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CLArithromycin for post-Stroke Pneumonia

Submission date
18/12/2024

Recruitment status
Recruiting

Registration date
14/03/2025

Overall study status
Ongoing

Last Edited
18/03/2025

Condition category
Respiratory

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
We want to find out if treatment with an antibiotic called clarithromycin, which might have additional effects such as reducing harmful inflammation in the lungs, can improve outcomes for people with a stroke who get a serious chest infection (pneumonia).
Around 100,000 people in the UK have a stroke each year. Pneumonia occurs in about 1 in 10 of these people in the first week after stroke. Pneumonia causes harmful inflammation in the lungs and is associated with much worse recovery, higher death rates and increased healthcare costs. How to prevent and treat pneumonia has been identified as a priority by people living with stroke.
Clarithromycin is currently only added to antibiotic treatment in around 1 in 10 people with pneumonia after a stroke. Previous research has suggested including clarithromycin might be beneficial for people who develop pneumonia after stroke. Clarithromycin has been used in clinical practice as an antibiotic for many years and the side-effects and drug interactions are well characterised.

Who can participate?
We aim to recruit 1166 patients from 45 hospital sites across the UK, within 7 days of admission for stroke who have developed pneumonia and will be started on antibiotic treatment that does not include clarithromycin.

What does the study involve?
Participants will be divided randomly into one of two groups: usual antibiotic therapy where clarithromycin is not included, or usual antibiotic therapy plus clarithromycin.
We will assess whether adding clarithromycin improves recovery from the stroke and pneumonia. We will also assess whether clarithromycin treatment affects mortality, quality of life, time spent at home, caregiver burden, readmission to hospital, recurrent strokes and healthcare costs. Safety of clarithromycin and total number of antibiotic doses will also be recorded.
Participation will last for approximately 90 days after enrolment in the trial.
This trial will tell us whether we should change practice in the NHS to include clarithromycin for the treatment of people who develop pneumonia soon after their stroke.

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

Where is the study run from?
NHS Greater Glasgow and Clyde (UK)
University of Glasgow (UK)

When is the study starting and how long is it expected to run for?
December 2024 to August 2029

Who is funding the study?
National Institute for Health and Care Research (NIHR) (UK).

Who is the main contact?
Prof. Craig J Smith, Craig.Smith-2@manchester.ac.uk

Contact information

Type(s)
Public, Scientific, Principal investigator

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
1009744

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
GN22ST525

Study information

Scientific Title
CLArithromycin for post-Stroke Pneumonia: A prospective, randomised open-label blinded-endpoint (PROBE) phase 3 multicentre trial

Acronym
CLASP

Study objectives
The primary objective of the trial is to determine whether 5 days of treatment with clarithromycin in addition to usual non-macrolide antibiotic treatment for Post Stroke Pneumonia improves patient outcomes at 90 days after stroke in comparison to usual antibiotic treatment.
This trial also seeks to determine whether 5 days of treatment with clarithromycin in addition to usual non-macrolide antibiotic treatment for Post Stroke Pneumonia:
• Reduces mortality at 90 days
• Increases home time by 90 days
• Reduces cardiovascular mortality at 90 days
• Reduces urgent or unplanned readmissions at 90 days
• Reduces recurrent stroke at 90 days
• Reduces major cardiovascular events at 90 days
• Improves quality of life at 90 days
• Improves stroke-related health status at 90 days
• Reduces caregiver burden at 90 days
• Is safe
• Is cost-effective from the perspective of NHS England

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 06/03/2025, Scotland A Research Ethics Committee (South East Scotland Research Ethics Service, Mainpoint, 102 Westport, Edinburgh, EH3 9ND, United Kingdom; +44 7814609032; Manx.Neill@nhs.scot), ref: 25/SS/0006

Study design
Interventional randomized parallel group controlled trial

Primary study design
Interventional

Study type(s)
Safety, Efficacy

Health condition(s) or problem(s) studied
Post Stroke Pneumonia

Interventions
Consented participants will be allocated to either the treatment arm or usual care in a 1:1 ratio via a web-based interface integrated into the electronic Case Report Form (eCRF).
• Intervention arm: Clarithromycin 500mg twice daily for 5 days total (route of administration will be determined by the local clinical team based on clinical condition and availability of route of administration in line with local policy) in addition to usual non-macrolide antibiotic treatment.
• Usual care: Local stroke unit usual non-macrolide antibiotic treatment.

All participants will be followed up at Day 7 (safety, intervention doses administered, other antibiotics administered, vital signs, examination findings, provision of contact details for follow-up) and Day 90 (remote collection of data required for outcomes).

Intervention Type
Drug

Phase
Phase III

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

Primary outcome(s)
Functional outcome is measured using the modified Rankin Scale (mRS) at Day 90

Key secondary outcome(s))
1. Mortality is measured using all-cause mortality at 90 days
2. Home time is measured using days spent in pre-admission usual place of residence at 90 days
3. Cardiovascular mortality is measured using cardiovascular mortality at 90 days
4. Urgent or unplanned readmissions is measured using non-elective admissions by 90 days
5. Recurrent stroke is measured using stroke at 90 days
6. Major cardiovascular events is measured using major cardiovascular events at 90 days
7. Quality of life is measured using EQ-5D-5L at baseline and 90 days
8. Stroke-related health status is measured using the Stroke Impact Scale (SIS) at 90 days
9. Caregiver burden is measured using the Zarit Caregiver Burden (ZBI-12) interview at 90 days
10. Safety is measured using Clostridioides difficile infection within 90 days and ventricular arrhythmia within 7 days
11. Cost-effectiveness is measured using health and social care resource use at baseline and up to 90 days.

Completion date
31/08/2029

Eligibility

Key inclusion criteria
1. Age ≥18 years
2. Acute stroke (ischaemic stroke or intracerebral haemorrhage [ICH]) within the past 14 days
3. Starting (or within 24 hours of starting) non-macrolide antibiotics for a new diagnosis of PSP
4. Written informed consent from participant or from Next of Kin / designated representative or consultee or Independent Physician if lacks capacity (by phone if required)
5. Women of childbearing potential must have a negative highly sensitive serum (beta-human chorionic gonadotropin [beta-hCG]) or urine test at screening

Participant type(s)
Patient

Healthy volunteers allowed

No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Requirement for macrolide therapy as usual care
2. Confirmed respiratory viral infection (e.g. COVID-19, influenza) at point of screening
3. Known antibiotic treatment for chest infection or pneumonia within the last two weeks (single doses or less than 3 days of treatment is allowed)
4. Known toxin positive C.difficile infection in the past 12 weeks
5. Contraindications or major cautions to macrolide antibiotic use:
5.1. Known hypersensitivity to clarithromycin, its excipients or other macrolide antibiotics
5.2. Established diagnosis of myasthenia gravis
5.3. Diagnosis of long QT syndrome
5.4. QTc interval >460ms on last ECG before screening
5.5. Known uncorrected hypokalaemia ($K^+ < 3.5$ mmol/l) which has not been corrected
5.6. Known uncorrected hypomagnesaemia ($Mg^{2+} < 0.85$ mmol/l) which has not been corrected
5.7. History of ventricular tachycardia
5.8. History of cardiac arrest
5.9. Severe hepatic impairment defined as AST, ALT or bilirubin > 3 times ULN or known diagnosis of cirrhosis
5.10. Current use of medicine(s) known to increase risk of QT prolongation that in the opinion of the investigator cannot reasonably be withheld for the duration of study treatment plus 3 days
5.11. Current use of medicine(s) that are contra-indicated in combination with clarithromycin that in the opinion of the investigator cannot reasonably be withheld for the duration of study treatment plus 3 days
6. Women of childbearing potential who are pregnant, breastfeeding or who are unwilling to use appropriate contraception or abstain from sexual intercourse for 3 days (72 hours) after the last dose of clarithromycin
7. Plan for imminent mechanical ventilation
8. End-of-life care
9. Previously randomised into the CLASP study

Date of first enrolment
30/03/2025

Date of final enrolment
30/11/2028

Locations

Countries of recruitment
United Kingdom

Study participating centre
-
United Kingdom
-

Sponsor information

Organisation
NHS Greater Glasgow and Clyde

ROR
https://ror.org/05kdz4d87

Organisation
University of Glasgow

ROR
https://ror.org/00vtgdb53

Funder(s)

Funder type
Government

Funder Name
National Institute for Health and Care Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

Use of data by applicants and other researchers will be permitted via a data sharing agreement for specific research questions and approved by a data sharing committee for 2 years after the main trial results are published. Thereafter, datasets generated during the study will then be deposited in a publicly available repository. Storage of anonymous research data is detailed in the Participant Information Sheet and Informed Consent Form.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file	version 1.0	12/12/2024	18/03/2025	No	No