ISRCTN25048895 https://doi.org/10.1186/ISRCTN25048895

Can an interleukin-1 receptor antagonist reduce inflammation following subarachnoid haemorrhage?

Submission date
12/05/2011

Recruitment status
No longer recruiting

Registration date
28/06/2011

Overall study status
Completed

Last Edited
25/05/2018

Condition category
Circulatory System

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

Plain English summary of protocol

Background and study aims
A subarachnoid haemorrhage (SAH) occurs when there is uncontrolled bleeding into the space surrounding the brain. The majority of SAH are caused when a bulging blood vessel in the brain bursts. The pooling of blood puts pressure on the brain, quickly leading to unconsciousness. A common complication of a SAH is where the arteries supplying the brain close up (vasospasm), causing the brain to become starved of oxygen. This often happens 3-10 days after the SAH and is known as delayed cerebral ischaemia (DCI). DCI is the most common cause of permanent disability and death after SAH, and so its prevention is a very important part of SAH treatment. Recent studies have shown that the chemicals in the blood responsible for inflammation such as interleukin-1 (IL-1) could be causing the vasospasm by irritating blood vessels. In the body, the action of IL-1 is blocked by a naturally occurring anti-inflammatory called interleukin1 receptor antagonist (IL1Ra). Drugs containing a manufactured version of IL-1Ra are used to treat diseases relating to inflammation, such as arthritis. One of these drugs which has been successful is Kineret. The aim of this study is to find out whether Kineret can reduce the amount of IL-1 in the body, and if this can help to prevent DCI.

Who can participate?
Adults who have had an acute subarachnoid haemorrhage within the past 72 hours.

What does the study involve?
Participants are randomly allocated into two groups. Those in the first group receive an injection of Kineret twice a day for up to 21 days after the SAH. Those in the second group do not receive any Kineret injections throughout the study period. Chemical indicators of inflammation (including IL-1) are measured using blood tests at the start of the study, then daily for 8 days and then again at days 14 and 21.

What are the possible benefits and risks of participating?
Not provided at time of registration

Where is the study run from?
Salford Royal Hospital (UK)

When is the study starting and how long is it expected to run for?
October 2011 to April 2014

Who is funding the study?
Medical Research Council (UK)

Who is the main contact?
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Contact information

Type(s)
Scientific

Contact name
Prof Pippa Tyrrell

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Additional identifiers

Clinical Trials Information System (CTIS)
2011-001855-35

Protocol serial number
MRC Ref: G1001252

Study information

Scientific Title
Does a subcutaneous interleukin-1 receptor antagonist reduce inflammation following subarachnoid haemorrhage?

Acronym
SC IL-1Ra in aSAH

Study objectives
A subcutaneous interleukin-1 receptor antagonist will reduce inflammation in patients with acute cerebrovascular disease and hence will subsequently improve outcome.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Full study R&D approval given on 14/09/2011, REC Ref: 11/NW/0390

Study design
Multi-centre single-blind open-label randomised controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Subarachnoid haemorrhage

Interventions
Current interventions as of 15/07/2013:
1. Study is a single-blind, open-label, randomised control trial of 140 patients. To be eligible to receive the drug, they must be within 72 hours of aneurysmal subarachnoid haemorrhage (aSAH), recruited from Salford Royal NHS Foundation Trust, The Walton Centre for Neurology and Neurosurgery and University Hospital North Staffordshire
2. Participants will be randomised to study treatment (IL-1Ra; Kineret®) or no study treatment
3. Participants will be stratified depending on time since ictus
4. Participants in treatment group will receive twice-daily (bd), subcutaneously administered IL-1Ra for maximum of 21 days post ictus (or discharge from study centre)
5. Baseline blood sample/assessment will be obtained following consent and prior to administration of study medication
6. Blood samples/assessments will be obtained daily to 8 days from ictus
7. Further blood samples/assessments will be obtained at days 14 and 21 from ictus unless discharged from study centre
8. Analysis of blood samples will measure the effect of IL-1Ra on inflammatory markers (including IL-6 and CRP)
9. Safety data will be obtained throughout in-patient stay and at 30 day telephone contact 10. Six month outcome data will be obtained by telephone Glasgow Outcome Score

Previous interventions:
1. Study is a single-blind, open-label, randomised control trial of 140 patients, who are eligible to receive drug within 72 hours of aneurysmal subarachnoid haemorrhage (aSAH) recruited to Greater Manchester Neuroscience Centre
2. Participants will be randomised to study treatment (IL-1Ra; Kineret®) or no study treatment
3. Participants will be stratified depending on time since ictus
4. Participants in treatment group will receive twice-daily (bd), subcutaneously administered IL-1Ra for maximum of 21 days post ictus (or discharge from study centre)
5. Baseline blood sample/assessment will be obtained following consent and prior to

administration of study medication
6. Blood samples/assessments will be obtained daily to 8 days from ictus
7. Further blood samples/assessments will be obtained at days 14 and 21 from ictus unless discharged from study centre
8. Analysis of blood samples will measure the effect of IL-1Ra on inflammatory markers (including IL-6 and CRP)
9. Safety data will be obtained throughout in-patient stay and at 30 day telephone contact 10. Six month outcome data will be obtained by telephone Glasgow Outcome Score

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Kineret®

Primary outcome(s)
To determine the effect of SC IL-1Ra on plasma IL-6 concentration from day 3 8 following ictus

Key secondary outcome(s))
1. To determine the effect of SC IL-1Ra on other plasma inflammatory markers on days 3 to 8 following the ictus of aSAH
2. To determine the effect of SC IL-1Ra on plasma inflammatory markers on day 14 and 21 following aSAH
3. To determine the effect of SC IL-1Ra on clinical outcome (Glasgow Outcome Score [GOS], modified Rankin Score [mRS], DCI [Delayed Cerebral Ischaemia] incidence, mortality) following aSAH
4. To obtain further feasibility and safety data in patients given SC IL-1Ra

Completion date
30/04/2014

Eligibility

Key inclusion criteria
1. Patients with confirmed spontaneous aSAH who are admitted to our neurosurgical department at SRFT where consent can be obtained and drug administered within 72 hours
2. No concomitant health problems that, in the opinion of the Principal Investigator (PI) or designee, would interfere with participation, administration of study treatment or assessment of outcomes including safety, for example, pre-existing malignancy
3. Renal function within normal limits (< 177 µmol/l)
4. Willing and able to give informed consent or consent available from a patient representative (personal) for study inclusion including agreement in principle to receive study intervention and undergo all study assessments
5. Aged 18 years or above

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Unconfirmed or uncertain diagnosis of spontaneous aSAH
2. Known or suspected infection in the preceding 2 weeks or at the time of consideration for the study
3. Known allergy to E. coli or any of the constituents of the study medication as established from the patient themselves, reliable representative and clinical records
4. Previous or concurrent treatment with recombinant IL-1Ra known at the time of study entry
5. Previous or current treatment with medication suspected of interacting with recombinant IL-1Ra, such as TNF-a inhibitors
6. Known to have participated in a clinical trial of an investigational agent or device in the previous 30 days or for the period determined by the protocol of the study the patient has taken part in
7. Known or planned pregnancy (pregnancy test to be performed in women of child-bearing potential) or breast-feeding
8. Clinically significant concurrent medical condition, at the PIs (or designees) discretion, which could affect the safety, tolerability, or efficacy in this study
9. Previous inclusion in the current study (known prior to inclusion).
10. Inability or unwillingness of patient or patients personal representative to give written informed consent
11. Likely to be transferred from the centre within eight days of admission

Date of first enrolment
01/10/2011

Date of final enrolment
30/04/2014

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Greater Manchester Neuroscience Centre and University of Manchester
Salford

United Kingdom
M6 8HD

Sponsor information

Organisation
Salford Royal NHS Foundation Trust (UK)

ROR
https://ror.org/019j78370

Funder(s)

Funder type
Research council

Funder Name
Medical Research Council (United Kingdom) (Grant ref: G1001252)

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, Medical Research Committee and Advisory Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

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	01/02/2018		Yes	No
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Study website	Study website	11/11/2025	11/11/2025	No	Yes