Tolerogenic dendritic cell therapy for rheumatoid arthritis.

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

Summary

ID

NL-OMON55219

Source
ToetsingOnline

Brief title
TOLERANT

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: ZonMW;programma translationeel onderzoek,Trajectum Pharma BV

Intervention

Keyword: cell therapy, rheumatoid arthritis, tolerance induction

Outcome measures

Primary outcome

Primary outcomes are the occurrence of (serious) adverse events including flares of disease activity in the four treatment groups, and the feasibility of generating sufficient numbers of TolDCB29 from RA patient apheresis product.

Secondary outcome

Secondary outcomes are the qualitative and quantitative B29-specific T cell response to treatment and the general immune reactivity to TolDCB29 administration. Our exploratory objective is the impact of the treatment on clinical parameters.

Study description

Background summary

In rheumatoid arthritis, immune cells cause joint inflammation and destruction in response to auto-antigens. Immunosuppressive therapies offer relief, but fail to induce tolerance to auto-antigens. Injection of antigen-loaded tolerogenic dendritic cells induces immune tolerance and ameliorates disease in arthritis models. We hypothesize that dendritic cell therapy with TolDCB29 is safe and induces immune tolerance in rheumatoid arthritis patients.

Study objective

We aim to demonstrate the safety and feasibility of intranodal TolDCB29 administration. Our secondary objectives are the characterization of B29-peptide specific immune reactivity in response to TolDCB29 treatment and the evaluation of the effect of the treatment on disease activity.

Study design

Phase I/II, open-label, dose-escalation clinical trial.

Intervention

Study participants will receive two intranodal injections with the TolDCB29 product with a four week interval. During the first phase of the study dose escalation is performed, in which the first group (n=3) receives two *low dose* injections, the second group (n=3) receives two *intermediate dose* injections, and the third group (n=3) receives two *high dose* injections. During the second phase, a fourth group (n=9) will receive the highest dosage without attributable serious adverse events thus far.

Study burden and risks

This study aims to demonstrate the safety of TolDCB29 therapy, and to investigate whether the treatment affects rheumatoid arthritis disease activity. Previous clinical trials with autologous DC in rheumatoid arthritis and with HSP peptide and protein in diabetes and RA were proven safe in the past. Serious risks for patients are therefore not expected. We anticipate that the treatment with TolDCB29 may confer a clinical benefit by restoring immune tolerance, which could allow for tapering of the current medication.
Patients included will undergo leukapheresis in Radboud UMC to harvest the cells, and will receive the treatment in UMC Utrecht after preparation of cells (within 3-6 weeks after leukapheresis). The TolDCB29 product will be administered in two injections with a four week interval in between. After each injection, vital functions will be monitored every 15 minutes during two hours. From the first injection onwards, they will be followed for twenty-four weeks, with detailed interviews, physical examination and laboratory testing every 4 weeks. Seventy mL of peripheral venous blood is collected at each of the five hospital visits for immunomonitoring.

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

- Diagnosis of rheumatoid arthritis according to the criteria which were valid at time of diagnosis (i.e. 1987 Rheumatoid Arthritis Classification or 2010 ACR/EULAR RA Classification Criteria).
- Age 18 years or older
- Stable dose, for at least 12 weeks, of any combination of disease-modifying anti-rheumatic drugs and glucocorticoids (maximum of 7,5 mg per day), with exception of those drugs that are part of the exclusion criteria.
- Disease in remission or in low disease activity, measured by disease activity score of 28 joints < 3.2 for at least 12 weeks
- Able and willing to give informed consent and to comply with the study protocol

Exclusion criteria

- Intramuscular or intra-articular glucocorticoid injection during 12 weeks prior to inclu-sion
- Use of JAK inhibitors
- Active or chronic infection (except fungal nail infection)
- Infection requiring hospitalization or IV antibiotics within 6 weeks of baseline
- Immunization with live vaccine within 6 weeks of baseline
- History of malignancy (except treated basal cell carcinoma of skin)
- Use of other investigational medicinal products within 30 days prior to study entry
- Major surgery within 8 weeks of baseline or planned within 12 weeks from

baseline
- Pregnancy, or women planning to become pregnant within the study period, or women who are breast feeding
- Hb<6 mmol/L; neutrophils< 2.00 x10^9/L; platelets <150x10^9/L; ALT/ALP>2x upper limit of normal; renal insufficiency (clearance < 60 ml/min) at screening visit.
- Poor venous access or medical condition precluding leukapheresis
- Serious or unstable co-morbidity deemed unsuitable by PI, e.g. COPD, cardiac failure
- Individuals of child bearing potential unwilling to use adequate contraception for dura-tion of study

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	17-08-2021
Enrollment:	18
Type:	Actual

Medical products/devices used

Product type:	Medicine
Generic name:	Somatic cells autologous

Ethics review

Approved WMO

Date:	05-01-2021
Application type:	First submission

Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	21-04-2021
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	10-08-2021
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	11-11-2021
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	27-06-2022
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	12-07-2022
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	16-09-2022
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

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
EudraCT	EUCTR2019-003620-20-NL
CCMO	NL71296.000.20