Safety and efficacy of vaccination with T cell-dependent and T cell-independent primary and recall antigens in patients with rheumatoid arthritis treated with anti TNF-* antibodies (adalimumab) or anti B cell therapy (Rituximab).

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To assess the effect of adalimumab and rituximab on the safety and efficacy of vaccination with T cell-dependent and T cell-independent primary and recall antigens.

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

Summary

ID

NL-OMON30739

Source
ToetsingOnline

Brief title
SEVRA

Condition

- Autoimmune disorders
- Ancillary infectious topics
- Joint disorders

Synonym
Rheumatoid arthritis RA Vaccination

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W,Abbott

Intervention

Keyword: Anti-TNF, B-cell therapy, Rheumatoid Arthritis, Vaccination

Outcome measures

Primary outcome

Percentage of patients with positive response to vaccination prior and post adalimumab or rituximab therapy, and measured 4 weeks after administration of the vaccins. Response is defined as a 2-fold increase in antibody levels to the administered antigens or as an absolute change in specific antibody of 1 g/mL, or seroconversion in patients with a non-protective baseline level of antibodies (<1/40).

Secondary outcome

To analyse the effect of RA disease parameters on vaccination and the influence of adalimumab and rituximab therapy on T and B cell response after vaccination as well as the relation T-B cell response.This will be done by analyzing T and B cell subsets, T cell cytokine production to specific antibody stimulus as measured by elispot and immunoglobuline subtypes.

Study description

Background summary

Infection is one of the leading causes of morbidity and mortality in patients with rheumatoid arthritis. Immunomodulating therapies may potentiate the already-increased tendency of these patients to develop serious infectious complications. As vaccination is one of the primary strategy to reduce the morbidity and mortality, several rheumatogists therefore suggest implementing vaccination in RA patients treated with anti -TNF.
Little is known about the effects of vaccination in patients with rheumatoid arthritis, and upto now, no data are available on patients with RA who are treated with adalinumab (anti TNFalpha) or rituximab (anti B cell) therapy.
In general there are 2 main vaccine catagories: T cell independent vaccines (conjugate vaccines) and T cell independent (polysaccharide) vaccines. In this study, we want to gain insight in the response of the immune system on T cell dependent and independent vaccines while being treated with anti-TNF alpha and after B cell depletion.

Study objective

To assess the effect of adalimumab and rituximab on the safety and efficacy of vaccination with T cell-dependent and T cell-independent primary and recall antigens.

Study design

This is a randomised patient control cross-over study.
All patients eligible for treatment with adalimumab or rituximab wil be asked to participate in this vaccination trial. To correct for a possible influence of one of the vaccines on the response to the other vaccines, patients will be randomised to 2 different vaccination schedules. One set of vaccines consists of a T cell-dependent primary antigen (KLH) combined with a T cell-independent antigen against pneumococci (Pneumovax®) and the Tetanus Toxoid recall antigen. The other set of vaccines consists of the T cell-dependent primary antigen against hepatitis A combined with the T cell-independent primary antigen against meningococci (Meningovax A+C®) and the polio recall antigen. Four weeks after the first immunization, adalimumab or rituximab treatment is initiated.
Six weeks after the start of adalimumab treatment rituximab treatment, patients cross-over to vaccination with the other set of vaccines.

Intervention

All patients will receive 2 sets of vaccines. The first set 4 weeks prior the initiation of anti-TNFalpha or Rituximab therapy, the second set 6 weeks after initiation of the therapy.

Study burden and risks

During the course of the study (16 weeks) all patients will receive 2 sets of

vaccines, each consisting one T cell dependent, one T cell independent and one recall antigen
There are no reasons to beleive the side-effects of this vaccination for the participants differ from vaccination of healthy volonteers.
Allergic reactions have been described after administration of each of the vaccins seperately. Local skin rash and painfull injection site are relatively common (1-10%). More severe or prolonged reactions are rare. They include fever (0.1%) and seizures (0.01%).
Next to the administration of the vaccines, all patients will visit the hospital 7 times and a total of 300 ml of blood will be drawn.

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

- RA diagnosed according to the revised 1987 criteria of the American College of Rheumatology (ACR) for at least 3 months
- Age 18-85 years
-Eligible for anti-TNF * or Rituximab therapy (according to the Dutch guidelines)

Exclusion criteria

- Pregnancy
- Breastfeeding
- Therapy within the previous 60 days with:
*any experimental drug
*alkylating agents, e.g. cyclophosphamide, chlorambucil
*monoclonal antibodies (including infliximab and etanercept)
*growth factors
*other cytokines
- A positive PPD skin test (> 4 mm induration)
- HIV infection
- History of severe allergic or anaphylactic reactions to vaccines
- Vaccination with KLH, Pneumovax, Meningovax, Polio or tetanus toxoid in the past 12 months
- Fever (orally measured > 38 °C), chronic infections or infections requiring anti-microbial therapy
- Manifest cardiac failure (stage III or IV according to NYHA classification)
- Progressive fatal disease/terminal illness

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-11-2006
Enrollment:	40
Type:	Anticipated

Ethics review

Approved WMO

Application type:	First submission
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
EudraCT	EUCTR2006-005666-39-NL
CCMO	NL14888.018.06