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The effect of Kineret® on brain biomarkers in patients with subarachnoid haemorrhage

Submission date
06/11/2008

Recruitment status
No longer recruiting

Registration date
18/12/2008

Overall study status
Completed

Last Edited
21/04/2020

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 spontaneous subarachnoid haemorrhage (SAH) is a serious medical condition caused by sudden bleeding over the surface of the brain. It is most often caused when a bulge in a blood vessel wall (brain aneurysm) bursts (ruptures) because the vessel wall has become weakened over time. Following rupture blood pools inside the skull (which cannot expand due to its rigid structure) leading to pressure on the brain and starving it of oxygen (cerebral ischaemia) causing further brain damage. To treat this, a hole is usually drilled into the skull and a tube (external ventricular drain) is placed inside so that the collected blood can escape, lowering pressure on the brain. When a person sustains a severe injury chemicals are released in the body to help start the healing process, such as the protein Interleukin–1 (IL–1) which triggers inflammation (swelling). Studies have shown that IL-1 actually contributes to the damage caused cerebral ischaemia. Kineret® is a drug which acts by blocking the action of IL-1. The aim of this study is to find out whether Kineret® can change the concentration of the inflammatory biomarkers (natural chemical indictors of inflammation) in the blood and cerebral spinal fluid (fluid that cushions the brain).

Who can participate?
Patients aged 16 years or over who have had a spontaneous subarachnoid haemorrhage (SAH) and have had an external ventricular drain (EVD) fitted.

What does the study involve?
Participants are randomly allocated to one of two groups. Those in the first group are a bolus (one-off large dose) injection of 500mg Kineret® into a vein (IV) over 1 minute. Immediately afterwards, the participants are started on a drip (infusion) of Kineret® which is given slowly, over 24 hours. Those in the second group are given a blous injection of a placebo (dummy) over one minute, followed by an infusion of saline (salt water) and placebo (dummy) over 24 hours. Participants in both groups have samples of blood and cerebral spinal fluid (CFS) taken at the start of the study and then after 6, 12, 24, 36, 48 and 72 hours in order to measure the concentration of the chemical indicators of inflammation (inflammatory biomarkers).

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

Where is the study run from?
Brain Injury Research Group, Salford Royal NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
June 2009 to April 2010

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

Who is the main contact?
Dr Pippa Tyrell
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Study website
http://www.hope-academic.org.uk/misah/Study2.html

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
2007-005836-98

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
MRC ref: G0502030; Protocol version 2 16-07-2008

Study information

Scientific Title
The effect of Kineret® on brain biomarkers in patients with subarachnoid haemorrhage: Double-blind randomised placebo-controlled trial

Study objectives
The presence of Kineret® in the cerebrospinal fluid (CSF) at concentrations that have been shown to be experimentally therapeutic decrease concentrations of inflammatory biomarkers in the CNS.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Added 05/06/2009: Wales REC approved on the 29th January 2009 (ref: 09/MRE09/1)

Study design
Single-centre double-blind randomised placebo-controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

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

Interventions
The study is a double-blind randomised controlled trial of Kineret® with participants with an external ventricular drain (EVD) inserted as part of their clinical care. Participants will be randomised to receive a regime of 500 mg bolus dose plus a 10 mg/kg/h intravenous infusion for 24 hours of Kineret® or placebo, which has been identified from a previous pharmacokinetic dose-finding study. Blood and CSF will be taken immediately prior to bolus dose of IMP/placebo (baseline); and at 6, 12 and 24 hours (during period of infusion) and then at 36, 48 and 72 hours (from time of bolus injection). A final sample will be obtained at Day 7 (study end) if the participant still has an EVD in-situ. Analysis of these samples will show the effect of Kineret® on inflammatory markers and allow the concentration of the markers to be measured.

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Interleukin-1 (IL-1), (Kineret®)

Primary outcome measure
To determine whether intravenously administered Kineret® causes a decrease in the concentration of central inflammatory biomarkers in the blood and CSF samples following SAH compared to placebo. The following markers will be assessed: C-reactive protein (CRP), IL-1RA, IL-1a, IL-1ß, IL-6, IL-8, IL-10

Blood and CSF samples will be taken immediately prior to bolus dose of IMP/placebo (baseline); and at 6, 12 and 24 hours (during period of infusion) and then at 36, 48 and 72 hours (from time of bolus injection). A final sample will be obtained at Day 7 (study end) if the participant still has an EVD in-situ.

Secondary outcome measures
No secondary outcome measures

Overall study start date
01/06/2009

Completion date
30/04/2010

Eligibility

Key inclusion criteria
1. Both males and females, aged 16 years or above
2. Patients with confirmed spontaneous subarachnoid haemorrhage (SAH) who have had an external ventricular drain (EVD) inserted as part of their clinical care
3. No concomitant health problems that, in the opinion of the Principal Investigator or Chief Investigator or designee, would interfere with participation, administration of study treatment or assessment of outcomes including safety, for example, pre-existing malignancy
4. No confirmed or suspected serious infection at the time of study entry
5. Renal function within normal limits (serum creatinine <177 µmol/l)
6. Willing and able to give informed consent or consent available from a patient representative (personal, usually the next of kin) for study inclusion including agreement in principle to receive study intervention and undergo all study assessments

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
32

Total final enrolment
18

Key exclusion criteria
1. Known or suspected infection at the time of consideration for the study
2. 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
3. Previous or concurrent treatment with anakinra or Kineret®; known at the time of study entry
4. Previous or current treatment with medication suspected of interacting with Kineret®, such as TNF-á inhibitors
5. Evidence of serious infection
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 pregnancy or breast-feeding
8. Clinically significant concurrent medical condition, which in the Chief Investigator's (or designee's) discretion, could affect the safety, tolerability, or efficacy in this study
9. Previous inclusion in current study (known prior to inclusion)
10. Inability or unwillingness of patient or patient's personal representative to give written informed consent

Date of first enrolment
01/06/2009

Date of final enrolment
30/04/2010

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Brain Injury Research Group
Salford Royal NHS Foundation Trust
Salford
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M6 8HD

Sponsor information

Organisation
Salford Royal Hospitals NHS Trust (UK)

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Research and Development Directorate
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lloyd.gregory@manchester.ac.uk

Sponsor type
Hospital/treatment centre

Website
http://www.hope-academic.org.uk/Academic/researchdevelopment/

ROR
https://ror.org/019j78370

Funder(s)

Funder type
Government

Funder Name
Medical Research Council (UK) (Grant ref: G0502030)

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

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Not provided at time of registration.

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results			21/04/2020	No	No
Results article	results	01/02/2016	21/04/2020	Yes	No
HRA research summary			28/06/2023	No	No