ISRCTN86837685 https://doi.org/10.1186/ISRCTN86837685

Evaluating the influence of abnormalities in immunity due to an extreme reaction to an infection (sepsis) on antibiotic use in critically ill patients

Submission date
08/12/2020

Recruitment status
No longer recruiting

Registration date
05/01/2021

Overall study status
Completed

Last Edited
27/04/2023

Condition category
Infections and Infestations

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

Plain English summary of protocol

Background and study aims
Sepsis is a life threatening condition due to infection in which the immune system has an abnormally over-active and under-active response (immunosuppression). Patients who have pronounced immunosuppression have a higher risk of getting further infections while in hospital, have a longer stay in hospital and even have a higher rate of death.

Patients with sepsis require treatment with antibiotics and the length of antibiotic course is often fixed. A trial (called ADAPT-sepsis https://www.isrctn.com/ISRCTN47473244) is currently underway to see whether two markers that can be measured in blood or 'biomarkers' (called procalcitonin (PCT) and c-reactive protein (CRP)), can reduce antibiotic use in patients with sepsis. The purpose is to see if using these biomarkers will reduce antibiotic use. These biomarkers are generally high at the start of the illness and when they fall to a certain level, the clinician will be advised to stop antibiotics.

Who can participate?
Patients enrolled in the ADAPT-sepsis trial.

What does the study involve?
As an observational study, participants will have four blood samples taken over a one-week period. These samples will be sent to a central laboratory for testing of white cell markers which will give a picture of immune function of patients. This observational study is a sub-study of an ongoing randomised controlled trial (ISRCTN47473244) and so all other procedures such as consent and clinical data collection will occur as part of the main trial.

What are the possible benefits and risks of participating?
Individual patients are unlikely to benefit from participating in this study. The amount of additional blood taken is small and is taken in most cases from an arterial or venous tube at the same time as blood required for routine clinical care. In exceptional cases, blood sampling is

from a vein using a needle. There may be a sharp scratch when the needle is inserted and possible bruising from the area from which the blood is taken.

Where is the study run from?
The Newcastle upon Tyne Hospitals NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
August 2020 to July 2024

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

Who is the main contact?
Dr Tom Ewen, Tom.Ewen@newcastle.ac.uk
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Contact information

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Public

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
209815

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
R121074, IRAS 209815, CPMS 45252, NIHR128374

Study information

Scientific Title
The Role of Immunosuppression in an antibiotic Stewardship intervention and its association with Clinical outcomes and antibiotic use: RISC-sepsis

Acronym
RISC-sepsis

Study objectives
As a mechanistic study embedded within a biomarker-guided antibiotic duration trial, this study will determine whether patients with sepsis-induced immunosuppression have prolonged duration of antibiotics and different trial outcomes.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 21/10/2020, South Central - Oxford C Research Ethics Committee (Level 3, Block B, Whitefriars Building, Lewins Mead, Bristol, BS1 2NT, UK; Tel: +44 (0)207 104 8379; oxfordc.rec@hra.nhs.uk), ref: 17/SC/0434

Study design
Prospective multi-centre exploratory cohort observational study embedded within the ADAPT-sepsis trial

Primary study design
Observational

Study type(s)
Other

Health condition(s) or problem(s) studied

Hospitalised adults who have been commenced on intravenous antibiotics for sepsis

Interventions
As an observational study, participant involvement will be limited to sampling of blood at 4 time points over a one-week period. Blood samples will be transferred to a central laboratory. Immune phenotype will be performed by measuring cellular surface markers by fluorescence-based flow cytometry. These markers will include but not limited to, HLA-DR, CD88, PD-1 and regulatory T cells.

ADAPT-sepsis study registration: https://www.isrctn.com/ISRCTN47473244

Intervention Type
Other

Primary outcome(s)
Immune phenotype measured using fluorescence-based flow cytometry of blood samples taken at ...
1. Monocyte HLA-DR
2. Neutrophil CD88
3. T cell, monocyte and neutrophil CD279
4. Percentage of regulatory T cells

Key secondary outcome(s))
Measured using patient records:
1. Total duration of antibiotic treatment to 28 days following randomisation (superiority) measured in days (24-hour time periods)
2. Antibiotic dose, measured as Defined Daily Dose to 28 days
3. Unscheduled care escalation/re-admission
4. Infection relapse/recurrence requiring further antibiotic treatment
5. Super-infection, defined as new infection at a different anatomical site
6. Suspected antibiotic adverse reactions
7. Time to ‘fit’ for hospital discharge

Completion date
31/07/2024

Eligibility

Key inclusion criteria
Patients enrolled in the ADAPT-sepsis trial. Patients are eligible if:
1. Hospitalised adult patients at least 18 years of age
2. Up to 24 hours of initiation of empiric intravenous antibiotic treatments for suspicion of sepsis
3. Likely to remain hospitalised and receiving intravenous antibiotic treatment for at least the next 72 hours
4. Requirement for critical care

Participant type(s)
Patient

Healthy volunteers allowed

No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
198

Key exclusion criteria
1. More than 24 hours since receiving first empiric intravenous antibiotic treatments for a suspicion of sepsis
2. Prolonged (greater than 21 days) antimicrobial therapy mandated (e.g. for endocarditis, cerebral/hepatic abscess, tuberculosis, osteomyelitis)
3. Severely immunocompromised (e.g. neutropenia, less than 500 neutrophils/microlitre)
4. All treatment for suspected sepsis likely to be stopped within 24 hours of its initiation because of futility
5. Consent declined
6. Previously enrolled in ADAPT-sepsis

Date of first enrolment
01/04/2022

Date of final enrolment
21/04/2023

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Royal Victoria Infirmary
The Newcastle upon Tyne Hospitals NHS Foundation Trust
Queen Victoria Road
Newcastle upon Tyne
United Kingdom
NE1 4LP

Sponsor information

Organisation
University of Manchester

ROR
https://ror.org/027m9bs27

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

Results and Publications

Individual participant data (IPD) sharing plan
Current IPD sharing statement as of 20/04/2021:
Following publication of the study's findings, publicly available summary data of immune phenotyping datasets will be made findable through those publications. Access to the full dataset will be made available via request to the chief investigator, Dr Tom Hellyer (thomas.hellyer@newcastle.ac.uk). Access requests will be considered in accordance with Newcastle University Data Sharing Policies and all external users submitting applications for access to data will require data sharing agreements in keeping with the NIHR requirements. The data use agreement must detail the agreed use and appropriate management of the data and include a requirement for recognition of the contribution of the researchers who generated the data and the original funder.

Patient will consent to archiving of data and data sharing limited to researchers for future research. All data will be available for peer review at the point of deposition and publication, and will be archived for a minimum of 10 years after publication.

Previous IPD sharing statement:
All data generated or analysed during this study will be included in the subsequent results publication.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article		09/12/2022	16/12/2022	Yes	No
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Study website	Study website	11/11/2025	11/11/2025	No	Yes