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LeoPARDS

Levosimendan for the Prevention of Acute Organ Dysfunction in Sepsis

Patient Information Sheet

You are being invited to continue taking part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish.

This sheet tells you the purpose of this study, what has happened and will happen to you if you continue taking part and provides more detailed information about how the study is being carried out. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to continue taking part. Thank you for reading this.

What is the purpose of the study?
We are investigating a treatment for septic shock. This is the low blood pressure that can occur when the body has an overwhelming infection. This is a medical emergency that requires urgent treatment with fluids and other drugs to help raise blood pressure. The low blood pressure can reduce the blood flow and delivery of oxygen to important organs in the body and impair the function of the heart. In turn this can cause these organs to stop working normally and can result in problems such as kidney failure.

The body normally produces stress hormones such as adrenaline to help raise blood pressure but it may be unable to do this when it is fighting an overwhelming infection. Treatment of septic shock includes giving patients adrenaline-like drugs via drips into a large vein. However, we know that adrenaline-like drugs can have side-effects.

We are investigating a different type of drug called levosimendan that works in a different way to adrenaline-type drugs. This drug is widely used in Europe for treating patients with heart failure but recently it has been shown that it could help patients with septic shock too. We plan to test if levosimendan improves blood flow to prevent organs failing and if it can reduce the side-effects of adrenaline type drugs.

Why have I been chosen?
You have been asked to take part in this study as your blood pressure has been low due to a severe infection and was being supported with powerful adrenaline-like drugs. We are planning to study 516 patients in total, admitted to different hospitals within the UK.

Do I have to take part?
It is up to you to decide whether or not to continue taking part. As many patients who have septic shock can initially be too ill to make decisions about participation, and treatment is an emergency, we have already spoken to your relatives / close friends / doctors about your participation and begun treatment as part of the study. If you do decide to continue in the study, you will be given this information sheet to keep and be asked to sign a consent form. If you decide to continue you are still free to withdraw at any time and without giving a reason. A decision to withdraw at any time will not affect the standard of care you receive.

What will happen to me if I take part?
This is a randomised study. Sometimes we need to make comparisons to see which way of treating patients is the best. People are put into groups and then compared. The groups are selected by a computer which has no information about the individual – i.e. so patients are put into the groups by chance. Each group then have a different treatment and these are compared.

You were assigned to one of two possible treatment groups. All patients in both groups are given all usual treatments. You may have been assigned to a group given an infusion of levosimendan for 24 hours or you may have been in the group given a placebo infusion instead of levosimendan. A placebo is a dummy treatment that looks like the real thing but is not. It contains no active ingredient.

This is a double-blind study. In a blind trial the patient does not know which treatment group they are in. In a double-blind trial, neither the patient nor the medical staff knows which treatment group the patient is in (although, if the medical team can find out if they need to). A double-blind study helps make sure the results of the trial are not affected by doctors' or patients' personal preferences. The drug was given at a standard rate that was reduced as necessary if serious side effects occurred. The drug was given for a period of 24 hours after which it was or will be stopped.

In some hospitals we are also collecting blood samples (the equivalent of five teaspoons on each of four occasions) and urine during your first week in the Intensive Care Unit. These samples will normally be collected from drips, lines and catheters already in place as part of your normal care. These samples will be used to measure levels of certain blood chemicals that we believe are important in severe infections and will allow us to evaluate the effects of levosimendan on the function of certain organs. Also, we will measure the amount of levosimendan in the blood samples from 80 patients to identify how quickly the drug is cleared from the body in septic shock. This requires an additional teaspoon of blood to be collected on an additional three occasions.

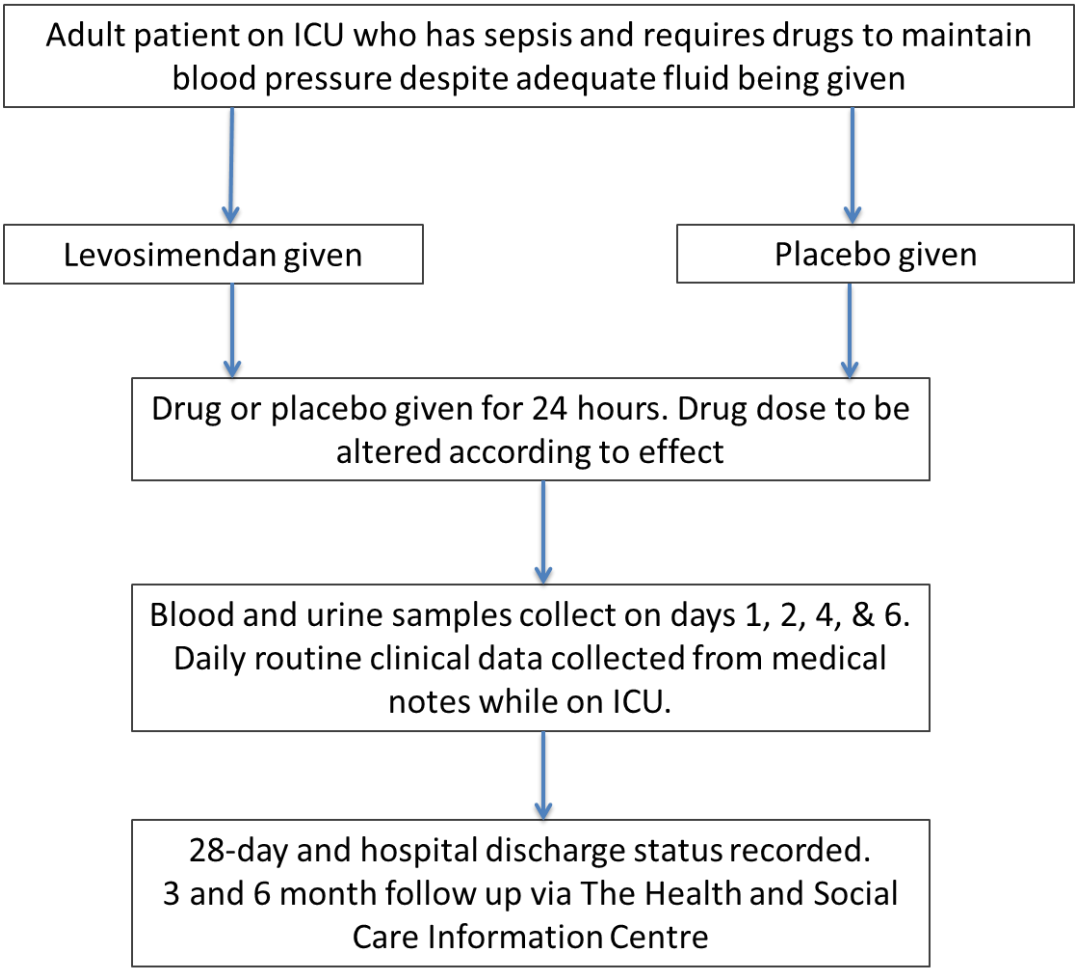
All samples will be coded and not contain any personal identifying information. These samples will initially be stored at this hospital and then be sent to Imperial College for storage and analysis. The samples for measurement of drug levels in the blood will be sent to Orion Pharmaceuticals, the manufacturer of the drug as they have the expertise needed to analyse these types of samples. Orion will not be given any personal identifying information. Samples will be stored beyond the end of this study in accordance with the Human Tissue Act.

What do I have to do?
You will not have to do anything different if you decide to continue in the study. The medical and nursing staff prescribed and administered the study drug to you, while on ICU along with your other normal medications. The study drug will be stopped after 24 hours (this may have already occurred). We will continue to collect daily clinical information from your medical notes relating to your condition throughout your stay in hospital. The study will not continue once you have left ICU other than to collect information about when you leave hospital.

With your consent, we will share your name, postcode and date of birth with the Health and Social Care Information Centre. This will enable the Health and Social Care Information Centre and other central UK NHS bodies to provide us with information about your health status after hospital discharge for up to 6 months.

If you do not wish continue in this study, no further information will be collected about you for the trial and the doctors will continue to provide you with whatever medical treatment is needed.

Treatment plan:



What is the drug that is being tested?

The drug being tested is called levosimendan. One of its main effects is that it improves the function of the heart. In fact, levosimendan drug was originally developed for the treatment of severe heart failure. However, researchers have shown that it has other effects on the body, including improving blood flow to certain organs such as the kidney, and have shown it may be of benefit in patients with septic shock. In small studies levosimendan was seen to improve kidney function as well as heart function in such patients. We therefore want to investigate whether levosimendan can improve organ function in septic shock and lead to better outcomes for patients.

What are the side effects of any treatment received when taking part?

Levosimendan has been given to around half a million patients with heart failure and it is generally accepted as being a safe drug with a low risk of side effects (less than 1%). The commonest side effect is a fall in blood pressure, which can be made less likely by ensuring patients have received enough fluid. This may have required the dose of adrenaline-like drugs that you were receiving to be increased temporarily, which is part of routine care within the ICU. Other much less common side effects are abnormal heart rhythms and low potassium levels. The doctors and nurses looking after you have and will watch carefully for these possible side effects and will treat them as necessary and even stop the study drug if needed.

What are the possible benefits of taking part?
It is possible that treatment with levosimendan may improve the function of certain organs for patients with septic shock. It may also reduce the use of adrenaline–type drugs and thus reduce their side effects. We cannot guarantee taking part in the study will benefit you directly but if this study shows a benefit then it might help improve the treatment of people with septic shock in the future.

What are the possible disadvantages and risks of taking part?
There is a small additional risk from taking part in this study due to the possible side effects of levosimendan. However, we know from the studies carried out previously that serious side effects are uncommon.

Blood samples need to be collected, but only in very small quantities. This will usually be done from existing lines, but it might be necessary to collect a sample from a new needle, which might result in some minor discomfort during collection and possibly a small bruise.

What if something goes wrong?
Imperial College London holds insurance policies which apply to this study. If in the unlikely event you experience serious and enduring harm or injury as a result of taking part in this study, you may be eligible to claim compensation without having to prove that Imperial College is at fault. This does not affect your legal rights to seek compensation. If you are harmed due to someone's negligence, then you may have grounds for a legal action.

If you wish to complain, or have any concerns about any aspect of the way you have been treated during the course of this study then you should immediately inform the local Investigator. The normal National Health Service complaints mechanisms are also available to you. If you are still not satisfied with the response, you may contact the Imperial AHSC Joint Research Office.

Will information from this study be kept confidential?
All information, including personal information, which is collected about you during the course of the research will be kept password protected and strictly confidential. Any information about you which leaves the hospital will have your name, hospital number and address removed and will be identified only by your Trial subject number, date of birth and initials, so that you cannot be recognised from it. This is with the exception of information obtained from The Health and Social Care Information Centre as described earlier Only the researchers, trial monitors on behalf of the Sponsor (Imperial College) and representatives of regulatory authorities and research ethics committees may have direct access to it. Other doctors in this hospital treating you, and your GP will be told of your participation in this study.

What will happen to the results of the research study?
The results of this study will be presented at medical meetings and published in scientific journals. Only group information and no personal information will be presented.

Who is organising and funding the research?
This study is being organised by doctors and scientists in Imperial College, London. It is funded by the National Institute for Health Research.

Who has reviewed the study?
All research in the NHS is looked at by an independent group of people called a Research Ethics Committee. This study has been reviewed and approved by the NRES Committee London - Harrow Ethics Committee. Patients and the public have also been involved in the design of the research and reviewing the study documents.

Who can I contact for independent research information?
If you have any questions about being in a research study, you can contact the Trust's Patient Advice Liaison Service (PALS). They will give you advice about who you can talk to for independent advice.