Using adalimumab serum concentration to choose a subsequent biological treatment in rheumatoid arthritis patients failing adalimumab treatment (ADDORA-switch): a blinded randomized superiority trail

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

Summary

ID

NL-OMON52747

Source
ToetsingOnline

Brief title
ADDORA-switch

Condition

- Autoimmune disorders

Synonym
Rheumatoide arthritis

Research involving

Human

Sponsors and support

Primary sponsor: Reade
Source(s) of monetary or material Support: ZonMw

Intervention

Keyword: Adalimumab, Failing, Rheumatoid arthritis, Second line biologic

Outcome measures

Primary outcome

The primary study endpoint is the difference in mean time weighted DAS28-CRP

after 24 weeks.

Secondary outcome

• percentage of patients with good or moderate response according the EULAR

response criteria after 12 and 24 weeks of treatment

• percentage of patients with minimal disease activity (DAS28-CRP<2.9) after 24

weeks

• percentage of non-responders to the subsequent biological after 24 weeks

• number of flares after 24 weeks

• numbers and severity of adverse events

• use of co-medication/rescue medication use

Study description

Background summary

A potential application of therapeutic drug monitoring is to predict efficacy after switch to another biological in the case of inefficacy of the previous biological in rheumatoid artritis patients. It has been shown that when

antidrug antibodies against a TNF blocker are detected (resulting in lower drug serum concentrations) in patients failing a TNF blocker, a normal response to a next TNF blocker can be anticipated. However, when clinical response is unsatisfactory and no antidrug antibodies against the first TNF blocker are detected (generally drug levels are adequate in this case), this predicts a lower response to a next TNF blocker. This means drug resistant failure in the former, compared to class resistant failure in latter category of patients. The current RA treatment strategy after failure of the first TNF-inhibitor is to start either a second TNF blocker or a non-TNF blocker. However, by channelling patients with sufficient adalimumab concentration, to a non-TNF class biological will provide higher chance of disease control. Patients with very low or undetectable drug levels have an equal high chance of disease control with a drug of the same class (i.e. another TNF blocker).

Study objective

The primary objective is to evaluate whether a switching strategy using adalimumab concentration (TDM) is superior to usual care in rheumatoid arthritis patients failing adalimumab treatment with regard to response rates. The secondary objectives are to evaluate the response rate after 12 weeks of treatment in both arms; to evaluate percentage of patients reaching minimal disease activity (DAS28-CRP<2.9) in both arms; to compare percentages of EULAR non-responders to the subsequent biological; to compare the number and severity of adverse events in both arms; to compare the use of co-medication/rescue medication use

Study design

Blinded randomized multi-centre trail

Intervention

Patients are randomly assigned to usual care or *drug concentration* guided switch. When randomized to the usual care group, patients are switched to TNFi (etanercept, infliximab, golimumab or certolizumab pegol) or a non-TNFi (abatacept, rituximab, tocilizumab, sarilumab, baricitinib, filgotinib, upadacitinib or tofacitinib), based on a secondary randomization schedule. When randomized to a non-TNFi, the treating rheumatologist will choose the specific TNFi or non-TNFi. In the *drug concentration guided* group, in patients with a concentration <1.0 mg/L adalimumab is switched to TNFi and in patients with a concentration >= 1.0 adalimumab is switched to a non-TNF-inhibitor (the same drugs and dosing as in usual care group).

Study burden and risks

Using serum drug levels may facilitate decision making regarding the subsequent

biological. Patients assigned to usual care group will not benefit from the aforementioned possible advantage. In addition, patients have to visit the outpatient clinic more often. Other burdens and risks seem not to be present.

Contacts

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Scientific
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Rheumatoid arthritis patient, according to ACR 1987/2010 criteria;
Failed treatment with adalimumab (defined as DAS28-CRP >2,9) and not treated with a subsequent biological DMARD (bDMARD) or target synthetic DMARD (tsDMARD)
Who has agreed to participate (written informed consent);
Age 18 years or older.
Received adalimumab for at least 10 weeks in standard dosing (40mg subcutaneously every other week, either in monotherapy or combined with

methotrexate or leflunomide)
Stop adalimumab due to inefficacy, either alone or combined with side effects

Exclusion criteria

Scheduled surgery during the follow-up of the study or other pre-planned reasons for treatment discontinuation
Life expectancy shorter than follow-up period of the study;
No possibility to safely receive an TNF-inhibitor or a non-TNF-inhibitor '
Treatment with another TNF inhibitor prior to adalimumab
Treatment with all non-TNFi options (abatacept, rituximab, sarilumab, tocilizumab, baricitinib, filgotinib, upadacitinib or tofacitinib) prior to adalimumab

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	31-07-2020
Enrollment:	84
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Enbrel / Benepali / Erelzi
Generic name:	Etanercept

Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Kevzara
Generic name:	Sarilumab
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Mab Thera / Rixathon / Truxima
Generic name:	rituximab
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Orencia
Generic name:	abatacept
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	RoActemra
Generic name:	Tocilizumab
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	24-09-2019
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	25-11-2019
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	09-06-2020
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	11-08-2020
Application type:	Amendment

Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	30-11-2020
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	15-07-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	12-04-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	EUCTR2019-001754-25-NL
CCMO	NL69841.091.19
Other	NL8210