Synovial Tissue characteristics in Rheumatoid Arthritis patients TreAted with their FIrst Tnf-inhibitor

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To find molecular pathways active in ST of RA patients who did not respond to TNFi after 3 months of treatment with their first TNFi. This may aid in clinical decision making (on the group level) and may lead to discovering new drug targets.

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

Summary

ID

NL-OMON47003

Source
ToetsingOnline

Brief title
STRATAFIT

Condition

- Autoimmune disorders

Synonym
arthritis, rheumatoid arthritis

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: Genentech

Intervention

Keyword: rheumatoid arthritis, synovial tissue, TNF-inhibitor

Outcome measures

Primary outcome

Synovial gene transcripts associated with non-response.

Secondary outcome

Blood biomarkers associated with non-response and with molecular and

immunological pathways in synovial tissue.

Study description

Background summary

~30% of rheumatoid arthritis (RA) patients do not demonstrate an adequate clinical response to TNF inhibitors (TNFi). We cannot predict which treatment will be effective in these patients and we do not know which pathways are still active in the synovial tissue (ST) of these patients.

Study objective

To find molecular pathways active in ST of RA patients who did not respond to TNFi after 3 months of treatment with their first TNFi. This may aid in clinical decision making (on the group level) and may lead to discovering new drug targets.

Study design

This is a single center observational study. The study is largely cross-sectional with a study visit 3 months after start of treatment with TNFi at which ultrasound (US) guided synovial biopsy sampling will be performed. A baseline study visit before initiation of treatment with TNFi is included in the design to be able to evaluate change in clinical disease activity upon treatment with TNFi and to be able to assess associations between immunological blood parameters at baseline and non-response to TNFi after 3 months. 3-4 Days after the biopsy visit, patients will have a telephone contact to evaluate complaints during and after the biopsy procedure.

Study burden and risks

Patients will have two study visits during the study, 3 months apart, at which they will undergo joint examination, and ultrasound of MCP-joints and of both wrists and knees.
In addition, at each study visit they will undergo blood sampling (at baseline 94.3ml and after 3 months 84.3 ml. The total amount of blood drawn in the study is 179ml. Patients may develop a hematoma at the site of venepuncture. To describe the patient population x-rays of hands and feet and of the biopsied joint will be performed at 3 months, if not performed in the last 12 months. In addition, at the 3 month study visit patients will undergo US guided synovial biopsy sampling of one wrist or knee or MCP-joint. Approximately 25% of patients will have minor discomfort after the procedure. This is effectively managed with simple analgesia (NSAIDs/paracetamol) and should dissipate after 24 hrs. Patients can walk after the procedure (applicable to patients undergoing synovial biopsy in knee joint) and can go home on the same day. Patients are asked to refrain from over exertion and should ideally be accompanied home by a friend/relative. Below is a list of most commonly experienced complications with arthroscopic procedures (approximate incidences in brackets; ref: synovialbiopsy.com):
i) Joint infection (0.2%)
ii) Deep venous thrombosis (0.2%)
iii) Haemarthrosis (1%)
iv) Neurological damage (0.02%)
v) Wound infection (0.5%)
vi) Thrombophlebitis (0.08%)
We expect the complication rate for US guided procedures to be significantly better.
Theoretically, patients may experience adverse events of lidocaine hydrochloride used for local anesthesia (as described in standard medication information).

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

* Age * 18 years
* Fulfilling 2010 American College of Rheumatology (ACR) / European League Against Rheumatism (EULAR) classification criteria for RA (Appendix A).
* DAS28 * 3.2
* At least one clinically active wrist or knee or MCP joint
* Start with aTNFi (all currently approved TNFi are allowed* infliximab (3 mg/kg at week 0, 2, 6 and 14), etanercept, adalimumab, golimumab, certolizumab pegol) within 4 weeks from the baseline study visit.
* Having insufficient response to treatment with * 2 conventional DMARDs.
* Current treatment with either methotrexate (*10 mg/week), sulfasalazine (*2000 mg/day), hydroxychloroquine (*200 mg/day), and/or leflunomide (*10 mg/day).
* Naïve to previous biological treatment regimens, including other TNFi, rituximab, abatacept, tocilizumab (and biosimilar equivalents).

Exclusion criteria

* Treatment with systemic glucocorticoids at a dose above 10 mg/day of prednisone or equivalent within 4 weeks of enrolment.
* Treatment with intra-articular glucocorticoids in a knee or wrist or MCP joint within 3 months of enrolment.
* Any rheumatic disease other than RA (except secondary Sjogren*s syndrome)

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	27-07-2018
Enrollment:	50
Type:	Actual

Ethics review

Approved WMO Date:	08-02-2017
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	25-04-2018
Application type:	Amendment
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	NL56944.041.16