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Liverpool Heart and Chest Hospital NHS
NHS Trust

NHS
National Institute for Health Research

A Pilot Randomised Control Trial, in Intensive Care Patients, Comparing Seven Days Versus Two Days Treatment With Empirical Antibiotics to Treat Hospital Acquired Infection of Unknown Origin

Randomised Evaluation of Antibiotic Treatment Duration in the Intensive Care Unit - READ-ICU

TRIAL - HTA Ref 08/13/38

Protocol version 5.0
Dated 29th September 2010

1 CONTACT DETAILS AND KEY PERSONNEL

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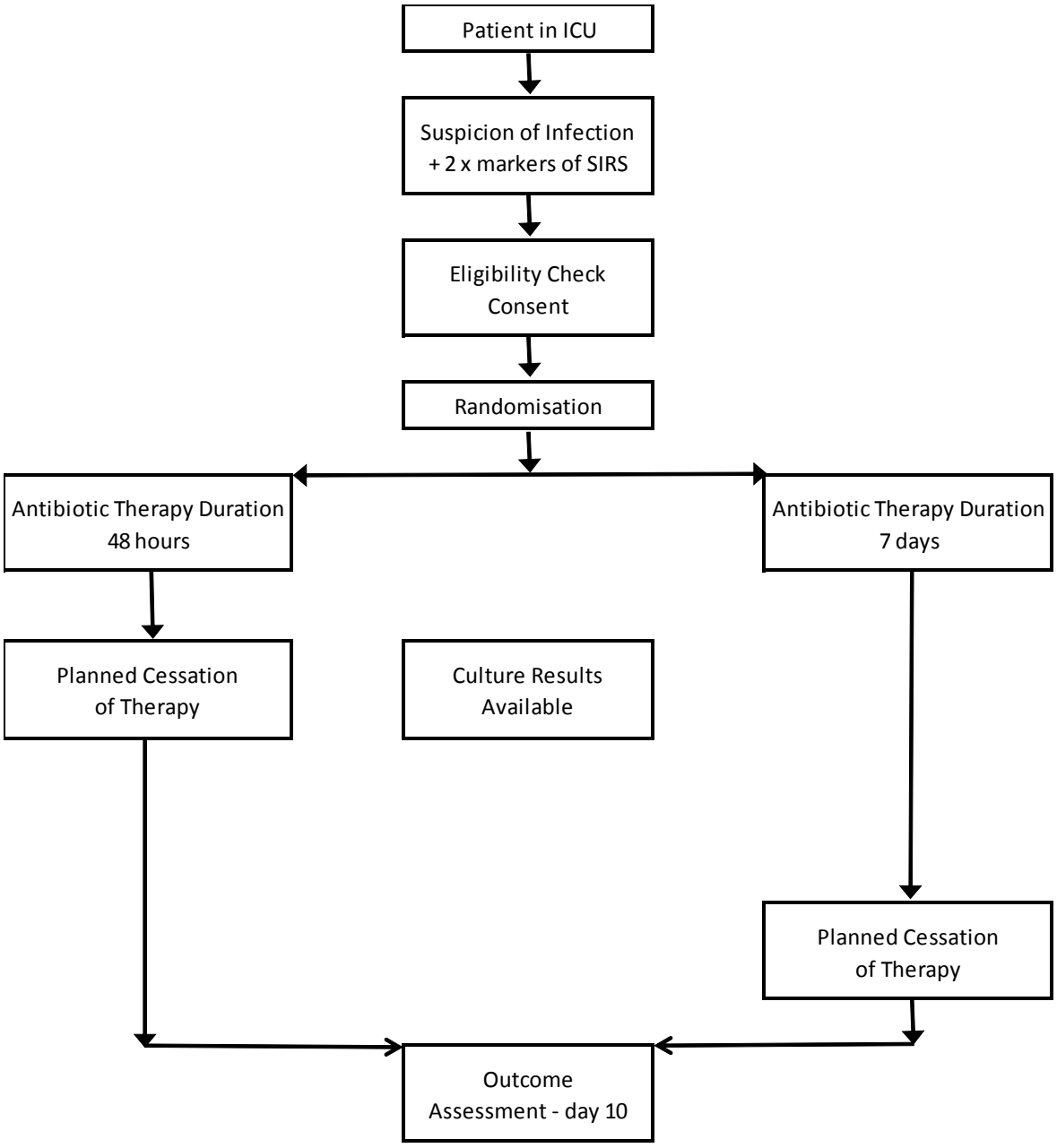
3 STUDY SUMMARY

Title of study	A pilot randomised control trial, in intensive care patients, comparing seven days versus two days treatment with empirical antibiotics to treat hospital acquired infection of unknown origin
Trial acronym	**R**andomised **E**valuation of **A**ntibiotic Treatment **D**uration in the **I**ntensive **C**are **U**nit **READ-ICU**
Study design	Single-centre, randomised, prospective clinical trial
No of subjects	60
Study timelines	Planning, ethics and start-up Sep 2009 - Dec 2009 Recruitment Jan 2010 - Dec 2010 End of follow-up Jan 2011 Analysis and reporting Jan 2011 – Mar 2011 Final report Apr 2011
Inclusion criteria	Patients in the intensive care unit with signs suggestive of new infection in the absence of positive microbiological cultures **AND** At least two of the four markers of systemic inflammatory response syndrome (SIRS): • temperature of >38^{0}C or <36^{0}C • tachycardia (>90 beats per minute) • tachypnoea (≥ 20 breaths per minute) • white blood count >12x10^9/L or <4x10^9/L
Exclusion Criteria	• Positive microbiological cultures before randomisation • Patients <18 years of age • Unable to obtain assent or consent • Patients enrolled in another study such that randomisation in READ-ICU would result in deviation from either protocol • Known allergy to treatment antibiotics
Primary outcome measure	The rate of death or initiation of antibiotic therapy after the completion of the treatment schedule allocated at randomisation
Secondary outcome measures	**Clinical** • Duration of ICU stay • Duration of Hospital stay • Duration of mechanical ventilation

	• Incidence of infection with clostridium difficile • Incidence of infection with MRSA **Economic** • Resource utilisation and costs **Feasibility** • The ratio of patients - screened : eligible : randomised • The incidence of cross-over between the randomised treatment groups • The accuracy of data collection assessed by a 20% source data verification check
Follow-up	Outcome measures will be assessed at day 10 or hospital discharge, whichever is sooner.

4 STUDY FLOW CHART



5 BACKGROUND

5.1 Hospital Acquired Infection in the Intensive Care Unit

Patients in intensive care units (ICUs) are at higher risk of hospital-acquired infections and sepsis than those in non-critical care areas [1]. Hospital-acquired sepsis is reported to occur in 10% to 70% of patients undergoing invasive mechanical ventilation, the rate varying with the patient population studied and diagnostic criteria used [5]. Despite the major advances in intensive care management sepsis and its complications remain the leading cause of mortality in ICUs [2]. Bloodstream infections (BSIs), pneumonias, and urinary tract infections (UTIs) are the most common hospital-acquired infections and are most often associated with the use of invasive devices [3]. Coagulase-negative staphylococcus BSIs have recently increased in frequency, and enterococci such as staphylococcus aureus have also been reported as causing BSIs in increasing numbers of ICUs. Recently, gram-negative bacilli have been reported more frequently than gram-positives in this setting. Fungal urinary tract sepsis has also increased [4].

5.2 Why New Treatment Strategies are Needed

Many patients with suspected sepsis in ICU are given antibiotics for the entire duration of stay to reduce the risk of complications, even in cases where there are no compelling positive microbiological results. To date most studies have focused on optimising antibiotic treatment for ventilator acquired pneumonia (VAP) that accounts for approximately 50% of antibiotics use in ICU [6-8] and the other proportion is for treatment of suspected sepsis often of unknown origin. Since clinical decisions for empirical antibiotic treatment are usually based on fever, purulent tracheal aspirates, increased white cell counts and heart rate, even if no x-ray changes are apparent, we hypothesise that prolonged treatments with antibiotics is unnecessary in cases where there are no confirmed organisms grown in blood cultures. In addition, other markers of sepsis may guide early diagnosis and decision making on necessity and duration of antibiotic treatment. On the basis of existing evidence from a recent retrospective study by Arts et al 2007 [9], suggesting that patients without proof of nosocomial infection receiving empirical antibiotics for longer than 4-days had higher 28-day mortality (32.1%) than those whose antibiotics were discontinued (7.7%), we hypothesised that 2-day antibiotic regime is sufficiently potent to eliminate any potential microbial threat in these patients. This is consistent with current international recommendations and guidelines that there is a need for continuous reassessment of antibiotic therapy with microbiology and clinical data to reduce duration when appropriate from the usual 7-10 days of antibiotic therapy guided by clinical response [10].

5.3 Current Dilemma

Although early identification and treatment of sepsis can have a major impact on the outcome of these patients [11], diagnosis of sepsis is generally difficult particularly in cases where there is no positive isolated microbiological growth. Whilst there has been no shortage of proposed markers of sepsis [12], two assays have emerged as increasingly relevant in recent years. These are the biphasic activated partial thromboplastin test (APTT) waveform and procalcitonin (PCT). The APTT waveform reflects light transmittance changes in plasma and septic patients have been found by several investigators to show an abnormal biphasic pattern. Increasing abnormality of this waveform correlates with real time clinical progression and its molecular mechanism is due to calcium dependent complexes between C-reactive protein (CRP) and very low density lipoprotein [13]. This has also been shown to be superior to CRP in the diagnosis of sepsis and the risk of mortality [9]. For PCT, the degree of rise in concentration can help differentiate between infectious and non-infectious complications in these patients, and indeed, PCT has been shown to be effective in differentiating infectious from non-infectious causes of acute respiratory distress syndrome [14]. Most recent work has shown that the use of PCT tests in combination with the biphasic APTT waveform can increase the specificity of the latter test in identifying sepsis [15]. Indeed, it has recently been shown that serial measurement of PCT may allow monitoring of a reduction in antibiotic treatment duration and exposure in patients with severe sepsis and septic shock without apparent harm [16].

5.4 Search For Evidence

We have completed a review of current trials registered in the ISRCTN Register, NHS Trusts Clinical Trials Register, MRC UK and National Institutes of Health (NIH) randomised trial records held on NIH ClinicalTrials.gov website. This yielded no present or past randomized trials of this nature. In addition, we conducted an extensive literature search of the NIH Pubmed, MEDLINE and EMBASE electronic databases between 1990 and January 2008.

Terms that were used for the search were "hospital-acquired infection", "antibiotics regimen in intensive care units" and "biphasic transmittance waveform APTT coagulation assay". The searches were limited to "human" and "English language". Reference lists of identified articles were scanned for additional potentially relevant publications in the Web of Science version 4.1.1, Institute for Scientific Information 2000 which identified all articles that cited the index publication.

However, evidence from randomised trials about the duration of antibiotic use is absent.

This pilot randomised trial will investigate whether 48 hours of antibiotic treatment is adequate can safely treat suspected sepsis in the ICU as compared to the traditional week-long course. In this pilot study, we will not be using biomarkers of sepsis as part of the entry criteria as this is not currently routine practice in most UK intensive care units. However, this study presents us with the opportunity to collect samples for procalcitonin and the APTT waveform to perform a retrospective analysis of their potential utility in a future full study.

5.5 Potential Benefits of the Trial

At our centre the monthly cost attributed to antibiotics use in our ICU is estimated to be £22,000. A substantial amount of savings of up to approx. £10,000 per month could be realised in our centre if treatment was limited to the first 48 hours of ICU care in cases where no infecting organisms can be isolated. This translates to even bigger savings to the NHS as a whole running into millions every year.

5.6 Study Objectives

The main objectives of this pilot study will be to provide preliminary data on the likely safety and efficacy of a reduced course of antibiotics for the treatment of ICU infections of unknown origin. In addition, we wish to identify the likely barriers to an effective recruitment to a full study, the appropriateness and reliability of outcome measures and the data collection methods.

6 STUDY DESIGN

This is a pilot, single-centre, randomised, prospective study designed to compare safety and efficacy of a reduced course of antibiotics to a more traditional seven day prescription, for the treatment of ICU infections of unknown origin. This study will be carried out in an intensive care unit (ICU) setting of a Tertiary Heart and Chest Hospital. Approximately 60 patients will be randomised to receive either 48 hours or 7 days of antibiotic treatment.

6.1 Selection of Patients

We will screen for trial entry, all ICU patients suspected of having an infection of unknown origin. Samples will be taken for microbiological culture testing at baseline. Initial patient status will be assessed by using APACHE II scoring system and documented in the case record form.

6.2 Inclusion Criteria

Patients in the intensive care unit with signs suggestive of new infection in the absence of positive microbiological cultures

AND

At least two of the four markers of systemic inflammatory response syndrome (SIRS):

- temperature of >38^{0}C or <36^{0}C
- tachycardia (>90 beats per minute)
- tachypnoea (≥ 20 breaths per minute)
- white blood count >12x10^9/L or <4x10^9/L

6.3 Exclusion Criteria

- Positive microbiological cultures before randomisation
- Patients <18 years of age
- Unable to obtain assent or consent
- Patients enrolled in another study such that randomisation in READ-ICU would result in deviation from either protocol
- Known allergy to treatment antibiotics

6.4 Randomisation

Eligible patients with appropriate assent or consent will be randomised in equal proportions between the two trial groups:

- Antibiotic treatment administered for **48 hours**
- Antibiotic treatment administered for **7 days**

Treatment assignment is based on the block method using randomly varying block sizes of 2, 4 and 6 to ensure numerical balance between the groups. An independent statistician will provide the randomisation tables. Randomisation will be revealed by telephone contact with the clinical trial unit. Investigators will be asked to confirm patient's initials, date of birth and eligibility criteria before randomisation occurs. The randomisation service will be available 09:00 –17:00 (UK time). Outside of these hours urgent randomisation will be performed by opening a sealed, opaque, serial numbered envelope. Once randomised, the patient will be enrolled into the study and will be followed for outcome measures.

6.5 Antibiotic Therapy

Patient less than 85 kg will be given a combination of Teicoplanin 400 mg twice a day for day 1, then 400 mg daily thereafter and Meropenem, 1 g three times a day for 2 days or 7 days, as allocated at randomisation. Patients over 85 kg will receive 6 mg/kg Teicoplanin twice a day for day 1, then 6 mg/kg daily thereafter. Meropenem dose remains the same independently of patient weight.

After completion of the treatment regime allocated at randomisation, additional antibiotic use will constitute an outcome measure and the reason for initiation will be documented in the trial case record forms. Antibiotic choice in this setting will be guided by culture information and clinical opinion. Anticipated reasons for extended therapy will include:

- Proven new or ongoing infection episode with positive microbiology
- X-ray or other imaging diagnostic information
- Poor physiological status believed to be related to infection

6.6 Sub-study Protocol

Blood samples for the analysis of biphasic APPT and procalcitonin levels will be taken at:

- Baseline
- 48 hours
- On the initiation of additional antibiotic therapy beyond the randomised schedule
- At day 10 or discharge whichever is the sooner

6.7 Withdrawal from the Trial

Patients can elect to withdraw from the trial at any time without prejudice to their care but every effort will be made to seek permission to track outcome measures for the normal duration of follow-up.

7 OUTCOME MEASURES

7.1 Timing of Outcome Measure Assessment

Outcomes will be assessed at 10 days after randomization or hospital discharge, whichever is the sooner.

7.2 Primary Clinical Outcome Measure

The rate of death or initiation of antibiotic therapy after the completion of the treatment schedule allocated at randomisation.

7.3 Secondary Clinical Outcomes

Duration of ICU stay

Duration of Hospital stay

Duration of mechanical ventilation

Incidence of infection with clostridium difficile

Incidence of infection with MRSA

7.4 Secondary Economic Outcomes

Resource utilisation and costs associated with each of the two pilot arms specifically ICU stay, hospital stay, mechanical ventilation, antibiotics and other medications, tests and procedures measured and valued up until the end of the follow-up period.

7.5 Secondary Feasibility Outcomes (Pilot Study Objectives)

The ratio of patients - screened: eligible: randomised

The incidence of cross-over between the randomised treatment groups

The accuracy of data collection assessed by a 20% source data verification check

8 SAMPLE SIZE

In common with most pilot studies, calculation of an accurate samples size is not possible due to the paucity of existing data. We will however, comply with previous recommendation for good practice that pilot randomised control trials should recruit a minimum number of 60 patients [19]. A preliminary audit of our ICU database suggests that on average about 10 patients /month in our ICU are treated for suspected infection. We aim to recruit at least 5 patients /month (50% recruitment rate) within the duration of 12 months.

9 DATA COLLECTION

A Manual of Operation containing relevant procedural instructions and definitions will be produced. Structured Case Record Forms (CRFs) will be used to record data at each stage of the patient journey through the trial. Trial documentation will be completed by specific Research Nurses working on the project (Claire Prince and Sandra Roberts). In addition, a medically qualified Clinical Research Fellow will be responsible for day to-day monitoring of recruitment activity and assist in maintaining the screening log and obtaining trial consent/assent. Trial related data will be transcribed into a bespoke, secure, password protected database in the Clinical Trials Unit.

Prospective monitoring of adverse and clinical events will start at randomisation and will continue until the end of the trial follow-up period. The Research Nurses will be

responsible for “tracking” each patient during their hospital stay to ensure that all tests are carried out and blood samples have been taken at the designated time. The reasons why an eligible patient does not proceed to randomisation will be recorded in the trial specific screening documentation and database.

9.1 Resource Utilisation Data Collection

Costs associated with each of the two pilot arms, length of intubation, ICU and hospital ward stay and medications will be estimated to the end of the follow-up period. The cost of antibiotics including the number of regimes used, and length of time on each regime in each arm will be calculated. A preliminary measure of key cost drivers will be estimated by applying routinely collected unit cost figures (NHS Reference costs and PSSRU unit costs), for ICU, ward and BNF prices for medications, to quantify resource utilisation over the length of the follow-up period of the study.

10 STATISTICAL ANALYSIS

The clinical and economic impact of 7 days versus 2 days antibiotic treatment will be examined. Categorical outcome measures will be examined using a Chi-square test or Fisher’s exact test as required. Length of ICU stay will be compared using the independent sample t-test or Mann-Whitney non-parametric test if necessary. The potential cost differences per patient will be estimated with confidence intervals. Exploratory analysis will be undertaken using Bayesian Value of Information methods described by Tan and Smith 1998 [20] that balance the benefit of detecting a minimally significant difference with at least a given power against the costs of the patient sample size and/or the risk that the research poses to patients (e.g. the probability of incompletely treating sepsis in the intensive care unit). The result of this analysis will provide guidance on the optimal sample size to use in a future RCT that would seek to evaluate the antibiotic regimen studied in this pilot study.

11 ETHICAL ARRANGEMENTS

The study will be conducted according to the principles of the Declaration of Helsinki (www.wma.net) and Good Clinical Practice, NHS Research Governance (www.doh.gov.uk), EU and NHS Governance Framework. The study will be sponsored by the Liverpool Heart & Chest Hospital NHS Trust. The trial protocol will be approved by an internal review board and the local Research Ethics Committees via the Integrated Research Application System. Approval from the ethics committee will be obtained if the consent form is updated or amended whenever new information becomes available that may be relevant to the patient. Patient’s right to privacy will be respected at all times to

comply with the Data Protection Act 1998 and Caldicott Principle. Medical records may be inspected for monitoring auditing purposes by individuals from the Clinical Trials Unit, Liverpool Heart & Chest Hospital NHS Trust. Patients consent to this as part of the written informed consent process. All information will be stored in a password protected NHS computer.

11.1 Risks and Anticipated Benefits for Trial Participants and Society

It is common practice to administer broad-spectrum empirical antibiotics to ICU patients who are suspected on clinical grounds of developing generalised nosocomial infection of unknown origin. However no evidence from prospective randomised studies is available to demonstrate risks associated with duration of antibiotic usage. The possible risks of taking part are common to all patients with suspected sepsis/infection. In addition, there is a possible small risk of recurrence of nosocomial infections associated with a reduced antibiotic treatment regimen. We anticipate that the risks associated with the trial are outweighed by potential benefits to the patients and society as whole as follows:

- Reduction in NHS costs by cutting overall ICU treatment costs
- Reduced risk of patients developing antibiotics resistant organisms
    - e.g. MRSA infection rate in ICU is currently at 10% of all admissions [21]
- Reduced risk of patients acquiring other infections
    - e.g. Clostridium difficile, estimated incidences at 2.2-3% of admissions [22]
- Reduced exposure of patients to unnecessary treatment with risk of allergic reactions

11.2 Informing Potential Trial Participants of Possible Benefits and Known Risks

The patient and family will be given information sheets, describing the nature of the study and a consideration of risks, benefits and implications for care. The content of the information sheets will have been approved by the ethics review process and internal mechanisms for oversight by our Trust Service Users Research Group.

Potential participants will be allowed some time for consideration but the nature of the clinical setting and the perceived imperative for early intervention means that the period for reflection may be limited to an hour. There will of course be opportunities for questions and dialogue with trial personnel. If a decision about trial participation cannot be made in this time scale the patient will be excluded from randomisation (a key aspect of the secondary feasibility outcome measures).

11.3 Obtaining Informed Consent from Participants Whenever Possible and Proposed Action When Fully Informed Consent is not Possible

In line with DIRECTIVE 2001/20/EC OF THE EUROPEAN PARLIAMENT of 2001 all research patients are required to provide written informed consent before enrolment in a trial. However, since most of the potential participants in this study will be under sedation or under the influence of anaesthetic agents, and therefore *incompetent*, in terms of understanding a research protocol and decision-making capacity an "assent" will be obtained from *surrogates* such as from a legal representative (next of kin or independent professional doctor/nurse). We have experience of conducting similar studies in Liverpool and procedures for obtaining assent are in place [11].

In summary, the research protocol will be approved in advance by our institutional Research & Development Committee. Before obtaining informed assent, information will be given in a language and at a level of complexity understandable to the patient's legal representative in both oral and written form by the investigator or designee. Legal representatives will not be coerced or unduly influenced in order for the patient to participate or remain in the trial. A legal representative will be given ample time and opportunity to inquire about details of the trial and all questions about the trial should be answered to the satisfaction of the representative. If the legal representative is unable to read the consent form, a witness should be present during the entire informed assent discussion. After the informed consent form is read to and signed by the legal representative, the witness should also sign the consent form, attesting that informed assent was freely given by the patient's legal representative. The patient's legal representative must receive a copy of the signed and dated informed consent form. When the patient gets better they will then be asked either in person or in writing if they are happy with this decision retrospectively and whether the information gathered on them as part of the study can be used. Patients that decline consent at this stage will not be included in the study and their results will not be used. Patient will be informed that they may withdraw or discontinue from the study anytime without giving an explanation and that their action will not affect their standard of care. Patient's that die after randomisation will have their data included in the final analysis, unless legal representatives raise objections.

12 TRIAL ADMINISTRATION AND DOCUMENTATION

12.1 Retention of Trial Documentation

The trial documentation and data will be stored in a secure storage facility within the Clinical Trials Unit for a period for at least 7 years after study completion.

12.2 Proposed Action to Comply with 'The Medicines for Human Use (Clinical Trials) Regulations 2004

The trial is not testing a new medicinal product. It is only comparing the duration of treatment with existing drugs not the type of antibiotics to be used for patient with sepsis therefore, “the medicines for human use Regulations 2004” do not apply. However, a request for authorisation to conduct this clinical trial or clarification shall be made to the licensing authority (i.e. the MHRA) by the sponsor of the trial.

12.3 Safety Reporting

The study procedures adopted here are part of normal clinical practice. Safety will be assessed by tracking the number and percentage of adverse events (AEs) up to discharge from hospital. Serious and other adverse events will be recorded and reported in accordance with the International Conference for Harmonisation of Good Clinical Practice (ICH GCP) guidelines/the European Clinical Trials Directive 2001/20/EC and the Sponsor’s Research Related Adverse Event Reporting Policy. ICH GCP requires that both investigators and sponsors follow specific procedures when reporting adverse/reactions in clinical trials. All serious adverse events **must** be reported to the steering committee and documented in CRFs. Such events result in death or are life-threatening, require hospitalisation or prolongation of existing hospitalisation, result in persistent or significant disability or incapacity or may have created a congenital anomaly or birth defect

Examples would include, but are not limited to:

- Deaths related or unrelated to infection/antibiotic treatment for healthcare-acquired infection
- Life-threatening bleeding
- Intracranial haemorrhage
- Cerebrovascular accident
- Profound thrombocytopenia (platelet counts≤ 50,000/mm^3)
- Occurrence of MRSA isolation
- Occurrence of Clostridium difficile infection
- Allergic reactions

12.4 Adverse Event

Any untoward medical occurrence in a patient or clinical trial subject to whom a medicinal product has been administered including occurrences which are not necessarily caused by or related to the product.

12.5 Adverse Reaction

Any untoward and unintended response to an investigational product related to any dose administered.

12.6 Unexpected Adverse Reaction

An adverse reaction, the nature or severity of which is not consistent with the information about the medicinal product in question set out in the summary of product characteristics (or investigator brochure) for that product).

12.7 Research Governance

The Liverpool Heart & Chest Hospital NHS Trust as the sponsor for this trial will ensure that the rights, safety, and wellbeing of participants will be safe guarded. Issues of consent and confidentiality are paramount in line with the *MRC Guidelines for Good Clinical Practice in Clinical Trials*. Individual patient medical information obtained as a result of this study is considered confidential and disclosure to third parties is prohibited. Patient confidentiality will be further ensured by utilising patient-identification code numbers to correspond to treatment data in the computer files. With appropriate patient authorisation, medical information may be given to the patient's personal physician or to other appropriate medical personnel responsible for his/her treatment. Data generated as a result of this trial are to be made available for inspection on request by the participating physicians, by the Ethics Committee and the regulatory authorities.

12.8 Interim Analysis and Stopping Rules

There is no planned interim analysis or stopping rules for the primary outcome measure, because by the time sufficient data has been accrued, the recruitment will almost be complete.

12.9 Major Protocol Violation

Major protocol violations will be documented including: failure to ensure adequate informed consent, recruitment of ineligible patient into the study on the basis of the inclusion and exclusion criteria and incorrect randomisation of a patient such that the patients are entered into the wrong treatment arm for clinical reasons. During the course of the trial, protocol deviations will be tracked.

12.10 Indemnity and Insurance

The Liverpool Heart & Chest Hospital NHS Trust is covered under the standard NHS indemnity sponsorship for the study.

12.11 Trial Organisation

12.11.1

(i) Steering Committee

Professor Paulo Lisboa, Dr Nigel Scawn, Dr Rod Stables, Mr Nathan Howes, Dr Nagesh Kalakonda, Dr Carlos Nistal De Paz, Dr Bashir Matata, Dr Mark Jackson, Dr Alan Haycox, Professor Cheng-Hock Toh, Mr Keith Wilson, Dr Steven Lane.

The Steering Committee will be responsible for finalising the protocol, discussing any required amendments, monitoring recruitment rates, ensuring the study runs to time and generally overseeing the running of the study. The TSC will include the principal investigators, lay patient representative in the TSC, expert TSC members, trial statisticians and trial co-ordinators. The TSC have responsibility for the day-to-day conduct of the trial.

(ii) Data Monitoring Committee

Dr Peter Booker, Dr Richard Wenstone, Dr Robert Harris, Dr Bashir Matata.

It is the only body involved in a trial that has access to the unblinded comparative data. The role of its members is to monitor these data and make recommendations to the TSC on whether there are any ethical or safety reasons why the trial should not continue. The safety, rights and well-being of the trial participants are paramount. The DMC considers the need for any interim analysis advising the TSC regarding the release of data and/or information. The DMC may be asked by the TSC, Trial Sponsor or Trial Funder to consider data emerging from other related studies. If funding is required above the level originally requested, the DMC may be asked by the Chief Investigator, TSC, Trial Sponsor or Trial Funder to provide advice and, where appropriate, information on the data gathered to date in a way that will not compromise the trial. Membership of the DMC should be completely independent[1], small (3 members) and comprise experts in the field, e.g. a clinician with experience in the relevant area and expert trial statistician.

[1] Independence, in respect of the DMC, is defined as independent from the Chief Investigator, TSC and Host Institution.

12.11.2 Study Director

Dr Nigel Scawn

12.11.3 Local Institution Governance

The Research Governance Department, LHCH NHS Trust

12.11.4 Independent Monitoring

The Research Governance Department, LHCH NHS Trust

The Clinical Trials Unit at the Liverpool Heart & Chest Hospital NHS Trust will undertake day-to-day management and co-ordination of the trial and are responsible for the collection, management, storage and analysis of all patient information.

12.11.5 Database Coordinator

Ian Kemp

12.11.6 Research Coordinators

Ian Kemp

12.11.7 Trial Statistician

Dr Steven Lane

12.12 Publication Policy

The investigators are committed to the publication and widespread dissemination of the results of the study. There is an agreed policy that the recommendation of any party concerning manuscripts or text shall be taken into consideration in the final preparation of scientific documents for publication and presentation. The Steering Committee will be responsible for finalising the protocol, discussing any required amendments, monitoring recruitment rates, ensuring the study runs to time and generally overseeing the running of the study. The trial protocol will be ISRCTN registered before the start of recruitment.

13 SERVICE USERS INVOLVEMENT

Our institution has established a Service Users Research Endeavour (SURE) group that has been active for more than 10 years. The SURE group is actively involved in our research as follows;

- Helps researchers to identify and ask the right questions in their project proposals
- Makes sure that the research questions are relevant to patients, people using the service and the public in general
- Gets involved in the research process itself, in terms of designing and managing service user-led projects
- Helps in analysis and dissemination of study results
- Assists final internal R&D study approval

This proposal has been reviewed by our patient service user group (SURE) and any opinions and comments incorporated. A patient representative will attend TSC meetings and be directly involved in decision making of trial process and then relay back information to the SURE groups on a regular basis.

14 TRIAL FUNDING

The pilot trial costs are £ 169,821.32 to be funded by a grant from the Health Technology Assessment programme. For the justification of costs and roles of team members please see the Finance Form for details of specific costs.

15 REFERENCES

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