A non-controlled trial of Anti-TNFa Chimeric Monoclonal Antibody (Infliximab, Remicade®) in Exudative Age Related Macular Degeneration.

No registrations found.

Ethical review	Positive opinion
Status	Recruitment stopped
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON20009

Source
NTR

Brief title
N/A

Health condition

Exudative Age Related Macular Degeneration.
Exudatieve leeftijdgebonden Macula Degeneratie

Sponsors and support

Primary sponsor: Erasmus Medisch Centrum
Dr. Molewaterplein 40
3015 GD Rotterdam
&
Oogziekenhuis Rotterdam
Schiedamse Vest 180
3011 BH Rotterdam
Source(s) of monetary or material Support: Centocor BV
Einsteinweg 32
2333 CD Leiden

Intervention

Outcome measures

Primary outcome

Absolute change in visual acuity (VA) versus baseline of the target eye. Target eye for primary endpoint is defined as the eye that is indicated by the patient as the most recent and worsening. VA change will be expressed as the absolute change in number of letters correctly identified at week 0 compared to week 52. VA will be determined as described in Chapter 20 of the Protocol.

Secondary outcome

1. Proportional changes in VA using ETDRS chart;

2. Proportion of target eyes that have a change in VA better than a loss of 15 letters on the ETDRS chart;

3. Proportion of target eyes that have a change in VA better than a loss of 30 letters on the ETDRS chart;

4. Time until decrease of VA > 15 letters on ETDRS chart;

5. Time until decrease of VA > 30 letters on ETDRS chart;

6. Change in contrast sensitivity using Pelli-Robson chart;

7. Change in area of the CNV lesion on photography and fluorescein angiography;

8. Change in quality of life measurements.

Study description

Background summary

Age-related macular degeneration (ARMD) results in a deterioration of the central retinal function, and is the leading cause of blindness in people over 50 years of age in Europe and the USA. Because of the localisation of the macula in the centre of the retina, advanced ARMD often leads to irreversible loss of vision and subsequently loss of social skills like reading ability.

Tumor necrosis factor (TNF) alpha is involved in various inflammatory processes as a

proinflammatory cytokine. Previously, it has been shown that inflammatory cells and inflammatory factors (complement H) are involved in the generation of ARMD. For example, TNF-alpha seems to be involved in destructive retinal membrane formation. Moreover, it has been shown recently that the visual acuity improved and, the pathological neovascularisation resolved in patients with ARMD during 6 months of treatment with anti-TNF-alpha. Based on these findings we propose “A non-controlled trial of Anti-TNFa Chimeric Monoclonal Antibody (Infliximab, Remicade®) in Exudative Age Related Macular Degeneration”.

Study objective

Treatment with Infliximab will reduce loss of visual acuity by 8 letters or better on the ETDRS chart.

Study design

N/A

Intervention

Infliximab (5mg/kg) in saline solution (0.9%) at weeks 0, 2, 6, 14, 22, 30, 38 and 46.

Contacts

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Eligibility criteria

Inclusion criteria

1. Have the capacity to understand and sign an informed consent form;

2. Men and women > 60 years of age;

3. Women must be postmenopausal (no menstrual period for a minimum of 1 year) or surgically sterilized. Men must agree to use adequate birth control measures during the study and for 6 months after the last infusion of infliximab;

4. A decrease in visual acuity within 2 months prior to study start, related to exudative ARMD, with an occult or a mixed (minimally classic) CNV that is at least partially subfoveal (i.e. on fluorescein angiogram, an occult or predominantly occult CNV is shown, within 200 ¨¬m of the centre of the Foveal area zone (FAZ));

5. A best corrected visual acuity (distance) of 0.125 (20/160 snellen equivalent, 0.9 logmar ETDRS equivalent or 40 letters read on ETDRS chart) or better in the study eye, which has been determined within 1 week prior to randomization and first treatment. Visual acuities will be measured using ETDRS charts at the moment of screening and during every visit of the study;

6. The screening laboratory test results must meet the following criteria:

a. WBC: ³ 3.5 x 109/L;

b. Hemoglobin for males ³ 8.6 mmol/L and females ³ 7.5 mmol/L;

c. Platelets 150-350 x 109/L;

d. Serum Creatinine £ 120 mmol/L or 1.5 times the upper limit of the normal range;

e. Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) should be within 3 times the upper limit of the normal range;

7. Are considered eligible according to the tuberculosis (TB) eligibility assessment, screening, and early detection of reactivation rules defined in Section 26 of the Protocol;

8. TB inclusion criteria:

a. Have no history of latent or active TB prior to screening;

b. Have no signs or symptoms suggestive of active TB upon medical history and/or physical examination;

c. Have had no recent close contact with a person with active TB or, if there has been such contact, will be referred to a physician specializing in TB to undergo additional evaluation

and, if warranted, receive appropriate treatment for latent TB prior to or simultaneously with the first administration of study agent;

d. Within 1 month prior to the first administration of study agent, either have a negative tuberculin skin test, as outlined in Section 17 of the Protocol, or have a newly identified positive tuberculin skin test during screening in which active TB has been ruled out and for which appropriate treatment for latent TB has been initiated either prior to or simultaneously with the first administration of study agent;

e. Have a chest radiograph (both posterior-anterior and lateral views), taken within 3 months prior to the first administration of study agent and read by a qualified radiologist, with no evidence of current active TB or old inactive TB.

Exclusion criteria

1. Ophthalmic exclusion criteria:

a. Inability to visualize the fundus due to corneal or important lenticular opacities;

b. Inability to obtain photographs to document CNV, e.g. due to allergy to fluorescein dye, ICG or lack of venous access;

c. Have a history of treatment for CNV in the study eye: including but not limited to confluent laser photocoagulation, submacular surgery, radiotherapy or macular scatter ('grid') laser photocoagulation;

d. Patients requiring ocular surgery within the initial 12 months of treatment, or who have had surgery in the prior 3 months;

e. Are participating in another ophthalmic clinical trial requiring follow-up examinations or are receiving, or have received any experimental systemic treatment for ARMD (e.g. retinoic acid, thalidomide) or any other investigational drug within 12 weeks prior to the start of study treatment;

f. Are subject to laser coagulation, acetazolamide, high dose systemic steroids (> 10 mg prednisolone daily or equivalent) or immunosuppressive therapy;

g. Have a tear (rip) of the RPE, a vitelliform-like lesion of the outer retina (e.g. as in pattern dystrophies or basal laminar drusen) or central serous retinopathy;

h. Have any additional ocular diseases which have irreversibly compromised or, during follow-up, could likely compromise the visual acuity of the study eye including amblyopia, uncontrolled glaucoma in one or both eyes (intraocular pressure >30mmHg), anterior ischemic optic neuropathy, diabetic macular edema, diabetic retinopathy;

i. Other retinal or ophthalmic disorders that could influence the macular area;

j. Previous retinal surgery;

k. High myopia (> 8 diopters);

l. History of macula affecting drugs (Hydrochloroquine, Chloroquine);

2. General medical exclusion criteria:

a. Women who are pregnant, nursing, or planning pregnancy within 6 months after the last infusion (this includes father's who plan on fathering a child within 6 months after their last infusion);

b. Known allergy against infliximab, Fluorescein dye, ICG dye;

c. Use of other systemic anti-inflammatory medication except NSAIDs and low dose systemic steroids (equal or less than 10 mg daily prednisolone or equivalent);

d. Have had any previous treatment with monoclonal antibodies or antibody fragments;

e. History of receiving human/murine recombinant products or a known allergy to murine products;

f. Documentation of seropositive for human immunodeficiency virus (HIV);

g. A positive test for hepatitis B surface antigen or hepatitis C;

h. Have a history of alcohol or substance abuse within the preceding 6 months that, in the opinion of the investigator, may increase the risks associated with study participation or study agent administration, or may interfere with interpretation of results;

i. Have a known history of serious infections (eg, hepatitis, pneumonia or pyelonephritis) in the previous 3 months;

j. Have or have had an opportunistic infection (eg, herpes zoster [shingles], cytomegalovirus, Pneumocystis carinii, aspergillosis, histoplasmosis, or mycobacteria other than TB) within 6 months prior to screening;

k. Are considered ineligible according to the TB eligibility assessment, screening, and early detection of reactivation rules defined in Section 26 of the Protocol;

l. Have a history of lymphoproliferative disease, including lymphoma or signs suggestive of possible lymphoproliferative disease such as lymphadenopathy of unusual size or location (eg, nodes in the posterior triangle of the neck, infraclavicular, epitrochlear, or periaortic area), or splenomegaly;

m. Currently have any known malignancy or have a history of malignancy within the previous 5 years, with the exception of basal cell or squamous cell carcinoma of the skin that has been fully excised with no evidence of recurrence;

n. Have current signs or symptoms of severe, progressive or uncontrolled renal, hepatic, hematologic, gastrointestinal, endocrine, pulmonary, cardiac, neurologic, or cerebral disease;

o. Are unable or unwilling to undergo multiple venipunctures because of poor tolerability or lack of easy access;

p. Use of any investigational drug within 30 days prior to screening or within 5 half-lives of the investigational agent, whichever is longer;

q. Treatment with any other therapeutic agent targeted at reducing TNF (eg, pentoxifylline, thalidomide, etanercept, adalimumab etc.) within 3 months of screening;

r. Presence of a transplanted solid organ (including a corneal transplant);

s. Have a concomitant diagnosis or history of congestive heart failure;

t. TB exclusion criteria:

1. Have a history of latent or active granulomatous infection, including TB, histoplasmosis, or coccidioidomycosis, prior to screening;

2. Have had a Bacille Calmette-Guerin (BCG) vaccination within 12 months of screening;

3. Have a chest radiograph within previous 3 months that shows an abnormality suggestive of a malignancy or current active infection, including TB;

4. Have had a nontuberculous mycobacterial infection or opportunistic infection (eg, cytomegalovirus, Pneumocystis carinii, aspergillosis) within 6 months prior to screening.

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-01-2006
Enrollment:	40
Type:	Actual

Ethics review

Positive opinion

Date:	10-01-2007
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	NL855
NTR-old	NTR869
Other	: OZR-2005-11
ISRCTN	ISRCTN01449944

Study results

Summary results

van Hagen PM, Baarsma GS, van Bilsen CE, Kuijpers RW, van Laar JA, van der Ent M, van Daele PL, Veeger NJ, Vingerling JR, Missotten TO. A noncontrolled trial of anti-TNF-α chimeric monoclonal antibody (infliximab, Remicade®) in exudative age-related macular degeneration. Acta Ophthalmol. 2014; Epub ahead of print Jun 22. PMID: 24953977