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The effects of tumour necrosis factor antagonism (Etanercept) in patients with acute coronary syndromes

Submission date
12/11/2012

Recruitment status
No longer recruiting

Registration date
14/01/2013

Overall study status
Completed

Last Edited
17/05/2016

Condition category
Circulatory System

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Heart attacks are caused by blood clots which form in the heart arteries and obstruct blood flow. These occur as a result of both acute and chronic inflammation occurring within the blood vessel walls. Tumour necrosis factor alpha (TNF-alpha) is an inflammatory molecule that may be instrumental in the development of artery inflammation that leads to heart attacks. The main aim of the study was to work out if specific anti-inflammatory treatment, suppressing the effects of TNF-alpha might be beneficial following a heart attack.

Who can participate?
We at the Royal Infirmary in Edinburgh recruited patients who have suffered heart attacks but who are otherwise well.

What does the study involve?
On the first day, patients underwent a forearm study which was carried out in a side room located within the Cardiology ward. This was to assess how well blood vessels are able to appropriately relax. This consisted of lying on a bed for 3 hours in a warm room. Some bands were placed around both arms which would tighten up for short periods and from time to time. A very small needle was placed in the artery of one arm and two plastic tubes (cannulae) were placed into the veins, one in each arm. This part of the study is associated with some slight discomfort and we use local anaesthetic to minimise this. Small amount of drugs (substance P, acetylcholine and sodium nitroprusside) were administered and samples of blood (up to 200 ml on each occasion) were taken from the cannulae. The drug doses are very small and should only affect the arm. They can cause flushing and some mild swelling in the forearm. The effects are however self-limiting and of short duration. The blood samples were analysed for components in the blood that play a part in the clotting and inflammatory mechanisms. Immediately after this patients were assigned by chance (randomised) to receive either an infusion of Etanercept or a dummy infusion (saline) over 30 minutes. There is therefore a one in two chance you will not receive the study drug. On the second day (24 hours later) you will undergo a second and final forearm study.

What are the possible benefits and risks of participating?
Treatment with anti-TNF-α monoclonal antibodies may have beneficial effects. We do not anticipate that you will experience any side effects from this drug (etanercept) although an allergic reaction to this drug may rarely occur.

Where is the study run from?
Edinburgh Royal Infirmary (UK)

When is the study starting and how long is it expected to run for?
May 2003 to August 2009

Who is funding the study?
British Heart Foundation (UK)

Who is the main contact?
1. Dr Gareth J Padfield (gareth.padfield@nhs.net)
2. Prof David E Newby (d.e.newby@ed.ac.uk)

Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

Protocol serial number
2001/R/CAR/01

Study information

Scientific Title
Cardiovascular effects of tumour necrosis factor alpha antagonism in patients with acute myocardial infarction: a first in man study

Study objectives
Inflammation causes and destabilises atheroma. Circulating tumour necrosis factor - alpha (TNF-α) concentrations are increased in acute coronary syndromes and is expressed at higher

concentrations in unstable atheromatous plaques. Treatment with anti-TNF-α monoclonal antibodies may have beneficial effects on vascular function (vasomotor and fibrinolytic function) and flow cytometric measures of platelet aggregation.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Lothian research and ethics committee, April 2001, ref: LREC/2001/4/18

Study design
Double-blind parallel-group randomised controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Acute myocardial infarction

Interventions
Patients presenting with acute myocardial infarction randomised to received an intravenous infusion of etanercept (10 mg) or saline placebo over 30 minutes.

Intervention Type
Drug

Phase
Phase II

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

Primary outcome(s)
Platelet monocyte aggregation, peripheral vasomotor and fibrinolytic function at baseline and again 24 hours later

Key secondary outcome(s))
Leukocyte count and plasma cytokine concentrations at baseline and again 24 hours later

Completion date
01/08/2009

Eligibility

Key inclusion criteria
1. A typical history of myocardial ischaemia lasting more than 20 minutes within 24 hours prior to admission

2. An elevated troponin I(>0.1µg/L) and/or electrocardiographic changes
3. Age ≥18 years of age, either sex
4. Screening full blood count (FBC) must meet the following criteria: healmoglobin (Hb) > 85g/L, white cell count (WCC) > 3.5 x 109/L, neutrophils > 1.5 x 109/L, platelets > 100 x 109/L
5. Subjects must be able to adhere to the study visit schedule and other protocol requirements
6. The subject must be capable of giving informed consent and the consent must be obtained prior to screening procedures

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Women of child bearing potential
2. Systolic blood pressure >190mmHg or <100mmHg
3. Malignant arrhythmias
4. Renal or hepatic failure
5. Severe or significant co-morbidity
6. Previous history of blood dyscrasia
7. Unable to tolerate the supine position
8. Opportunistic infection within the previous 6 months, human immunodeficiency virus, serious infection within the previous 2 months, chronic/recurrent infection
9. A history of malignancy within the previous 5 years, lymphoproliferative disease, or multiple sclerosis/ other demyelinating disorder
10. Patients with diabetes mellitus (type 1 or insulin-dependent)
11. Patients with systemic inflammatory disorder
12. Use of any investigational drug within 1 month prior to screening or within five half-lives of investigational agent, whichever is longer
13. Treatment with any other therapeutic agent targeted at reducing TNF (e...g pentoxifylline, thalidomide, etanercept etc) within 3 months of screening
14. Known recent substance abuse (drugs or alcohol)
15. Poor tolerability of venepuncture or lack of adequate venous access for required blood sampling during the study period

Date of first enrolment
01/05/2003

Date of final enrolment
01/08/2009

Locations

Countries of recruitment
United Kingdom

Scotland

Study participating centre
University of Edinburgh
Edinburgh
United Kingdom
EH16 4SU

Sponsor information

Organisation
University of Edinburgh (UK)

ROR
https://ror.org/01nrxwf90

Funder(s)

Funder type
Charity

Funder Name
British Heart Foundation (UK)

Alternative Name(s)
the_bhf, The British Heart Foundation, BHF

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

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	results	01/09/2013		Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes