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A non-controlled trial of anti-Tumour Necrotising Factor alpha (anti-TNFa) chimeric monoclonal antibody (Infliximab, Remicade®) in exudative age-related macular degeneration

Submission date 16/07/2007	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 16/07/2007	**Overall study status** Completed	
Last Edited 28/10/2021	**Condition category** Eye Diseases	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

OZR-2005-11, NL855 (NTR869)

Study information

Scientific Title
A non-controlled trial of anti-Tumour Necrotising Factor alpha (anti-TNFa) chimeric monoclonal antibody (Infliximab, Remicade®) in exudative age-related macular degeneration

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

Ethics approval required
Old ethics approval format

Ethics approval(s)
Full approval received from the local medical ethics committee (Medisch Ethische ToetsingsCommissie [METC]) on the 12th January 2006 (ref: MEC-2005-249).

Study design
Non-randomised, non-controlled, clinical trial

Primary study design
Interventional

Secondary study design
Non randomised controlled trial

Study setting(s)
Not specified

Study type(s)
Treatment

Participant information sheet

Health condition(s) or problem(s) studied
Exudative age-related macular degeneration

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

Intervention Type
Drug

Phase
Not Specified

Drug/device/biological/vaccine name(s)
Infliximab, Remicade®

Primary outcome measure
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.

Secondary outcome measures
1. Proportional changes in VA using ETDRS chart, measured at baseline, weeks 2, 6, 14, 22, 30, 38, 46, 52 and 72
2. Proportion of target eyes that have a change in VA better than a loss of 15 letters on the ETDRS chart, measured at baseline, weeks 2, 6, 14, 22, 30, 38, 46, 52 and 72
3. Proportion of target eyes that have a change in VA better than a loss of 30 letters on the ETDRS chart, measured at baseline, weeks 2, 6, 14, 22, 30, 38, 46, 52 and 72
4. Time until decrease of VA greater than 15 letters on ETDRS chart, measured at baseline, weeks 2, 6, 14, 22, 30, 38, 46, 52 and 72
5. Time until decrease of VA greater than 30 letters on ETDRS chart, measured at baseline, weeks 2, 6, 14, 22, 30, 38, 46, 52 and 72
6. Change in contrast sensitivity using Pelli-Robson chart, measured at baseline, weeks 2, 6, 14, 22, 30, 38, 46, 52 and 72
7. Change in area of the CNV lesion on photography and fluorescein angiography, measured at weeks 22 and 52
8. Change in quality of life measurements, measured at weeks 6, 22, 38 and 52 (using the 36-item Short Form health survey [SF-36] and the National Eye Institute Visual Function Questionnaire-25 [NEI-VFQ25])

Overall study start date
01/01/2006

Completion date
31/12/2007

Eligibility

Key inclusion criteria
1. Have the capacity to understand and sign an informed consent form
2. Men and women older than 60 years of age
3. Women must be postmenopausal (no menstrual period for a minimum of one year) or surgically sterilised. Men must agree to use adequate birth control measures during the study and for six months after the last infusion of infliximab
4. A decrease in visual acuity within two months prior to study start, related to exudative ARMD, with an occult or a mixed (minimally classic) Choroid Neovascularisation (CNV) that is at least partially subfoveal (i.e. on fluorescein angiogram, an occult or predominantly occult CNV is shown, within 200 µm 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 one week prior to randomisation 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:
6.1. White Blood Cells (WBC): greater than or equal to 3.5 x 10^9/L
6.2. Haemoglobin for males greater than or equal to 8.6 mmol/L and females greater than or

equal to 7.5 mmol/L
6.3. Platelets 150 - 350 x 10^9/L
6.4. Serum creatinine less than 120 mmol/L or 1.5 times the upper limit of the normal range
6.5. Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) should be within three 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

TB inclusion criteria:
1. Have no history of latent or active TB prior to screening
2. Have no signs or symptoms suggestive of active TB upon medical history and/or physical examination
3. 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 specialising 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
4. Within one month prior to the first administration of study agent, either have a negative tuberculin skin test, 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
5. Have a chest radiograph (both posterior-anterior and lateral views), taken within three 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

Participant type(s)
Patient

Age group
Senior

Sex
Both

Target number of participants
40

Total final enrolment
13

Key exclusion criteria
Ophthalmic exclusion criteria:
1. Inability to visualise the fundus due to corneal or important lenticular opacities
2. Inability to obtain photographs to document CNV, e.g. due to allergy to fluorescein dye, Indocyanine Green (ICG) or lack of venous access
3. 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
4. Patients requiring ocular surgery within the initial 12 months of treatment, or who have had surgery in the prior three months
5. 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
6. Are subject to laser coagulation, acetazolamide, high dose systemic steroids (greater than 10 mg prednisolone daily or equivalent) or immunosuppressive therapy
7. Have a tear (rip) of the Retinal Pigment Epithelium (RPE), a vitelliform-like lesion of the outer retina (e.g. as in pattern dystrophies or basal laminar drusen) or central serous retinopathy
8. 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 greater than 30 mmHg), anterior ischemic optic neuropathy, diabetic macular oedema, diabetic retinopathy
9. Other retinal or ophthalmic disorders that could influence the macular area
10. Previous retinal surgery
11. High myopia (greater than 8 dioptres)
12. History of macula affecting drugs (hydrochloroquine, chloroquine)

General medical exclusion criteria:
1. Women who are pregnant, nursing, or planning pregnancy within six months after the last infusion (this includes father's who plan on fathering a child within six months after their last infusion)
2. Known allergy against infliximab, fluorescein dye, ICG dye
3. Use of other systemic anti-inflammatory medication except Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) and low dose systemic steroids (equal or less than 10 mg daily prednisolone or equivalent)
4. Have had any previous treatment with monoclonal antibodies or antibody fragments
5. History of receiving human/murine recombinant products or a known allergy to murine products
6. Documentation of seropositive for Human Immunodeficiency Virus (HIV)
7. A positive test for hepatitis B surface antigen or hepatitis C
8. Have a history of alcohol or substance abuse within the preceding six 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
9. Have a known history of serious infections (e.g., hepatitis, pneumonia or pyelonephritis) in the previous three months
10. Have or have had an opportunistic infection (e.g., herpes zoster [shingles], cytomegalovirus, Pneumocystis carinii, aspergillosis, histoplasmosis, or mycobacteria other than TB) within six months prior to screening
11. Are considered ineligible according to the TB eligibility assessment, screening, and early detection of reactivation rules
12. Have a history of lymphoproliferative disease, including lymphoma or signs suggestive of possible lymphoproliferative disease such as lymphadenopathy of unusual size or location (e.g., nodes in the posterior triangle of the neck, infraclavicular, epitrochlear, or periaortic area), or splenomegaly
13. Currently have any known malignancy or have a history of malignancy within the previous five years, with the exception of basal cell or squamous cell carcinoma of the skin that has been fully excised with no evidence of recurrence
14. Have current signs or symptoms of severe, progressive or uncontrolled renal, hepatic, haematological, gastrointestinal, endocrine, pulmonary, cardiac, neurological, or cerebral disease
15. Are unable or unwilling to undergo multiple venipunctures because of poor tolerability or lack of easy access
16. Use of any investigational drug within 30 days prior to screening or within five half-lives of the investigational agent, whichever is longer
17. Treatment with any other therapeutic agent targeted at reducing TNF (e.g., pentoxifylline,

thalidomide, etanercept, adalimumab etc.) within three months of screening
18. Presence of a transplanted solid organ (including a corneal transplant)
19. Have a concomitant diagnosis or history of congestive heart failure

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 three months that shows an abnormality suggestive of a malignancy or current active infection, including TB
4. Have had a non-tuberculous mycobacterial infection or opportunistic infection (e.g., cytomegalovirus, Pneumocystis carinii, aspergillosis) within six months prior to screening

Date of first enrolment
01/01/2006

Date of final enrolment
31/12/2007

Locations

Countries of recruitment
Netherlands

Study participating centre
Erasmus Medisch Centrum
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3015 GD

Sponsor information

Organisation
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Sponsor type
Hospital/treatment centre

Website

http://www.erasmusmc.nl/content/englishindex.htm

ROR
https://ror.org/018906e22

Funder(s)

Funder type
Industry

Funder Name
Centocor (The Netherlands)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan
Not provided at time of registration

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		22/06/2014	28/10/2021	Yes	No