A pilot study examining the effect of abatacept in ANCA associated vasculitis (AAV)

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Main objective:To assess the relapse rate (defined by clinical and biochemical parameters) over 24 months in patients with acute AAV presenting at first diagnosis of relapse, after 12 months of treatment with abatacept in combination with steroids...

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

Summary

ID

NL-OMON31540

Source
ToetsingOnline

Brief title
ABAVAS clinical trial

Condition

- Autoimmune disorders
- Joint disorders
- Vascular disorders NEC

Synonym
ANCA Associated Vasculitis (AAV), Wegener granulomatosis

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum

Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: ABAVAS, ANCA, Vasculitis

Outcome measures

Primary outcome

Response to treatment will be measured by:

the relapse rates in patients who achieved remission over 24 month study period

Secondary outcome

Response to treatment will also be measured by:

- The proportion of patients in sustained remission at 6, 12, 18 months and 24

months;

- The time to remission;

- The average steroid dosage at 6, 12, 18 and 24 months;

- Proportion of patients switching to cyclophosphamide;

- The time to ANCA negativity by immunofluorescence or negative anti-PR3 or

anti-MPO Ab test by ELISA;

- Urinary MCP-1 measurement to assess disease activity;

- Quality of life scoring;

- Vasculitis damage index scoring.

Study description

Background summary

The ANCA associated vasculitides (AASV), namely Wegener*s granulomatosis, microscopic polyangiitis, and renal limited vasculitis are autoimmune,

multi-system, progressive diseases which untreated can lead to rapidly progressive renal failure and death.
Randomised, prospective, clinical trials have demonstrated the efficacy of immunosuppressive treatments for vasculitis and have defined treatment protocols at different disease points. The current *gold standard* treatment for active AASV with glomerulonephritis is cyclophosphamide with steroids. However the standard treatment is associated with significant morbidity and mortality, largely due to infections and malignancy with cumulative cyclophosphamide dosing. Other effective treatments for AASV are being sought, with safer side effect profiles. In a randomized clinical trial, we previously demonstrated that Methotrexate in combination with prednisolone was as effective as cyclophosphamide and prednisolone. Relapse rate was, however, unacceptable high in both arms of this study.
Abatacept is well tolerated in humans with a good safety profile. Abatacept is now being increasingly used for other (non-ANCA) autoimmune conditions such as lupus and rheumatoid arthritis.
ABAVAS has been designed to test the hypothesis that Abatacept leads to a higher rate of sustained remission compared to standard therapies (MTX/steroids) with an equal rate of adverse events and reduced cyclophosphamide and prednisolon exposure as treatment for active, non-life-threatening AASV.

Study objective

Main objective:

To assess the relapse rate (defined by clinical and biochemical parameters) over 24 months in patients with acute AAV presenting at first diagnosis of relapse, after 12 months of treatment with abatacept in combination with steroids and methotrexate or placebo in combination with steroids and methotrexate.

Secondary objectives:

To assess the clinical efficacy of abatacept combined with MTX + steroids vs placebo and MTX + steroids by measuring:
1. The sustained remission rate
2. Time to remission
3. The average steroid dosage at 6, 12, 18 and 24 months in abatacept and placebo groups respectively
4. Time to ANCA megativity by immunofluorescence or negative anti PR3 or anti MPO Ab test by ELISA
5. Proportion of patients defaulting to cyclophosphamide therapy
6. Proportion of patients unable to stick with trial protocol
7. Degree of chronic disease activity
8. Health related quality of life

9. Number of adverse events

Study design

Multinational, randomized, double-blind, placebo-controlled, two-arm parallel design study of 24 months duration to the primary endpoint. This is an exploratory study. Subjects will be randomized 1:1 to receive either abatacept or placebo on top of MTX + CS for the first 12 months of the study and then be maintained on MTX only.

In order to maximise recruitment in a short time period (12 months) 15-20 centres would be required. This realistically would require a pan-european approach.

Intravenous injections of Abatacept or placebo will be given at day 1, 15, 29 at therafter each month for 12 months.
Dose: <60 kg: 500 mg
>60 to <100 kg: 750 mg
>100 kg: 1 gram

Intervention

Yes, standard therapy with or without abatacept.
14 x intravenous injection

Study burden and risks

AAV are severe diseases that are treated with cyclophosphamide and prednisolon. Side effects of this toxic therapy result in a lot of morbidity and even sometimes mortality (around 10-20% of patients). Recently, we demonstrated in a RCT that MTX in combination with corticosteroids is as effective as cyclophosphamide/corticosteroids in mild forms of AAV. During this RCT, however, relapse rate was unacceptable high in both arms of the study (70% within 18 months). With Abatacept/MTX/Prednisolon we hope that a more stable remission can be induced than with MTX/Prednisolon without increases of adverse events. Abatacept has been proven to be safe in RA. Side effects that occur are transfusion related. Theoretically also more infections can be induced by abatacept.

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

Active ANCA-associated vasculitis

Exclusion criteria

Pregnancy and malignancy, severe life threatening disease, renal insufficiency.

Study design

Design

Study phase:	2
Study type:	Interventional

Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-05-2008
Enrollment:	4
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Orencia
Generic name:	Abatacept
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	31-07-2008
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Approved WMO

Date:	01-10-2008
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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	EUCTR2006-001859-35-NL
Other	NC T00482066
CCMO	NL18440.068.08