INTENT: immunogenicity in patients failing response on anti-TNF - phase 1: immunogenicity and pharmacokinetics in patients failing to respond to TNF inhibitors. - phase 2: clinical effectiveness of subsequent TNF inhibitor treatment and predictive value of pharmacokinetics and immunogenicity.

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1. To determine the proportion of patients developing anti-drug antibodies (ADA) detectable with an antigen binding test (ABT, radioimmunoassay) in patients experiencing inefficacy of their first TNF inhibitor treatment (phase 1).2. To study...

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

Summary

ID

NL-OMON43571

Source
ToetsingOnline

Brief title
INTENT: immunogenicity in patients failing response on anti-TNF

Condition

- Joint disorders
- Epidermal and dermal conditions

Synonym
psoriasis, reumatic disease

Research involving
Human

Sponsors and support

Primary sponsor: Jan van Breemen Instituut
Source(s) of monetary or material Support: Pfizer b.v.

Intervention

Keyword: anti-TNF, immunogenicity, prediction

Outcome measures

Primary outcome

Phase 1:

Amongst patients that perceive inefficacy of their first TNF inhibitor, the

percentage of patients that test positive for anti-drug antibodies, detectable

with a radioimmunoassay.

Phase 2:

Efficacy:

- RA: minimal disease activity (DAS28 < 2.6)

- AS: ASDAS, inactive disease (>1.3)

- PsA: minimal disease activity**

- Pso: PASI 75

**MDA is defined as a score of at least 5 out of 7 from the following outcome measures: TJC (0-68) *1, SJC (0-66) *1, PASI *3, patient pain VAS *15 (scale 0-100), patient global disease activity VAS *15 (scale 0-100); HAQ score *0.5, and tender entheseal points *1(using Leeds Enthesitis Index, LEI).

Immunogenicity: the percentage of patients that test positive for anti-drug antibodies, detectable with a radioimmunoassay

Secondary outcome

Phase 2:

Efficacy:

- RA: SDAI remission. Effect on HaQ.

- AS: ASDAS, minimal disease activity (<2.1); BASDAI50 response.

- PsA: ACR 20, 50, 70. Effect on HaQ.

- Pso: PASI 50, PASI 90. Effect on DLQI.

Study description

Background summary

Presently there are five TNF inhibitors approved for clinical use in rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis and psoriasis, i.e. infliximab, adalimumab, etanercept, golimumab and certolizumab pegol. Potentially, all biologicals can induce an unwanted immune response, which is associated with diminished serum drug levels and a diminished treatment response. The incidence of anti-drug antibodies (ADA) is dependent on the therapeutic itself e.g. dosing scheme/route of administration, and other factors like study population, use of concomitant medication and assay techniques used to measure these antibodies. It is known that the presence or absence of ADA has implications for response to a second TNF inhibitor.

Since low or absent serum drug levels are associated with lack or loss of

clinical response, therapeutic drug monitoring (TDM) would be an important tool in clinical decision making in patients with inflammatory diseases.

Study objective

1. To determine the proportion of patients developing anti-drug antibodies (ADA) detectable with an antigen binding test (ABT, radioimmunoassay) in patients experiencing inefficacy of their first TNF inhibitor treatment (phase 1).
2. To study response to a subsequent TNF inhibitor treatment after patients experienced inefficacy of a first TNF inhibitor (phase 2).
3. To investigate the predictive value of ADA and drug levels for response to subsequent TNF inhibitor treatment (phase 1 and 2).

Study design

Prospective observational multicenter European cohort study in RA, PsA, AS and PsO patients.
Trough serum samples (for drug level and anti-drug antibody testing 1st TNF inhibitor) and clinical data will be obtained from patients with inflammatory diseases (RA, AS, PsA and Pso) failing to respond to their first TNF inhibitor as judged by the treating rheumatologist or dermatologist (baseline, phase 1). Treatment failure is defined as inefficacy of the drug (primary or secondary), patients with other reasons of treatment failure, such as side effects, will not be included in this study.
Patients in whom treatment is switched to a second TNF-inhibitor enter phase 2 of this study. In this phase, at 3-4 months a second trough sample (for drug level and anti-drug antibody testing 2nd TNF inhibitor) and clinical data, and at 6 months clinical data will be collected.

Study burden and risks

The additional burden consists of an extra blood sample taken at moments that this would already have been done in view of routine patient care.

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

Phase 1:
- patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA), ankylosing spondylitis (AS) or psoriasis (Pso) treated with a first TNF inhibitor (adalimumab, infliximab, etanercept, golimumab or certolizumab pegol) in daily clinical practice across different European countries.
- TNF inhibitor treatment has been initiated and continued until failure at dose and interval according to label (adalimumab 40 mg every other week (eow); etanercept 50 mg once weekly or 25 mg twice weekly; golimumab 50 mg once monthly; certolizumab pegol 200 mg eow; infliximab 3 mg/kg per 8 weeks (RA), infliximab 5 mg/kg per 6-8 weeks (AS), infliximab 5 mg/kg per 8 weeks (PsA or Pso).
- Inefficacy of first TNF inhibitor (both 'primary' and 'secondary' failure) resulting in switch of therapy.
- planned treatment with a second TNF inhibitor.
- written informed consent.;Phase 2:
- participation in phase 1.
- first TNF inhibitor treatment is switched to second TNF inhibitor treatment (at labeled dose).

Exclusion criteria

Phase 1:
- current TNF inhibitor treatment is not the first TNF inhibitor ever used for this patient.

- first TNF inhibitor treatment switched due to other reasons than inefficacy (e.g. side effects).
- serum sample not taken at trough (=prior to the next infusion/injection with the TNF inhibitor for patients on drug).;Phase 2:
- treatment is switched to other treatment than TNF inhibitor.
- serum sample not taken at trough (prior to the next infusion/injection with the TNF inhibitor).

Study design

Design

Study phase:	4
Study type:	Observational non invasive
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	17-02-2015
Enrollment:	100
Type:	Actual

Ethics review

Approved WMO Date:	15-12-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-11-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	

Date:	22-03-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-10-2016
Application type:	Amendment
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	NL51186.048.14