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Low dose etanercept for the treatment of patients with ankylosing spondylitis

Submission date
21/01/2011

Recruitment status
No longer recruiting

Registration date
21/01/2011

Overall study status
Completed

Last Edited
12/10/2016

Condition category
Musculoskeletal Diseases

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
In people with ankylosing spondylitis (AS) a protein called tumour necrosis factor (TNF) is overproduced in the body, causing inflammation and damage to bones, cartilage and tissue. A number of drugs have been developed that block the action of TNF and so can reduce this inflammation. One of these anti-TNF drugs is called Etanercept. At the moment the recommended dose for Etanercept is 50 mg per week. This is given as an injection under the skin each week. We are trying to find out if this 50 mg amount is the optimum dose for people with AS. People with rheumatoid arthritis also take Etanercept to ease their joint pain and stiffness. Research has shown that taking lower doses of the drug still produces a good response. At the moment we do not know if this is also true for people with AS. We want to find out if a lower weekly dose of Etanercept still produces a good clinical response for people with AS. If so, this may reduce the side effects this drug can cause.

Who can participate?
People with AS living in Norfolk who are about to start taking Etanercept are being invited to take part in this research.

What does the study involve?
Everyone who takes Etanercept is followed up at routine out-patient clinics every 3 months to see how they are getting on. Not everyone who takes Etanercept finds it helps them and three out of ten people see no difference in their symptoms. People taking part in the study will be asked to complete a series of questionnaires about their AS symptoms, quality of life and general health and well-being. No additional tests or procedures are required to take part in the study. After six months, those people who find Etanercept helps their symptoms will be randomly allocated to one of two groups. One group will continue to take Etanercept at the standard 50 mg dose whilst the other group will have their weekly dose reduced by half. Whichever group people are in, they will continue to take Etanercept for a further six months as part of the study. They will attend two more routine out-patient visits (three months apart) where the same questionnaires will be completed. If they are in the lower dose group and there is evidence that their symptoms are getting worse, the dose of Etanercept will be put back up to the standard 50 mg. In total, people will be involved in the study for one year.

What are the possible benefits and risks of taking part?
Those people in the lower dose group may find they experience fewer side effects than those people who continue on the standard recommended dose. The information we get from this study will help improve the treatment of people with AS in the future. People involved in the study will have slightly longer clinic visits (between ten minutes and half an hour). Some people put in the lower dose group may find the drug stops working or does not work as well as it did before.

Where is the study run from?
This research is taking place at two NHS hospitals in Norfolk, the Norfolk & Norwich Hospital and the James Paget Hospital.

When is the study starting and how log is it expected to run?
The study started in October 2010 and finished in August 2013.

Who is funding the study?
This study is funded by Pfizer Pharmaceuticals (UK).

Who is the main contact for the study?
Dr Karl Gaffney, Consultant Rheumatologist at the Norfolk & Norwich Hospital

Contact information

Type(s)
Scientific

Contact name
Dr Frances Elender

Contact details
Colney Lane
Colney
Norwich
United Kingdom
NR4 7UY
-
frances@elenderlimited.com

Additional identifiers

Clinical Trials Information System (CTIS)
2010-020913-10

Protocol serial number
9375

Study information

Scientific Title

An open label, pilot, multicentre, stepdown, randomised controlled trial to examine whether etanercept 25 mg once weekly is effective in maintaining a clinical response in patients with ankylosing spondylitis who have responded to 50 mg once weekly

Acronym
ANSWERS

Study objectives
Study aims:
1. To investigate whether etanercept 25 mg once weekly is effective in maintaining a clinical response in patients with AS who have responded to 50 mg once weekly
2. To assess measurements of efficacy and adverse effects in low and high dose groups

Ethics approval required
Old ethics approval format

Ethics approval(s)
North West 2 Ethics Committee - Liverpool Central approved on the 06/08/2010 (ref: 10/H1005 /52)

Study design
Multicentre randomised open label controlled interventional treatment trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Topic: Musculoskeletal; Subtopic: Musculoskeletal (all Subtopics); Disease: Musculoskeletal

Interventions
Patients attending hospital rheumatology out-patient clinics who fulfil the NICE eligibility criteria for AS will be initiated on Etanercept (Enbrel®) 50 mg once weekly. After a six month lead-in phase, responders to Etanercept (as defined by NICE criteria) will be randomly assigned to either step down to 25 mg once weekly dose or continue with 50 mg once weekly.

Follow up length: 6 months
Study entry: single randomisation only

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Etanercept

Primary outcome(s)
Maintenance of 50% reduction in Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and/or fall by greater than or equal to 2 units at 3 and 6 months post-randomisation

Key secondary outcome(s))
1. AS response criteria (ASAS 20,40,5 of 6 & Partial Remission)
2. Bath Ankylosing Spondylitis Metrology Index (BASMI)
3. Bath Ankylosing Spondylitis Functional Index (BASFI)
4. Ankylosing Spondylitis Quality of Life Questionnaire. (ASQoL)
5. Standard measure of health outcome (EQ-5D)
6. Proportions of patients discontinuing therapy for different reasons

All secondary outcome measures will be measured at the same time point as the primary outcome measure (i.e. BASDAI) which is one year post baseline (6 months post randomisation).

Completion date
31/08/2013

Eligibility

Key inclusion criteria
At screening/baseline:
The participant will be placed on etanercept 50 mg once weekly providing:
1. Diagnosis of AS according to the modified New York criteria
2. Confirmation of sustained active spinal disease, demonstrated by:
2.1. BASDAI score of at least 4 units
2.2. At least 4 cm on a 0-10cm spinal pain visual analogue scale (VAS)
2.3. Both severity measures demonstrated on two occasions at least 12 weeks apart without any change of treatment
3. Conventional treatment with two or more NSAIDs taken sequentially at maximum tolerated or recommended dosage for 4 weeks have failed to control symptoms
4. Participant has clinically acceptable results from laboratory screening test
5. Male or Female, aged 18 - 80 years
6. Participant is willing and able to give informed consent to participate in the study
7. Able (in the Investigators opinion) and willing to comply with all study requirements

At randomisation:
The participant will be randomised to 50 mg or 25 mg etanercept providing:
1. An adequate response to treatment has been achieved, with response defined as:
1.1. Reduction of the BASDAI score to 50% of the pre-treatment value, or
1.2. Reduction in BASDAI by 2 or more units, and
1.3. Reduction of the spinal pain VAS by 2 cm or more
2. The participant finds etanercept acceptable and wishes to continue treatment

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group

Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
At screening/baseline:
The participant will not enter the study if ANY of the following apply:
1. Previous treatment with any licensed or experimental anti TNF therapy
2. Chronic infection of the upper respiratory tract (e.g. sinusitis), chest (e.g. bronchiectatic lung disease), urinary tract or skin (e.g. paronychia, chronic ulcers, open wounds)
3. Serious infections (such as pneumonia or pyelonephritis) in the previous 3 months
4. Any ongoing or active infection or any major episode of infection requiring hospitalisation or treatment with intravenous (IV) antibiotics within the preceding 30 days and/or orally administered antibiotics in the preceding 15 days
5. Received any live (attenuated) vaccines within four weeks of screening visit
6. Known immunosuppressive disease or treatment with immunosuppressive drugs
7. Active/latent tuberculosis as identified by local screening guidelines
8. Stable corticosteroid use 10 mg OD taken in the 4 weeks prior to screening
9. History of hepatitis B or C
10. Significant concurrent cardiovascular disease including; uncompensated congestive heart failure, myocardial infarction within 12 months, unstable angina pectoris, uncontrolled hypertension
11. Cancer or a history of cancer (other than resected cutaneous basal cell carcinoma, and in situ cervical cancer) within five years of entering the screening period
12. Significant renal or hepatic impairment
13. Leukopaenia (WBC less than 3000 x 10^6/L) and/or neutropeania (WBC less than or equal to 1500 x 10^6/L)
14. Thrombocytopaenia (platelets less than 150 x 10^9/L)
15. Demyelinating disorders such as multiple sclerosis
16. Women who are pregnant, lactating or of childbearing potential not using contraception
17. Scheduled elective surgery/procedures requiring general anaesthesia during the study
18. Allergy to latex (the needle cover of the syringe contains latex)
19. Presence of any other significant and uncontrolled medical condition, which in the investigator's opinion precludes the use of etanercept
20. Unable to give informed consent
21. Unable/unwilling to comply with study procedures
22. Not available for followup assessments
23. Received treatment with an investigational drug within 12 weeks prior to study screening
24. History of back injury or trauma which confounds the clinical scenario

At randomisation:
The participant will not be randomised if ANY of the following apply:
1. An adequate response to etanercept 50 mg per week has not been achieved by the end of the 6 month lead in period
2. The participant wishes to discontinue treatment with etanercept
3. On the basis of adverse reactions, the treating physician considers the participant should withdraw from treatment with etanercept

Date of first enrolment
18/10/2010

Date of final enrolment
31/08/2013

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Colney Lane
Norwich
United Kingdom
NR4 7UY

Sponsor information

Organisation
Norfolk and Norwich University Hospital NHS Foundation Trust (UK)

ROR
https://ror.org/01wspv808

Funder(s)

Funder type
Industry

Funder Name
Pfizer (formerly Wyeth) (UK)

Alternative Name(s)
Pfizer Inc., Pfizer Consumer Healthcare, Davis, Charles Pfizer & Company, Warner-Lambert, King Pharmaceuticals, Wyeth Pharmaceuticals, Seagen, Pfizer Inc

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes