Regulating Rheumatoid Arthritis

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

Summary

ID

NL-OMON52768

Source
ToetsingOnline

Brief title
Regulating RA

Condition

- Autoimmune disorders
- Joint disorders

Synonym
rheumatoid arthritis

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: Health Holland,Reuma NL,Trajectum Pharma BV

Intervention

Keyword: immune regulation, rheumatoid arthritis

Outcome measures

Primary outcome

Novel insights into various aspects of faulty immune regulation in RA, as well

as the prerequisites for the development, implementation, and immunological

monitoring of immune regulation restoring therapies in RA patients.

Secondary outcome

NA

Study description

Background summary

Current therapies for rheumatoid arthritis (RA) successfully suppress disease symptoms albeit often at the cost of side-effects such as infections. Furthermore the underlying pathology of RA, immune deregulation, is not restored by these therapies, often causing patients to remain on long-term immunosuppressive medication. Novel cell therapy-based methods are being developed with the aim of strengthening the patient*s natural immune regulation. Such tolerogenic cell therapy methods involve the ex vivo training or engineering of the patient*s own immune cells (tolerogenic dendritic cells (tolDC) or regulatory T cells), which are subsequently injected back into the patient. The hope is that cellular immunotherapy will reduce or completely end the need for long-term use of immunosuppressive medication in these patients. We have identified four challenges that in our opinion need to be addressed before the efficacy of tolerogenic cell therapies for RA can be properly tested.

Study objective

The aim of this study is to better understand various prerequisites for the development, implementation, and immunological monitoring of immune regulation restoring therapies in RA patients. To meet this aim, the study is divided into four equally important challenges with their corresponding objectives:
Challenge 1: Defining in- and exclusion criteria for tolDC therapy. In this

objective we will investigate the phenotype and functionality of tolDC generated from peripheral blood of RA patients in comparison to those from healthy individuals. We will study how the use of various types of immunosuppressive medication and the disease activity affect the ability to generate functional tolDC from peripheral blood of RA patients.
Challenge 2: Establishing assays for monitoring of antigen-specific T cell responses in RA patients. In objective 2 we will develop assays for the detection of antigen-specific regulatory T cell responses in support of auto-antigen targeted immunotherapy clinical trials in RA.
Challenge 3: Identifying T cell receptor sequences for engineered Treg therapy. In objective 3 we will identify and characterize antigen-specific T cell receptors for auto-antigen targeted engineered Treg therapy strategies.
Challenge 4: Characterizing the metabolic signature of Treg from RA patients and healthy controls. In objective 4 we will compare the metabolic signatures of Treg of RA patients and healthy controls. This will provide insight into how RA and current RA therapies affect Treg metabolic characteristics.

Study design

Observational cross-sectional study

Study burden and risks

Participants will undergo a physical examination (to determine disease activity) and a single venepuncture (a maximum of 80 mL blood). Patients may elect to participate multiple times, requiring renewed informed consent, but never more than two times per year. As blood is primarily taken together with routine blood sampling, no additional burden arises for the patient. The participants of this study will not directly benefit from participation in this study.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

• Age range: >18 years
• Diagnosed with Rheumatoid arthritis
• Use of one or several small molecule anti-rheumatic drugs. Combination with biologicals is allowed.
• Blood from healthy controls is obtained via the *mini-donor dienst* of the UMC Utrecht or purchased as buffy coats from Sanquin, and is anonymous, except for the age and sex

Exclusion criteria

None

Study design

Design

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

Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	23-03-2023
Enrollment:	125
Type:	Actual

Ethics review

Approved WMO

Date:	16-08-2022
Application type:	First submission
Review commission:	METC NedMec

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	NL74568.041.21