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Subcutaneous interleukin-1 receptor antagonist (SC IL-1RA) in Stroke Study

Submission date
22/07/2013

Recruitment status
No longer recruiting

Registration date
22/07/2013

Overall study status
Completed

Last Edited
21/05/2019

Condition category
Nervous System Diseases

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

Plain English summary of protocol

Background and study aims
A stroke is a serious condition where the blood supply to a part of the brain is cut off, usually by a blood clot blocking an artery (ischaemic stroke) or a bleed (haemorrhagic stroke). A large proportion of stroke victims suffer from long-term complications depending on the area of the brain that is affected, which can affect their ability to move, speak or even their cognitive function (memory loss, difficulty reasoning and confusion). When a person sustains a severe injury chemicals are released in the body to help start the healing process and trigger inflammation (inflammatory biomarkers). Following a stroke, patients have abnormally high levels of inflammatory biomarkers in their blood and brain, including the protein interleukin-1 (IL-1). Increased inflammation is associated with more severe brain damage and the patient is more likely to die or be severely disabled. Interleukin-1 receptor antagonists (IL-1Ra) are drugs which work by blocking the action of IL-1 to reduce inflammation. IL-1Ra is currently licensed as a treatment for rheumatoid arthritis and given to patients via injections under the skin. The aim of this study is to find out if skin injections of IL-1Ra will also work to reduce inflammation after stroke.

Who can participate?
Adults who have had a stroke but are otherwise healthy

What does the study involve?
Participants are randomly allocated to receive twice daily injections of either IL-1Ra or a placebo (dummy drug). The first injection is given within 6 hours of stroke with five further doses given at 12 hourly intervals for 3 days (six injections in total). All participants receive standard care for ischaemic stroke, including treatment to dissolve the blood clot (thrombolysis), if needed. Blood samples are taken at the start of the study. Participants undergo assessments, together with four further blood samples for measurement of inflammatory biomarkers at multiple times over 57 days, to determine whether IL-1Ra causes a decrease in the level of inflammatory biomarkers in the blood within 3 days after stroke and also 57 days after. Participants' level of disability and length of hospital stay are assessed at 1 and 3 months. Safety data on all participants is collected throughout the study.

What are the possible benefits and risks of participating?
There are no benefits expected from taking part. Risks include those associated with the drug being tested (IL-1Ra). The participant information sheets explain the side-effects relate to it being given as a treatment for rheumatoid arthritis, when it is given for a long time (months or years). The drug is only given for a very short time in this study (3 days). In studies that have given the drug over short periods (for severe infections, subarachnoid haemorrhage or stroke) there has been no evidence of increased infections. However, studies in patients with rheumatoid arthritis who have been on long term treatment have shown a small possibility of an increased risk of infections, some of which were classed as serious. Previous studies also showed that after long-term use of the drug, the body may make antibodies to the drug, with a possible risk of allergy to the drug. This is a rare but potentially serious side-effect. Participants are advised that If they think they may have received this drug or a similar drug, either as part of their general care or as part of another study, they should discuss this with the researcher but they may be excluded from taking part in this study. Some patients also experience a slight skin reaction following injection of the drug. These small red patches usually occur when the drug is given for longer periods e.g. more than 3 days. In the unlikely event this should occur, the participant is given the option to withdraw or to continue and receive the full six injections. The participant is also advised that they may experience some discomfort and bruising as a result of the blood sampling. Researchers try to collect research blood samples at the same time as blood is taken for normal clinical purposes, to reduce discomfort.

Where is the study run from?
Salford Royal NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
March 2015 to October 2016

Who is funding the study?
Stroke Association (UK)

Who is the main contact?
Mrs Sharon Hulme
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Contact information

Type(s)
Scientific

Contact name
Mrs Sharon Hulme

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Additional identifiers

Protocol serial number
14764

Study information

Scientific Title
Does subcutaneous interleukin-1 receptor antagonist reduce inflammation after ischaemic stroke compared to placebo? (SC IL-1Ra in Stroke study)

Acronym
SC IL-1RA in Stroke Study

Study objectives
The aim of this study is to investigate whether skin injections of IL-1Ra twice a day for 3 days will reduce inflammation in the blood of stroke patients.

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES Committee North West - Greater Manchester South, 26/9/2013, ref: 13/NW/0460

Study design
Randomised interventional trial; Design type: Treatment

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Topic: Stroke Research Network; Subtopic: Acute Care; Disease: In hospital study

Interventions
Participants will receive twice daily, SC injections of either Kineret© or placebo.

Added 06/04/2017:
Participants will be randomised to subcutaneous administered of Kineret (anakinra) or placebo by a third-party, web-based computerised system. All participants will receive the first dose of study treatment (Kineret or placebo) within 6 hours of stroke onset. Five further doses will be given at 12 hourly intervals; a total of 6 injections over 72 hours. A blood sample will be obtained prior to randomisation and this will be repeated at 7am on the following 3 days. This will be used to measure levels of inflammation in the blood. Participation in the study will not delay clinical care or discharge from the hospital. All participants will be contacted by telephone at 30 days

post-stroke, to check for adverse events and at 3 months post-stroke to measure recovery or level of ability using a standard questionnaire called modified Rankin Scale. This will complete study participation.

Intervention Type
Drug

Phase
Phase II

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

Primary outcome(s)
Current primary outcome measures as of 06/04/2017:
Level of IL6, using ELISA within 3 days of stroke onset

Previous primary outcome measures:
Reduction in inflammatory biomarkers; Timepoints: Between 6 hours and 5-7 days post stroke

Key secondary outcome(s))
Added 06/04/2017:
1. Levels of other inflammatory markers, measured using ELISA or Luminex at within 3 days of stroke onset
2. Clinical outcome at 3 months following ischaemic stroke, measured using:
2.1. The National Institutes of Health Stroke Scale, or NIH Stroke Scale (NIHSS)
2.2. The modified Rankin Score (mRS)
2.3. Survival (mortality) , measured using hospital records
2.4. Length of hospital stay (LOS), measured using a telephone survey

Completion date
28/02/2017

Eligibility

Key inclusion criteria
1. Patients with confirmed ischaemic stroke who are admitted to the Comprehensive Stroke Centre at Salford Royal NHS Foundation Trust (SRFT) where consent can be obtained and drug administered within 6 hours
2. National Institutes of Health stroke scale (NIHSS) score between 4-26
3. 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, preexisting malignancy
4. Renal function within normal limits (< 177 µmol/l)
5. Willing and able to give informed consent or consent available from a patient representative (personallegal) for study inclusion including agreement in principle to receive study intervention and undergo all study assessments
6. Aged 18 years or above

Healthy volunteers (recruited to provide a one-off 20ml blood sample only)
1. Between 18 and 80 years, in good health

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
80

Key exclusion criteria
Patient group:
1. Unconfirmed or uncertain diagnosis of ischaemic stroke or rapid improving symptoms
2. Haemorrhagic stroke
3. NIHSS <4 or >26
4. 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
5. Previous or concurrent treatment with recombinant IL1Ra known at the time of study entry
6. Previous or current treatment with medication suspected of interacting with recombinant IL1Ra, such as TNFa inhibitors
7. 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
8. Known or planned pregnancy (pregnancy test to be performed in women of childbearing potential) or breastfeeding
9. Clinically significant concurrent medical condition, at the PIs (or designees) discretion, which could affect the safety, tolerability, or efficacy in this study
10. Previous inclusion in the current study (known prior to inclusion)
11. Evidence of current infection or infection within the past 4 wk
12. Inability or unwillingness of patient or patients personal representative to give written informed consent

Healthy volunteers (recruited to provide a oneoff 20ml blood sample only)
1. Current acute medical problems or taking medication for chronic conditions

Date of first enrolment
01/11/2013

Date of final enrolment
30/04/2016

Locations

Countries of recruitment

United Kingdom

England

Study participating centre
Hope Hospital
Salford
United Kingdom
M6 8HD

Sponsor information

Organisation
Salford Royal NHS Foundation Trust

ROR
https://ror.org/019j78370

Funder(s)

Funder type
Charity

Funder Name
Stroke Association (UK)

Alternative Name(s)
TheStrokeAssociation, TheStrokeAssoc

Funding Body Type
Private sector organisation

Funding Body Subtype
Associations and societies (private and public)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are/will be available upon request from Prof. Craig Smith. Anonymised individual-level data will be available from 01 /09/2018 for 15 years on request for legitimate, public sector researchers for statistical analysis compatible with the consent process by electronic transfer within the EU. Consent from participants was obtained. No specific dates or other data that could potentially identify individuals. Data is subject to EU and UK data protection legislation and archived subject to standard operating procedures at Salford Royal NHS Foundation Trust.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/05/2018		Yes	No
HRA research summary			28/06/2023	No	No