint assessment of tender and swollen joints for articular involvement) (at all time points); Worsening in SLICC/ACR Damage Index (SDI) score (at week 52); Health-related quality of life (HRQoL), assessed with EQ-5D-5L, FACIT-F, Medical Outcomes Study 36-item Short Form health survey (SF-36), Epworth Sleepiness scale (ESS) and Lupus-QoL (at week 26 and week 52); Impact of anti-SARS-CoV-2 antibodies of different isotypes (IgA, IgG, IgM) on attainment of or time to BICLA, SRI, LLDAS and DORIS, change in SLEDAI-2K, PhGA, PGA and SDI scores, change in organ specific index scores, and HRQoL outcomes.

Study description

Background summary

3TR (Taxonomy, Treatment, Targets and Remission) is a transdisciplinary consortium with the aim to perform a longitudinal multi-dimensional molecular analysis in patients with autoimmune, allergic and inflammatory diseases. Systemic lupus erythematosus (SLE) is one of the chronic disorders that will be investigated for possible shared biomolecular pathways.

SLE is a complex and heterogeneous autoimmune disease of only partially unraveled etiology, characterized by the production of autoantibodies, tissue deposition of immune complexes, and eventually tissue damage across multiple organ systems. The natural history of SLE is characterized by relapses or flares alternated with periods of remission. Flares are associated with accrual of organ damage independently of other risk factors, both contributing to a considerable morbidity. Although remission is the desirable target of SLE, a failure to achieve at least the so-called Lupus Low Disease Activity State (LLDAS) increases the risk of subsequent damage or flare. Despite the fact that important advances have been achieved over the years regarding the understanding and management of the disease, SLE pathogenesis still is poorly understood. Still, a major advance in the treatment of SLE and the prevention

of its complications is expected to come from a clear comprehension of the mechanisms of response to therapies or, conversely, of escape to sustained response to them.

There remains an unmet need of identification of patients who can be expected to best benefit from SLE therapies. By analyzing biomolecular characteristics, we aim to identify new biomarkers to predict response and non-reponse to current therapies, and predict flares. More insight in the pathogenesis will offer future possibilities for the identification of new treatments and will contribute to improved diagnostics and monitoring in SLE through personalized therapy.

Study objective

1. To determine biomarkers of response and non-response to treatment for active SLE in a prospective study where patients will be allocated to therapy according to current clinical practice and the EULAR guidelines (response biomarker study; 3TR SLE 2).
2. To determine biomarkers of flare in patients with a clinically stable or quiescent SLE over an observational period of a maximum of 24 months (flare biomarker study; 3TR SLE 1).

Study design

This is a European observational cohort study, in which patients from multiple European centers participating in 3TR will be recruited for a longitudinal clinical follow-up and collections of several samples (e.g. blood, urine, saliva, and relevant tissues) from the same individual at multiple time points.

For the SLE study a two-step study has been designed, and comprises:
1. The flare biomarker study (3TR SLE 1) is considered a *feeding* phase before the main part, but patients who meet the inclusion criteria for 3TR SLE 2 will be directly included in this second study.
2. The response biomarker study (3TR SLE 2), which is the main part.

Study burden and risks

There are 2-8 time points of this study depending on patient characteristics. If possible, the study visits will be planned on the same day as a regular clinical visit. Collection of blood, urine, stool, and saliva only causes a small inconvenience. Completing the questionnares will take a maximum of 30 minutes per visit. Patients can additionally consent to undergo biopsies of the skin (collection of kidney biopsy is standard care); these procedures carry only a small risk in terms of pain, infection and bleeding, which in most cases can be treated with painkillers, antibiotics or adequate pressure on the wound.

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

- Flare biomarker study:
1. Age at the time of inclusion >= 18 years.
2. Diagnosis of SLE according to the EULAR/ACR criteria.
3. BILAG C, D or E only.
4. No restriction regarding current or previous therapies, except for hydroxychloroquine (HCQ) or chloroquine treatment which should be administered unless contraindicated or documented intolerance in the past.
- Response biomarker study:
1. Age at the time of inclusion >= 18 years.
2. Diagnosis of SLE according to the EULAR/ACR criteria.
3. Patients should have at least one of the following: i. active arthritis, attributed to SLE (BILAG A or B in the musculoskeletal domain). ii. active skin

disease, attributed to SLE (BILAG A or B in the mucocutaneous domain). iii. active biopsy-proven lupus nephritis (LN; ISN/RPS class III, IV or V), with or without extrarenal organ involvement. iv. active CNS involvement as a main manifestation (with or without other organ involvement) along with initiation of new treatment for CNS involvement (BILAG A or B in the neuropsychiatric domain).
4. Stable standard therapy for at least 30 days, including hydroxychloroquine (HCQ) or chloroquine treatment, unless contraindicated or documented intolerance.

Exclusion criteria

- Flare biomarker study:
1. Pregnancy (at baseline).
2. Initiation or intensification of immunosuppressive therapy or a prednisone equivalent dose of > 10 mg/day within 30 days prior to baseline.
- Response biomarker study:
1. Serological activity only without signs of clinically active disease.
2. Pregnancy (at baseline).

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):	05-06-2023
Enrollment:	63
Type:	Actual

Ethics review

Approved WMO Date:	14-04-2023
Application type:	First submission
Review commission:	METC Amsterdam UMC

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	NL77212.029.22