A Multicenter Study of the Efficacy and Safety of the Human Anti-TNF Monoclonal Antibody Adalimumab in Subjects with Inactive Non-infectious Intermediate-, Posterior-, or Pan-uveitis

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Ocular infections, irritations and inflammations
Study type	Interventional

Summary

ID

NL-OMON39341

Source
ToetsingOnline

Brief title
N/A

Condition

- Ocular infections, irritations and inflammations

Synonym
eye inflammation, Uveitis

Research involving
Human

Sponsors and support

Primary sponsor: AbbVie B.V.
Source(s) of monetary or material Support: AbbVie GmbH & Co KG

Intervention

Keyword: Efficacy, Inactive uveitis, Placebo, Safety

Outcome measures

Primary outcome

The primary efficacy endpoint is the Time to Treatment Failure. Treatment

Failure in this study is defined by the occurrence of a uveitis flare (i.e.,

loss of disease control) as patients are tapered off their corticosteroids.

Secondary outcome

* Proportion of subjects who were able to taper down to 5 mg/day of prednisone

without meeting Treatment Failure criteria

* Proportion of subjects who discontinued prednisone without meeting Treatment

Failure criteria

* Change in Vitreous Haze grade (NEI/SUN criteria) in each eye from Baseline to

the Final/Early Termination visit

* Change in logMAR BCVA in each eye from Baseline to the Final/Early

Termination visit

* Time to OCT evidence of macular edema in at least one eye

* Change in central retinal thickness in each eye from Baseline to the

Final/Early Termination visit

* Change in NEI Visual Functioning Questionnaire score (VFQ-25) from Baseline

to the Final/Early Termination visit

Study description

Background summary

Uveitis refers to inflammation in the uveal tract of the eye which includes the iris, ciliary body, and choroid. In addition, diseases in which the retina is affected are also often included under the term "uveitis." According to the Standardization of Uveitis Nomenclature (SUN) working group, uveitis can be classified according to the primary anatomical location of the inflammation - anterior-, intermediate-, posterior- or pan uveitis (affecting all three areas).

Globally, there is a clear unmet medical need for additional effective therapies in patients with non-infectious intermediate-, posterior- and pan-uveitis who require chronic corticosteroid therapy and are at risk for the long-term side effects of corticosteroids. These types of uveïtis also have a higher risk of vision loss compared to patients with anterior uveïtis.

Immunosuppressive agents have been used as corticosteroid-sparing or additive therapy in intermediate-, posterior- or pan-uveitis but these have not been thoroughly studied, are not effective in all patients and also carry risk of certain adverse effects.

Study objective

The objective of this study is to evaluate the efficacy and safety of adalimumab 80 mg loading dose followed by 40 mg dose given every other week (eow) subcutaneously (SC) starting at Week 1 compared with placebo in subjects with inactive non-infectious intermediate-, posterior-, or pan uveitis.

Study design

A randomized, double-masked, placebo-controlled, multicenter study

Intervention

40mg adalimumab SC every other week

Study burden and risks

The patient will have 23 scheduled visits during the study. At the screening visit a PPD test, a pregnancy test and an ECG will be done. Every 4 weeks several test will be done(OCT, Tonometry, ETDRS and a slitlamp exam), blood will be drawn and the patient will be asked to complete several health questionnaires. Every 12 weeks the patient will get a physical exam and an urine pregnancy test.

Previous studies have shown significant efficacy of adalimumab and other anti-TNFs in patients with adalimumab. The intended efficacy of adalimumab in patients with uveitis could have a positive influence on their quality of life. It is highly probable that, as a result of the adalimumab therapy, the uveitis will not flare.

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

1. Subject is >= 18 years of age.;2. Subject is diagnosed with non-infectious intermediate-, posterior- or pan-uveitis.;3. Subject that for >= 28 days prior to the Baseline visit has inactive disease, and is taking >= 10 mg of oral prednisone to maintain this inactive state and fulfillment of all 3 of the following criteria based on the Investigators' clinical judgment at the Screening and Baseline visits for both eyes:;* Subject without active, inflammatory

chorioretinal and/or inflammatory retinal;vascular lesion.;* Subject with Anterior Chamber Cell grade <= 0.5+ according to SUN criteria.;* Subject with Vitreous Haze grade <= 0.5+ according to NEI/SUN criteria.;4. Subject is on oral prednisone 10 to 35 mg/day (or oral corticosteroid equivalent) at Baseline and the dose has not been increased in the past 28 days or decreased in the past 14 days.;5. Subject must have a documented history of experiencing at least one disease flare within 18 months of the Screening visit. This flare has to occur during or up to a maximum of 28 days after tapering off the oral corticosteroid therapy.;6. Subjects who do not have previous, active or latent TB.

Exclusion criteria

• Subject with isolated anterior uveitis.;• Subject with confirmed or suspected infectious uveitis, including but not limited to infectious uveitis due to TB, cytomegalovirus (CMV), Human T-Lymphotropic Virus Type 1 (HTLV-1), Whipple's disease, herpes zoster virus (HZV), Lyme disease, toxoplasmosis, ,and herpes simplex virus (HSV).;• Subject with serpiginous choroidopathy.;• Subject with corneal or lens opacity that precludes visualization of the fundus or that likely requires cataract surgery during the duration of the trial.;• Subject with intraocular pressure of > or = 25 mmHg and on > or = 2 glaucoma medications or evidence of glaucomatous optic nerve injury.;• Subject with best corrected visual acuity (BCVA) less than 20 letters (ETDRS [Early Treatment Diabetic Retinopathy Study]) in at least one eye at the baseline visit.;• Subject with intermediate uveitis or panuveitis that has signs of intermediate uveitis (e.g., presence or history of snowbanking or snowballs) and symptoms and/or Magnetic Resonance Imaging (MRI) findings suggestive of a demyelinating disease such as multiple sclerosis. All subjects with intermediate uveitis or panuveitis that have signs of intermediate uveitis (e.g., presence or history of snowbanking or snowballs) must have a brain MRI within 90 days prior to the Baseline visit.;• Subject has previous exposure to anti-TNF therapy or any biologic therapy (except intravitreal anti VEGF therapy) with a potential therapeutic impact on non-infectious uveitis.;• Subject on concomitant immunosuppressive therapy other than methotrexate, cyclosporine, mycophenolate mofetil or an equivalent drug to mycophenolate mofetil (e.g., mycophenolic acid), azathioprine or tacrolimus within 28 days of Baseline or has discontinued an immunosuppressive therapy including methotrexate, cyclosporine, mycophenolate mofetil or an equivalent drug to mycophenolate mofetil (e.g., mycophenolic acid), azathioprine or tacrolimus within 28 days of Baseline.;• If entering the study on one concomitant immunosuppressive therapy, dose has not been stable for at least 28 days prior to the Baseline visit or is not within the following allowable doses at the Baseline visit:;- Methotrexate (MTX) < or = 25 mg per week;- Cyclosporine < or = 4 mg/kg per day;- Mycophenolate mofetil < or = 2 grams per day or an equivalent drug to mycophenolate mofetil (e.g., mycophenolic acid) at an equivalent dose approved by the Medical Monitor;- Azathioprine < or = 175 mg per day;- Tacrolimus (oral formulation) <= 8 mg per day.;• Subject has received Retisert® (glucocorticosteroid implant) within 3 years prior to the Baseline visit or has had complications related to the device.;Subject has had Retisert® (glucocorticosteroid implant) removed within 90 days prior to the Baseline visit or has had complications related to the removal of the device.;• Subject has received intraocular or periocular corticosteroids within 90 days prior to the Baseline visit.;• Subject with proliferative or severe non-proliferative diabetic retinopathy or clinically significant

macular edema due to diabetic retinopathy.;• Subject with neovascular/wet age-related macular degeneration.;• Subject with abnormality of vitreo-retinal interface (i.e., vitreomacular traction, epiretinal membranes, etc.) with the potential for macular structural damage independent of the inflammatory process.;• Subject with cystoid macular edema unless the retinal changes are persistent, residual and stable as defined by the Standardization of Uveitis Nomenclature (SUN) criteria (persistent is > 3 months duration).;• Subject has received Ozurdex® (dexamethasone implant) within 6 months prior to the Baseline visit.;• Subject has received intravitreal methotrexate within 90 days prior to the Baseline visit.;• Subject has received intravitreal anti-VEGF therapy:;- within 45 days of the Baseline visit for Lucentis® (ranibizumab) or Avastin® (bevacizumab);;- or within 60 days of the Baseline visit for anti-VEGF Trap (Aflibercept).;• Subject on cyclophosphamide within 30 days prior to the Baseline visit.

Study design

Design

Study phase:	3
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):	10-02-2011
Enrollment:	5
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Decortin
Generic name:	prednison
Product type:	Medicine

Brand name:	Humira
Generic name:	adalimumab
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Placebo
Generic name:	placebo

Ethics review

Approved WMO Date:	28-07-2010
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	01-11-2010
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	28-06-2011
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	13-09-2011
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	26-09-2011
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	01-11-2011

Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	25-11-2011
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	14-12-2011
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	15-05-2012
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	31-05-2012
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	05-07-2012
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	11-07-2012
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	15-10-2012
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO Date:	06-11-2012
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	05-12-2012
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	12-12-2012
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	28-02-2013
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	16-04-2013
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	11-07-2013
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	25-07-2013
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	05-08-2013
Application type:	Amendment

Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	06-08-2013
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	13-03-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	03-04-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	04-07-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	04-08-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	EUCTR2009-016008-22-NL
CCMO	NL32595.078.10