A Multicenter Study of the Efficacy and Safety of the Human Anti-TNF Monoclonal Antibody Adalimumab as Maintenance Therapy in Subjects Requiring High Dose Corticosteroids for Active Non infectious Intermediate-, Posterior-, or Pan-uveitis

Published: 28-07-2010
Last updated: 01-05-2024

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 as maintenance therapy in subjects...

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

Summary

ID

NL-OMON39258

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
Source(s) of monetary or material Support: AbbVie BV

Intervention

Keyword: Adalimumab, Multicenter, Placebo, Uveitis

Outcome measures

Primary outcome

The primary efficacy endpoint is the Time to Treatment Failure. Treatment Failure is defined in the table on page 30 of the protocol for Week 6 and all other visits thereafter.

Secondary outcome

1. Change in Vitreous Haze grade (NEI/SUN criteria) in each eye from Week 6 to the Final/Early Termination visit

2. Change in logMAR BCVA in each eye from Week 6 to the Final/Early Termination Visit

3. Time to OCT evidence of macular edema in at least one eye on or after Week 6

4. Change in central retinal thickness in each eye from Week 6 to the Final/Early Termination visit

5. Change in NEI Visual Functioning Questionnaire (VFQ-25) score from Week 6 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). Patients with intermediate-, posterior- or pan uveitis are at a higher risk for vision loss compared to patients with anterior uveitis.

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.

The intended efficacy of adalimumab in patients with uveïtis could have a positive influence on their quality of life. It is highly probable that the uveïtis symptoms will improve significantly as a result of the adalimumab therapy. Previous studies have shown significant efficacy of adalimumab and other anti-TNFs in patients with adalimumab (page 24-25 of the protocol).

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 as maintenance therapy in subjects requiring high dose corticosteroids for active non-infectious intermediate-, posterior-, or pan-uveitis.

Study design

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

Intervention

Subjects will be randomized to receive adalimumab 80 mg subcutaneous (SC) loading dose followed a week later by 40 mg eow starting at Week 1 (Arm 1) or matching placebo as loading and eow doses (Arm 2) in a 1:1 ratio.
All subjects will receive a standardized prednisone burst of 60 mg/day at study

entry followed by a protocol-defined mandatory taper schedule in which all patients continuing in the study will be off prednisone no later than Week 15.

Study burden and risks

The patients will have 24 scheduled visits during the study. At the screening visit a PPD test, a pregnancy test, urinalysis test and an ECG will be done. During every study visit several tests (OCT, Tonometry, EDTRS and slit lamp exam) will be done, blood will be drawn and a chest X-ray will be made. The patients will also be asked to complete some questionnaires. Every 12 weeks the patient will get a physical exam and an urine pregnancy test.

Contacts

Public
AbbVie

Wegalaan 9
Hoofddorp 2132JD
NL
Scientific
AbbVie

Wegalaan 9
Hoofddorp 2132JD
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Subject is >= 18 years of age.;Subject is diagnosed with non-infectious intermediate-, posterior- or pan-uveitis.;Subject must have active disease at the Baseline visit as defined by the presence of at least 1 of the following parameters in at least one eye despite at least 2 weeks of maintenance therapy with oral prednisone at a dose of >= 10 mg/day to <= 60 mg/day (or oral corticosteroid equivalent):;* Active, inflammatory, chorioretinal and/or inflammatory retinal vascular lesion;* >= 2+ anterior chamber cells (Standardization of Uveitis Nomenclature [SUN] criteria);* >= 2+ vitreous haze (National Eye Institute [NEI]/SUN criteria);Subject is on oral prednisone at a dose of >= 10 mg/day to <= 60 mg/day (or oral corticosteroid equivalent) for at least 2 weeks prior to Screening and remains on the same dose from Screening to Baseline visit.;Subjects who do not have previous, active or latent TB.

Exclusion criteria

1. Subject with isolated anterior uveitis.;2. Subject with prior inadequate response to high-dose oral;corticosteroids.;3. Subject with confirmed or suspected infectious uveitis, including but not limited to;infectious uveitis due to TB, cytomegalovirus (CMV), Lyme disease,;toxoplasmosis, Human T-Lymphotropic Virus Type 1 (HTLV-1) infection,;Whipple's disease, herpes zoster virus (HZV) and herpes simplex virus (HSV).;4. Subject with presumed ocular histoplasmosis syndrome (POHS).;5. Subject with ocular masquerade syndromes, such as ocular lymphoma.;6. Subject with serpiginous choroidopathy.;7. Subject has a contraindication to pupil dilation with mydriatic eyedrops.;8. Subject with corneal or lens opacity that precludes visualization of the fundus or;that likely requires cataract surgery during the duration of the trial.;9. Subject with intraocular pressure of >= 25 mmHg and on >= 2 glaucoma medications;or evidence of glaucomatous optic nerve injury.;10. 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.;11. 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.;12. Subject has previous exposure to anti-TNF therapy or any biologic therapy (except;intravitreal anti-vascular endothelial growth factor [VEGF] therapy [See Exclusion;Criterion No. 43]) with a potential therapeutic impact on non infectious uveitis.;13. Subject on more than 1 immunosuppressive therapy (not including corticosteroids);at Baseline.;14. 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 at Baseline.;15. If entering the study on 1 concomitant immunosuppressive therapy, dose has been;increased within the last 28 days prior to Baseline visit or is not within the;following allowable doses at the Baseline visit:;* Methotrexate (MTX) <= 25 mg per week;* Cyclosporine <= 4 mg/kg per day;* Mycophenolate mofetil <= 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 <= 175 mg per day;*Tacrolimus (oral formulation) <= 8 mg per day;16. Subject with prior or current use of chlorambucil.;17. 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.;18. Subject has received intraocular or periocular corticosteroids within 30 days prior;to the Baseline visit.;19. Subject with history of prior ocular surgery within 90 days prior to the Baseline visit with the exception of refractive laser surgery or retinal laser photocoagulation or YAG (neodymium-doped yttrium aluminium garnet) posterior capsulotomy. These three exceptions are exclusionary within 30 days prior to Baseline.;20. Subject with any planned (elective) eye surgery within the next 80 weeks from;Baseline.;21. Subject with proliferative or severe non-proliferative diabetic retinopathy or;clinically significant macular edema due to diabetic retinopathy.;22. Subject with neovascular/wet age-related macular degeneration.;23. 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.;40. Subject with severe vitreous haze that precludes visualization of the fundus at the;Baseline visit.;41. Subject has received Ozurdex® (dexamethasone implant) within 6 months prior to;Baseline visit.;42. Subject has received intravitreal MTX within 90 days prior to the Baseline visit.;43. 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).;51. Subject with intolerance to high-dose oral corticosteroids (equivalent of oral prednisone 1 mg/kg/day or 60 to 80 mg/day).;52. 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

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:	02-08-2013
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)

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	EUCTR2009-016095-68-NL
CCMO	NL32051.078.10