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Adjunctive rifampicin to reduce early mortality from Staphylococcus aureus bacteraemia

Submission date
20/01/2012

Recruitment status
No longer recruiting

Registration date
26/01/2012

Overall study status
Completed

Last Edited
02/11/2018

Condition category
Infections and Infestations

[X] Prospectively registered

[X] Protocol

[_] Statistical analysis plan

[X] Results

[_] Individual participant data

Plain English summary of protocol

Background and study aims
Staphylococcus (S) aureus is a bacteria normally found on the skin. It can cause severe infections, with a reputation as a super-bug when it is resistant to antibiotics, for example, meticillin-resistant S. aureus (MRSA). In the community S. aureus causes serious skin infections (e.g. cellulitis), whilst in hospital it may infect wounds, intravenous lines (used to inject drugs or fluids) and other implanted medical devices (e.g. artificial heart valves and joints). S. aureus is especially dangerous when it infects the bloodstream (bacteraemia). Despite the incidence of S. aureus bacteraemia the best way to treat this infection remains uncertain. Doctors do not know which antibiotics are the most effective, how long these should be given, and whether starting treatment with a combination of antibiotics is better than starting with just one. Current UK guidelines recommend at least 14 days treatment with a single antibiotic for S. aureus bacteraemia, but acknowledge the lack of evidence supporting this recommendation. We want to find out whether or not giving an extra antibiotic, called rifampicin, in addition to the standard antibiotic, will help sick people with S. aureus blood infections. We want to know if rifampicin prevents some of them from dying, or whether it makes no difference to survival but just gives more side-effects and/or encourages the bug to become resistant. At the moment we do not know whether taking extra rifampicin is better or the same or even worse this is the reason we are doing the study.

Who can participate?
Patients admitted to hospital who are found to have S. aureus infection.

What does the study involve?
ARREST is designed as a placebo-controlled trial. A placebo is a dummy treatment such as a pill which looks like the real treatment (rifampicin) but it contains no active ingredient. Everyone in the study will get the same standard antibiotic that they would have received if they decided not to join the study. In addition , you will have an equal chance of getting rifampicin for 2 weeks or getting a placebo which looks like rifampicin for 2 weeks on top of this standard antibiotic. Whether you get extra rifampicin or extra placebo will be chosen by chance by a computer.

What are the possible benefits and risks of participating?
Taking rifampicin may help you fight S. aureus blood infection better. Whether you get

rifampicin or a placebo, we will monitor you very carefully throughout your treatment and detect early any complications of the infection or side-effects of the drugs. Entering this study may not directly benefit you, but the information we get from the ARREST study will help to guide the best way to treat patients like you in the future. Rifampicin, like all medicines, has unwanted side-effects, which are sometimes serious. Serious side effects happen in fewer than 1 in 100 people and it may be necessary to stop the study drug after which the problem usually goes away. The most important side-effect of rifampicin is that is can cause inflammation of the liver. This can cause vomiting and abdominal pain. Regular blood tests will be performed during the study to watch for this side-effect. The other common side-effect of rifampicin is that it can turn urine, tears and sweat an orange colour. This is completely harmless and goes away completely when the drug is stopped. Finally, rifampicin increases the way the body breaks down some drugs. This can mean that these drugs become less effective. For example, rifampicin can stop the oral contraceptive pill working. The study doctor will check with the you what medication you are on before starting the study so that she/he can ensure rifampicin will not effect you.

Where is the study run from?
The study will take place across several clinics in National Health Service (NHS) hospitals across the UK.

When is the study starting and how long it is expected to run for?
The study will start in November 2012 and will run for four years. You will be followed up for 12 weeks, and more information on health status may be obtained by looking at medical notes for five years thereafter.

Who is funding the study?
National Institute of Health Research.

Who is the main contact?
Professor Guy Thwaites
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Contact information

Type(s)
Scientific

Contact name
Prof Guy Thwaites

Contact details
Centre for Clinical Vaccinology and Tropical Medicine (CCVTM)
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United Kingdom
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Additional identifiers

Clinical Trials Information System (CTIS)
2012-00344-10

Protocol serial number
HTA 10/104/25

Study information

Scientific Title
Adjunctive Rifampicin to Reduce Early mortality from STaphylococcus aureus bacteraemia: a multi-centre, randomised, double blind, placebo-controlled trial

Acronym
ARREST

Study objectives
Adjunctive rifampicin will enhance killing of S. aureus early in the course of antibiotic treatment, sterilise infected foci and blood faster, and thereby reduce the risk of dissemination, metastatic infection and death.

More details can be found at: http://www.nets.nihr.ac.uk/projects/hta/1010425
Protocol can found at: http://www.nets.nihr.ac.uk/__data/assets/pdf_file/0003/81723/PRO-10-104-25.pdf

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES Committee London - Westminster, 24/05/2012, ref:12/LO/0637

Primary study design
Interventional

Study design
Parallel-group randomised double-blind placebo-controlled multi-centre trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
S. aureus (meticillin-susceptible or resistant) infection, acute infection

Interventions
2 weeks of rifampicin or placebo in addition to standard antibiotic therapy

Intervention Type
Drug

Phase
Not Applicable

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

Primary outcome(s)
Current primary outcome measures as of 09/11/2016:
Bacteriological failure/death through 12 weeks from randomisation

Previous primary outcome measures:
1. All cause mortality through 14 days from randomisation
2. Bacteriological failure/death through 12 weeks from randomisation

Key secondary outcome(s)
Current secondary outcome measures as of 09/11/2016:
1. All cause mortality through 14 days from randomisation
2. Death or clinically defined treatment failure or disease recurrence by 12 weeks (clinical failure being assessed by an independent endpoint committee blind to the treatment allocation)
3. Duration of bacteraemia (blood cultures will be taken on days 3 and 7 following randomisation)
4. Adverse events (grade 3/4 adverse events, serious adverse events)
5. Modification of any treatment (including concomitant medications) due to drug interactions
6. Development of rifampicin resistant S. aureus
7. Cost-effectiveness of rifampicin

Previous secondary outcome measures:
1. Death or clinically defined treatment failure or disease recurrence by 12 weeks (clinical failure being assessed by an independent endpoint committee blind to the treatment allocation)
2. Duration of bacteraemia (blood cultures will be taken on days 3 and 7 following randomisation)
3. Adverse events (grade 3/4 adverse events, serious adverse events)
4. Modification of any treatment (including concomitant medications) due to drug interactions
5. Development of rifampicin resistant S. aureus

Completion date
17/01/2017

Eligibility

Key inclusion criteria
1. Adults (18 years or older)
2. Staphylococcus aureus (meticillin-susceptible or resistant) grown from at least one blood culture
3. Less than 96 hours of active antibiotic therapy for the current infection (added 09/11/2016: not including rifampicin and excluding stat doses)
4. Patient or legal representative (LR) provides written informed consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Key exclusion criteria
1. Infection not caused by S. aureus alone in the opinion of the treating physician (e.g. S. aureus is considered a blood culture contaminant, or polymicrobial culture with another organism likely to be contributing clinically to the current infection)
2. Sensitivity results already available and demonstrate rifampicin resistant S. aureus (defined by British Society for Antimicrobial Chemotherapy in vitro disc susceptibility testing)
3. Treating physician considers rifampicin is contraindicated for any reason
4. Treating physician considers rifampicin treatment is mandatory for any reason
5. Suspected active infection with Mycobacterium tuberculosis
6. Previously been randomised in ARREST for a prior episode of S. aureus bacteraemia

Date of first enrolment
26/11/2012

Date of final enrolment
28/10/2016

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Guy's and St Thomas' NHS Foundation Trust
United Kingdom
SE1 9RT

Study participating centre
Oxford University Hospitals NHS Trust
United Kingdom
OX3 7LE

Study participating centre

University College London Hospitals NHS Foundation Trust
United Kingdom
NW1 2BU

Study participating centre
Royal Free London NHS Foundation Trust
United Kingdom
NW3 5NU

Study participating centre
King's College Hospital NHS Foundation Trust
United Kingdom
SE5 9RS

Study participating centre
Brighton and Sussex University Hospitals NHS Trust
United Kingdom
BN2 5BE

Study participating centre
The Royal Liverpool and Broadgreen University Hospitals NHS Trust
United Kingdom
L7 8XP

Study participating centre
Sheffield Teaching Hospitals NHS Foundation Trust
United Kingdom
S10 2JF

Study participating centre
Cambridge University Hospitals NHS Foundation Trust
United Kingdom
CB2 0QQ

Study participating centre

Royal United Hospital Bath NHS Trust
United Kingdom
BA1 3NG

Study participating centre
Royal Devon and Exeter NHS Foundation Trust
United Kingdom
EX2 5DW

Study participating centre
Plymouth Hospitals NHS Trust
United Kingdom
PL6 8DH

Study participating centre
Hull and East Yorkshire Hospitals NHS Trust
United Kingdom
HU3 2JZ

Study participating centre
South Tees Hospitals NHS Foundation Trust
United Kingdom
DL6 1JG

Study participating centre
Heart of England NHS Foundation Trust
United Kingdom
B9 5SS

Study participating centre
St George's Healthcare NHS Trust
United Kingdom
SW17 0QT

Study participating centre

Portsmouth Hospitals NHS Trust
United Kingdom
PO6 3LY

Study participating centre
University Hospital Southampton NHS Foundation Trust
United Kingdom
SO16 6YD

Study participating centre
Blackpool Teaching Hospitals NHS Foundation Trust
United Kingdom
FY3 8NR

Study participating centre
The Leeds Teaching Hospital NHS Trust
United Kingdom
LS1 3EX

Study participating centre
University Hospitals Coventry and Warwickshire NHS Trust
United Kingdom
CV2 2DX

Study participating centre
Aintree University Hospital NHS Foundation Trust
United Kingdom
L9 7AL

Study participating centre
Bradford Teaching Hospitals NHS Foundation Trust
United Kingdom
BD9 6RJ

Study participating centre

County Durham and Darlington NHS Foundation Trust
United Kingdom
DH1 5TW

Study participating centre
Dartford & Gravesham NHS Trust
United Kingdom
DA2 8DA

Study participating centre
North Bristol NHS Trust
United Kingdom
BS10 5NB

Study participating centre
North Cumbria University Hospitals
United Kingdom
CA2 7HY

Study participating centre
University Hospitals of Leicester NHS Trust
United Kingdom
LE1 5WW

Study participating centre
Wirral University Teaching Hospital NHS Foundation Trust
United Kingdom
CH49 5PE

Study participating centre
The Newcastle upon Tyne Hospitals NHS Foundation Trust
United Kingdom
NE7 7DN

Study participating centre

Salford Royal NHS Foundation Trust
United Kingdom
M6 8HD

Sponsor information

Organisation
Medical Research Council (MRC) (UK)

ROR
https://ror.org/03x94j517

Funder(s)

Funder type
Government

Funder Name
Health Technology Assessment Programme

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

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
	results				

Results article	protocol	01/10/2018		Yes	No
Protocol article		18/12/2012		Yes	No
HRA research summary	Study website		28/06/2023	No	No
Study website		11/11/2025	11/11/2025	No	Yes