ISRCTN10086050 https://doi.org/10.1186/ISRCTN10086050

To determine if critically ill patients with acute respiratory failure treated with carbocisteine, hypertonic saline, or both, experience increased hydration of airway mucus.

Submission date
01/07/2022

Recruitment status
No longer recruiting

Registration date
04/07/2022

Overall study status
Ongoing

Last Edited
09/04/2025

Condition category
Respiratory

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

Plain English summary of protocol

Background and study aims

When patients are critically ill, one of the main complications is called ‘acute respiratory failure’. This is when a patient’s illness causes their lungs to fail to work (lung failure). Patients need to be admitted to the Intensive Care Unit (ICU) and often need to have a breathing machine, or ventilator, to help them breathe and ensure that enough oxygen gets into their blood. However, one problem that can occur as a result of being on a ventilator, is difficulty clearing secretions (mucus, or sputum) from the lungs. Not being able to clear secretions from the lungs can make breathing harder, and this may result in developing a lung infection.

In some cases, medications called ‘mucoactives’ may be prescribed for patients to reduce the problem of thick secretions. Mucoactives are medications that work to help clear secretions from the airways. Two examples of mucoactives are ‘Carbocisteine’ and ‘Hypertonic saline’. Carbocisteine can help by changing the thickness and stickiness of secretions, which may help clear mucus from the lungs. It is given to patients in the ICU whilst they are on a breathing machine, in either liquid form or as powder dissolved in water, via the patient’s feeding tube. Hypertonic saline is salty water that is delivered into the airways via a device called a nebuliser, which turns the salty water into a mist. The mist may stimulate coughing to help clear thick secretions from the lungs.

A study called MARCH is already investigating whether using one, or both, of these mucoactives (carbocisteine and hypertonic saline), really helps patients when they have difficulty clearing secretions, and if as a result, this means patients spend less time on the breathing machine (ventilator).

This study is named EME and is a part of the MARCH study. The EME Study hopes to find out biologically the ways these mucoactives might work to help clear secretions from the airways and so shorten the time patients need a ventilator to breathe. This information will allow doctors to prescribe the correct amount of medication to help critically ill patients, and improve lung failure treatments for patients in the future.

Who can participate?
Patients who have provided their consent to be enrolled in the main MARCH trial and to have biological samples (airway secretions) collected and analysed.

What does the study involve?
Samples of airway secretions will be taken from patients in the MARCH study who are being treated by one of these mucoactives, both of them, or neither of them. The EME study will test the samples to measure their thickness, stickiness, and the level of inflammation present.

What are the possible benefits and risks of participating?
The information gained from the tests on the biological samples will benefit doctors and patients as it will improve treatments for patients with lung failure in the future. We do not anticipate any risks associated with being the EME part of this study. All patients enrolled in the MARCH study will be carefully monitored.

Where is the study run from?
The Trial Coordinating Centre is the Northern Ireland Clinical Trials Unit (NICTU) (UK). The Sponsor is the Belfast Health and Social Care Trust (BHSCT) (UK).

When is the study starting and how long is it expected to run for?
From May 2022 to November 2025

Who is funding the study?
National Institute for Health and Care Research (NIHR) Efficacy and Mechanism Evaluation Programme (UK)

Who is the main contact?
Dr Naomi Dickson
MARCH@nictu.hscni.net

Study website
https://nictu.hscni.net/march-trial/

Contact information

Type(s)
Principal Investigator

Contact name
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Type(s)
Scientific

Contact name
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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
293630

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
IRAS 293630, NIHR130454, CPMS 51165

Study information

Scientific Title
Is the mechanism of action of hypertonic saline and/or carbocisteine in the treatment of patients with acute respiratory failure due to an increase in mucus hydration?

Acronym
MARCH EME

Study objectives
Treatment of critically ill patients with ARF with carbocisteine, hypertonic saline, or both, will lead to increased mucus hydration and changes in sputum viscosity and elasticity.

Ethics approval required
Old ethics approval format

Ethics approval(s)

Approved 29/06/2022, Faculty of Medicine, Health & Life Sciences (MHLS) Research Ethics Committee (REC) (Research & Enterprise Directorate, Queen's University Belfast, 63 University Road, Belfast, BT7 1NN, United Kingdom; +44 (0)28 9097 2529; facultyrecmhls@qub.ac.uk), ref: MHLS 22_79

Study design
Multi-centre, exploratory mechanistic, observational cohort study embedded within the MARCH trial

Primary study design
Observational

Secondary study design
Cohort study

Study setting(s)
Hospital

Study type(s)
Other

Participant information sheet
Not available in web format, please use contact details to request a MARCH trial participant information sheet as the samples are collected via this study.

Health condition(s) or problem(s) studied
Critically ill patients with acute respiratory failure (ARF)

Interventions
Sputum samples will be collected from patients recruited to the MARCH clinical trial (https://www.fundingawards.nihr.ac.uk/award/NIHR130454).
The proposed study will involve collection of sputum samples from patients randomised to each of the four trial groups:
1. Carbocisteine plus usual airway clearance management
2. Hypertonic saline plus usual airway clearance management
3. Carbocisteine and hypertonic saline plus usual airway clearance management
4. Usual airway clearance management alone
Sputum samples will be collected at 3 time-points during the study; baseline (Day 0) (at randomisation), Day 3, and Day 7. The solids concentration of mucus will be measured and dynamic rheology measurements will be recorded including G' and G" of samples from which the Tc value will be obtained. Inflammatory mediators will be measured by ELISA.

Intervention Type
Other

Primary outcome measure
Percentage mucus solid content (dry-to-wet weight ratio) of sputum measured from sputum samples collected at baseline and 3 days

Secondary outcome measures

1. Percentage mucus solid content (dry-to-wet weight ratio) of sputum measured from sputum samples collected at baseline and 7 days
2. Sputum elasticity (G') and viscosity (G'') (and yield stress, Tc) measured using dynamic rheology of sputum samples collected at baseline and 3 days
3. Sputum IL-6, IL-8, and 8-isoprostane levels measured by ELISA of sputum samples collected at baseline and 3 days
4. Sputum elasticity (G') and viscosity (G'') (and yield stress, Tc) measured using dynamic rheology of sputum samples collected at baseline and 7 days
5. Sputum IL-6, IL-8, and 8-isoprostane levels measured by ELISA of sputum samples collected at baseline and 7 days

Overall study start date
01/05/2022

Completion date
30/11/2025

Eligibility

Key inclusion criteria
1. Participating in the MARCH trial
2. Provide consent to have biological samples (airway secretions) collected and analysed and the data generated from these analyses to be used

Participant type(s)
Patient

Age group
Adult

Lower age limit
16 Years

Sex
Both

Target number of participants
360 patients

Key exclusion criteria
1. Suspected/confirmed COVID disease
2. Do not meet the MARCH trial inclusion criteria

Date of first enrolment
01/08/2022

Date of final enrolment
30/04/2025

Locations

Countries of recruitment
England

Northern Ireland

Scotland

United Kingdom

Wales

Study participating centre
Royal Victoria Hospital
274 Grosvenor Road
Belfast
United Kingdom
BT12 6BA

Study participating centre
Bristol Royal Infirmary
Marlborough Street
Bristol
United Kingdom
BS2 8HW

Study participating centre
Sunderland Royal Hospital
Kayll Road
Sunderland
United Kingdom
SR4 7TP

Study participating centre
Belfast City Hospital
51 Lisburn Rd
Belfast
United Kingdom
BT9 7AB

Study participating centre
Royal Infirmary of Edinburgh at Little France
51 Little France Crescent
Old Dalkeith Road
Edinburgh
Lothian
United Kingdom
EH16 4SA

Study participating centre
Royal Liverpool University Hospital NHS Trust, Royal Liverpool University Hospital, Prescot Street, Liverpool, L7 8XP
Prescot Street
Liverpool
United Kingdom
L7 8XP

Study participating centre
Royal Cornwall Hospitals NHS Trust
Royal Cornwall Hospital
Treliske
Truro
United Kingdom
TR1 3LJ

Study participating centre
Mersey Care NHS Trust at Aintree Hospital
C/o University Hospital Aintree
Fazakerley Hospital
Lower Lane
Liverpool
United Kingdom
L9 7AL

Study participating centre
Manchester Royal Royal Infirmary
Cobbett House
Oxford Road
Manchester
United Kingdom
M13 9WL

Study participating centre
Wythenshawe Hospital
Southmoor Road
Wythenshawe
Manchester
United Kingdom
M23 9LT

Study participating centre
Western General Hospital
Crewe Road South
Edinburgh
Lothian
United Kingdom
EH4 2XU

Study participating centre
Royal Stoke University Hospital
Newcastle Road
Stoke-on-trent
United Kingdom
ST4 6QG

Study participating centre
Watford General Hospital
60 Vicarage Road
Watford
United Kingdom
WD18 0HB

Study participating centre
The Royal Oldham Hospital
Rochdale Road
Oldham
United Kingdom
OL1 2JH

Study participating centre
University Hospital (coventry)
Clifford Bridge Road

Coventry
United Kingdom
CV2 2DX

Study participating centre
Southmead Hospital
Southmead Road
Westbury-on-trym
Bristol
United Kingdom
BS10 5NB

Study participating centre
John Radcliffe Hospital
Headley Way
Headington
Oxford
United Kingdom
OX3 9DU

Study participating centre
Glasgow Royal Infirmary
84 Castle Street
Glasgow
United Kingdom
G4 0SF

Study participating centre
Preston Acute Hospitals NHS Trust
Royal Preston Hospital
Sharoe Green Lane North
Fulwood
Preston
United Kingdom
PR2 9HT

Study participating centre
Royal Devon & Exeter Foundation Hospital
Barrack Road

Exeter
United Kingdom
EX2 5DW

Study participating centre
Morriston Hospital
Heol Maes Eglwys
Cwmrhydyceirw
Swansea
United Kingdom
SA6 6NL

Study participating centre
Queen Elizabeth University Hospital
1345 Govan Road
Glasgow
United Kingdom
G51 4TF

Study participating centre
Derriford Hospital
Derriford Road
Crownhill
Plymouth
United Kingdom
PL6 8DH

Study participating centre
William Harvey Hospital
Kennington Road
Willesborough
Ashford
United Kingdom
TN24 0LZ

Study participating centre
Northern General Hospital
Northern General Hospital NHS Trust
C Floor, Huntsmnan Building
Herries Road
Sheffield

United Kingdom
S5 7AU

Study participating centre
Aberdeen Royal Infirmary
Foresterhill Road
Aberdeen
United Kingdom
AB25 2ZN

Study participating centre
University College London Hospitals NHS Foundation Trust
250 Euston Road
London
United Kingdom
NW1 2PG

Study participating centre
Pinderfields General Hospital
Aberford Road
Wakefield
United Kingdom
WF1 4DG

Study participating centre
Sandwell District General Hospital
Lyndon
West Bromwich
United Kingdom
B71 4HJ

Study participating centre
Northern Devon Healthcare NHS Trust
North Devon District Hospital
Raleigh Park
Barnstaple
United Kingdom
EX31 4JB

Study participating centre
University Hospital Monklands
Monkscourt Avenue
Airdrie
United Kingdom
ML6 0JS

Sponsor information

Organisation
Queen's University Belfast

Sponsor details
Research, Governance, Ethics and Integrity
Queen’s University Belfast
63 University Road
Belfast
Northern Ireland
United Kingdom
BT7 1NN
+44 (0)28 90245133
researchgovernance@qub.ac.uk

Sponsor type
University/education

Website
http://www.qub.ac.uk/

ROR
https://ror.org/00hswnk62

Funder(s)

Funder type
Government

Funder Name
National Institute for Health 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

Funder Name
Health Technology Assessment Programme

Alternative Name(s)
NIHR Health Technology Assessment Programme, HTA

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Funder Name
Efficacy and Mechanism Evaluation Programme

Alternative Name(s)
NIHR Efficacy and Mechanism Evaluation Programme, EME

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Planned publication of results in a high-impact peer-reviewed journal. Planned publication of protocol in a leading peer-reviewed respiratory journal.

Intention to publish date
30/11/2026

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study will be available upon request following publication of the primary and secondary outcomes. Formal requests for data should be made in writing to Prof Cliff Taggart (Chief Investigator) via the Trial Manager (Naomi Dickson; MARCH@nictu.hscni.net) at the Northern Ireland Clinical Trials Unit (NICTU) and will be reviewed on a case by case basis in collaboration with the Sponsor.

IPD sharing plan summary
Available on request