

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	☐ Prospectively registered ☐ Protocol
Registration date 20/07/2015	Overall study status Completed	☐ Statistical analysis plan ☒ Results
Last Edited 10/05/2021	Condition category Circulatory System	☐ 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

MAHSC CTU
550 Wilmslow Road
Manchester
United Kingdom
M20 4BX

Additional identifiers

Clinical Trials Information System (CTIS)

2014-000591-26

Protocol serial number

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

Primary study design

Observational

Study design

Study Type: Observational; Design type: Cohort study

Study type(s)

Diagnostic

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(s)

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.

Key secondary outcome(s)

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

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

Healthy volunteers allowed

No

Age group

Adult

Sex

All

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

United Kingdom

England

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

ROR

<https://ror.org/03v9efr22>

Funder(s)

Funder type

Government

Funder Name

NIHR Efficacy and Mechanism Evaluation Programme (UK)

Results and Publications

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