Using adalimumab serum concentration to choose a subsequent biological DMARD in rheumatoid arthritis patients failing adalimumab treatment

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON24414

Source
NTR

Brief title
ADDORA-switch

Health condition

Rheumatoid arthritis

Sponsors and support

Primary sponsor: Reade Rheumatology Research Institute
Source(s) of monetary or material Support: ZonMw, Sanquin diagnostics

Intervention

Outcome measures

Primary outcome

The primary objective is to evaluate whether a switching strategy based on adalimumab

concentration is superior to usual care switching in rheumatoid arthritis patients failing adalimumab treatment with regard to mean time weighted DAS28CRP at 28 weeks.

Secondary outcome

The secondary objectives include comparing response rates (EULAR good response), percentages of patients reaching low disease activity or remission (DAS28-CRP<2.9/2.4), percentages of non-responders to the subsequent biological, number and severity of adverse events and co-medication/rescue-medication use

Study description

Background summary

Over the last decades biopharmaceuticals such as agents against tumor necrosis factor (TNF), are frequently prescribed to optimize rheumatoid arthritis treatment. Although TNF-inhibitors such as adalimumab, etanercept and infliximab, have improved the treatment of rheumatoid arthritis, a proportion of patients discontinue the treatment because of inefficacy or intolerance. Where TNF-inhibitor have failed, mainly two treatment approaches are available: switch to another TNF-inhibitor or to a biological with a different mode of action (notably rituximab, abatacept or tocilizumab) or to a target synthetic DMARDs. The EULAR recommendation for the management of rheumatoid arthritis advocate that any biologic agent including a subsequent TNF-inhibitor can be used with equal chance for effect in case of non-response to a previous TNF-inhibitor. Although it seems that indeed on a group level response to a non-TNF-inhibitor is comparable to a second TNF-inhibitor after the first TNF-inhibitor has failed, using therapeutic drug monitoring could identify subgroups of patient who would benefit more from either a non TNF-inhibitor or a TNF-inhibitor as next treatment. Here we explore the underlying pathophysiological mechanisms for this hypothesis. Nonresponse on adalimumab in RA can have different causes. Firstly, the patient might not be sensitive to TNF blockade at all, or the patient develops this trait later on (primary nonresponse or secondary nonresponse). In these patients, switching to a non-TNF-inhibitor might conceptually be superior to starting a second TNF-inhibitor. However, in other patients nonresponse (either primary or secondary) might be caused by inefficient drug concentration because of development of antidrug antibodies against adalimumab. In these patients a TNF-inhibitor might be just as effective as a non-TNF-inhibitor, as these patients have drug- but not class failure. Thus, testing of adalimumab levels might be helpful in channelling patients to their most optimal treatment.However, a diagnostic study comparing a serum concentration guided versus usual care switching strategy has not yet been performed.

Study objective

We hypothesis that a switching strategy based on adalimumab concentration is superior to usual care switching in rheumatoid arthritis patients failing adalimumab.

Study design

-2,4,12,24 weeks

Intervention

Rheumatoid arthritis patients failing adalimumab treatment will be randomly assigned to switching strategy using drug concentration or usual care switching

Contacts

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Eligibility criteria

Inclusion criteria

Rheumatoid arthritis patient, according to ACR 1987 or ACR/EULAR 2010 criteria;
Recently 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);
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;
Age 16 years or older.

Exclusion criteria

Treatment with another TNF inhibitor prior to adalimumab
Treatment with all non-TNFi options (abatacept, rituximab, sarilumab and tocilizumab) prior

to adalimumab
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

Study design

Design

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

Recruitment

NL

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

IPD sharing statement

Plan to share IPD: Yes

Plan description
To avoid duplication of research, the gathered data will be shared once all desirable data analysis have been performed and the results are published

Ethics review

Positive opinion

Date:	03-12-2019
Application type:	First submission

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
NTR-new	NL8210
Other	Commissie Mensgebonden Onderzoek Regio Arnhem-Nijmegen : METC 2019-5397 CCMO NL69841.091.19 EudraCT 2019-001754-25

Study results

Summary results
N/A