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Imaging cerebral neuro-inflammation in acute and chronic cerebrovascular disease: a predictor of outcome and biomarker for guiding treatment (IN-CVD)

Submission date
15/04/2015

Recruitment status
No longer recruiting

Registration date
20/07/2015

Overall study status
Completed

Last Edited
10/05/2021

Condition category
Circulatory System

[_] 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, life-threatening medical condition that occurs when the blood supply to part of the brain is cut off, which can result in tissue damage. In order to predict the extent of injury and symptoms, we must take into account the severity and length of time for which the blood supply is reduced. However, recent studies have shown that the inflammation surrounding the damaged area may also add to the extent of injury and following symptoms. We can measure the inflammation in the brain shortly after a patient has had a stroke using an imaging method called positron emission tomography (PET). PET scans produce detailed three-dimensional images of the inside of the body by detecting the radiation given off by a substance called a radiotracer that is injected into the blood stream. Brain damage and inflammation causes an increase in translocator protein (TSPO) due to the responding microglial cells in the brain. A new radiotracer, [18F]GE180, can be used to detect levels of TSPO. It is anticipated that the new radiotracer will help to identify the swollen areas in the brain, meaning that we will be able to identify the amount of swelling around the damaged tissue. This study aims to evaluate the association between microglial cell activation and the outcome in stroke patients.

Who can participate?
Adult stroke patients.

What does the study involve?
During the first year of the study, we will compare the new radiotracer [18F]GE180 with another conventional radiotracer called [11C]-R-PK11195. This will allow us to confirm that the new radiotracer will be tolerable for the patients and that it will produce clear images. Once we have compared the two radiotracers, we continue the study using the new radiotracer only. The results of the PET scans will be compared to the overall injury caused by the stroke (measured by physical examinations at 3 months after the stroke). We aim to use this comparison as a predictor for the long-term effects of stroke.

What are the possible benefits and risks of participating?
This study will not impact on the patients' standard health care and the results will not be used to assist treatment.

Where is the study run from?
Manchester Academic Health Science Centre (UK).

When is the study starting and how long is it expected to run for?
From May 2015 to November 2017.

Who is funding the study?
The Christie NHS Foundation Trust (UK).

Who is the main contact?
Dr Rebecca Robinson

Contact information

Type(s)
Scientific

Contact name
Dr Rebecca Robinson

Contact details
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Additional identifiers

EudraCT/CTIS number
2014-000591-26

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
18820

Study information

Scientific Title
Imaging cerebral neuro-inflammation in acute and chronic cerebrovascular disease: a predictor of outcome and biomarker for guiding treatment (IN-CVD)

Acronym

IN-CVD

Study objectives
Acute stroke is part of the spectrum of cerebrovascular disease (CVD). Inflammation occurs around the damaged tissue and blood vessels which can increase the severity of stroke. Microglial cells are an important type of cell that have several functions in supporting nerve cells, including regulating the inflammatory response in the brain. The brain damage and inflammation means that there is an increase in translocator protein (TSPO) due to the responding microglial cells. This study aims to evaluate the association between microglia activation and the outcome in stroke patients. PET (positron emission tomography) can be used to image the inflammation in the brain. This is done by using an imaging agent that binds to the TSPO. [18F]GE180 is a newly developed imaging agent with good selectivity for TSPO.

More details can be found here: http://public.ukcrn.org.uk/Search/StudyDetail.aspx?StudyID=18820

Ethics approval required
Old ethics approval format

Ethics approval(s)
Liverpool Central NRES Committee North West, 03/03/2015, ref: 15/NW/0032

Study design
Study Type: Observational; Design type: Cohort study

Primary study design
Observational

Secondary study design
Cohort study

Study setting(s)
Hospital

Study type(s)
Diagnostic

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
Topic: Stroke; Subtopic: Prevention; Disease: In hospital study

Interventions
The first year of the trial (phase 1) will be dedicated to assessing the technical feasibility, and comparing the new imaging agent ([18F]GE180) with an existing agent ([11C](R)PK11195). It is hoped that the agents are technically comparable. [11C](R)PK11195 is unable to be used in routine clinics due to the reduced halflife (20 minutes), which is too short to allow routine clinical procedures but the new agent has a halflife of 110 minutes, which would be able to be used in clinics.

Assuming phase 1 of the study is successful the study can progress to phase 2 (on approval by the IDMC). In phase 2 of the study, patients will only have a PET scan using the new agent imaging. Data will be collected on a further 40 patients, ensuring that by the end of the trial there will be data on 50 stroke patients. The data from the entire study will be used to identify the microglial activation and determine if a correlation between with clinical outcome and inflammation can be demonstrated.

Intervention Type
Other

Phase
Phase II

Primary outcome measure
Correlation between inflammation and the clinical outcome at 3 months after having a stroke. The clinical outcome is measured using the National Institutes of Health Stroke Scale Assessment (NIHSS), and the Modified Rankin Scale Assessment (mRS). These will be able to determine the extent of injury caused by the stroke.

Secondary outcome measures
Tolerability of the [18F]GE-180 scan as assessed by a patient-completed questionnaire asked at the end of the scans.

Overall study start date
01/05/2015

Completion date
01/12/2019

Eligibility

Key inclusion criteria
1. Ischemic stroke in middle cerebral artery territory
2. Mild to moderate severity (Modified Rankin Scale score 2 or 3)

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
Planned Sample Size: 50; UK Sample Size: 50

Total final enrolment
10

Key exclusion criteria
1. Neurological diagnosis of neurodegenerative disease
2. Inability to understand study information and/or express willingness to consent to the study due to communication difficulties (patients that wish to consent but are unable to sign or mark the consent form due to mobility issues may give their consent orally in the presence of at least one witness, who must sign the consent form as evidence that the information was accurately explained to and understood by the subject and that consent was freely given)
3. History of brain surgery, brain tumour, neuroinflammatory or neurodegenerative disease
4. Severe uncontrolled systemic illness
5. Patients in whom carotid endarterectomy/carotid stenting is due to be carried out within three months of recruitment to the study
6. Treatment with other drugs known to influence microglial activation, e.g. minocycline or cortical steroids (2 weeks prior to date of stroke)
7. Pregnancy
8. Contraindications to MRI scanning

Date of first enrolment
01/06/2015

Date of final enrolment
01/12/2018

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
MAHSC CTU
550 Wilmslow Road
Manchester
United Kingdom
M20 4BX

Study participating centre
Salford Royal Foundation Trust
United Kingdom
M6 8HD

Sponsor information

Organisation
The Christie NHS Foundation Trust

Sponsor details
Christie Hospital
550 Wilmslow Road
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England
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M20 4BX

Sponsor type
Hospital/treatment centre

ROR
https://ror.org/03v9efr22

Funder(s)

Funder type
Government

Funder Name
NIHR Efficacy and Mechanism Evaluation Programme (UK)

Results and Publications

Publication and dissemination plan
To be confirmed at a later date

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		01/02/2020	10/05/2021	Yes	No
HRA research summary			28/06/2023	No	No