AUCKLAND CITY HOSPITAL

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Participant Information and Prior Consent

A phase III randomised controlled trial of continuous beta-lactam infusion compared with intermittent beta-lactam dosing in critically ill patients (**BLING III**)

ICU:	**Department Critical Care Medicine, Auckland City Hospital**	**Ethics Committee Ref:**	**18-NTA-08**
Local investigator:	**Dr. Colin McArthur**	**Contact Phone Number:**	**09 3074949 ext. 24800**

WHAT IS THE PURPOSE OF THIS INFORMATION SHEET?

Our intensive care unit (ICU) is participating in a study comparing two different administration methods of beta-lactam antibiotics: continuous intravenous (IV) infusion, given continuously over 24 hours into the vein, or intermittent IV infusion, given at regular intervals over 24 hours into the vein.

The aim of study is to determine the best administration method for patients with suspected or confirmed infection that will allow doctors in the future to make informed decisions about which administration method they should use prescribe.

The purpose of this information sheet is to inform you about this study so that you can decide whether you **would like to participate in the study**.

It is important that you understand this information sheet. It includes details we think you need to know about the study. We will go through this information sheet with you and answer any questions you may have, take as much time as you need. You may want to discuss this with others. Participation in this study is entirely voluntary (your choice). All patients in this ICU receive the best possible care whether they participate in research studies or not.

WHAT IS THE PURPOSE OF THE STUDY?

Patients suffering from severe infections are sometimes managed in the ICU where they may require antibiotics and other therapies to support the functions of the body.

The purpose of this study is to determine whether critically ill adults with infection who require a beta-lactam antibiotic have better survival 90 days after going into the study if the antibiotics are given via continuous infusion as compared to intermittent infusion.

Beta-lactam antibiotics are a group of antibiotics commonly used to treat infection. Currently, beta-lactam antibiotics are most commonly given to patients as intermittent infusions, that is, given into the vein (IV) at regular intervals 3 or 4 times a day. However, giving beta-lactam antibiotics as a continuous infusion into the vein over 24 hours may mean that antibiotic levels in the blood remain more consistent and may be more effective at killing bacteria. Previous studies in humans have not been large enough to show if there is any benefit to patients by giving beta-lactam antibiotics this way. The purpose of this research is to explore whether beta-lactam antibiotics work better when they are administered by 24 hour continuous infusion as opposed to multiple intermittent infusions each day.

The antibiotics being studied are registered drugs currently used to treat infection. You will receive one of these antibiotics to treat your infection regardless of whether or not you are enrolled in the study. You may also receive other antibiotics and medications as part of your treatment and this will not affect your involvement in the study.

This study is endorsed by the Australian and New Zealand Intensive Care Society Clinical Trials Group.

WHAT WILL MY PARTICIPATION IN THE STUDY INVOLVE?

This study will include 7000 ICU patients from New Zealand, Australia, South Africa, Malaysia, The United Kingdom and Europe. Around 500 patients will be from New Zealand. The study will take about 4 years to complete and results will be known in about 5 years.

If you decide to participate then you will be "randomised" into one of two groups. Randomisation means that you are put into a group by chance (like flipping a coin). There is no way to predict which group you will be assigned to. There is a 50% chance of receiving the antibiotics via continuous infusion and 50% chance of receiving the antibiotics intermittently. Neither the study staff, nor the doctors involved in your care choose which group you will be in.

Group 1: Continuous infusion antibiotics

If you are randomised to this group, following an initial dose, the antibiotic will be administered continuously into the vein over the 24 hour period.

Group 2: Intermittent infusion antibiotics

If you are randomised to this group, the antibiotics will be administered via an intermittent infusion into the vein over 30 minutes, 3-4 times a day.

For all study participants

All study participants receive the same dose of the antibiotic over 24 hours regardless of which group they are randomised to. The only difference between the two groups is the method of administration, that is, whether the antibiotic is given by continuously or intermittently.

If you still require the antibiotic when you leave the ICU, you will receive this via the standard administration method used on the ward.

You will be followed by the ICU research team to collect study data including age, sex, hospital admission dates, severity of disease, reason for ICU admission and underlying disease etc. We also collect data regarding signs and symptoms of your infection, blood test results, any side effects and health status at the time of ICU and hospital discharge.

Following discharge from hospital

When you are discharged from hospital, a research coordinator will contact you or another nominated person by telephone around 90 days after going into the study. The purpose of this call will be to see how you are recovering. The research coordinator will also ask you, or another person chosen by you, some questions about your quality of life, which should only take about 10 minutes. If there are any concerns about the health or wellbeing of the participant during these telephone calls the research coordinator will discuss these with them and may, with the participants permission, inform their General Practitioner (GP) or other healthcare professional. If it is not possible to obtain permission from the participant the research coordinator can advise the nominated person on who they should contact for further help and support.

WHAT ARE THE POSSIBLE BENEFITS AND RISKS OF THIS STUDY?

In any clinical trial, side effects, both expected and unexpected, are possible. In spite of all reasonable precautions, participants might develop medical complications from participating in this study. We do not expect any side effects beyond those associated with usual care for patients in the ICU. Regardless of participation in this study, your doctor has prescribed a beta-lactam antibiotic to treat your infection.

As you will be in the ICU when the antibiotics are given, you will be closely monitored and treated immediately if problems arise.

You may experience side effects from participating in this study. However, these side effects exist even if you did not participate in this research study because all patients with infections will be prescribed antibiotics to treat the infection. Although the beta-lactam antibiotics (piperacillin-

tazobactam and meropenem) have been given to many patients over many years and are in regular and current use, there may be additional unforeseen or unknown risks.

If at any point during the study your doctor felt it was not in your best interests to continue to receive the beta-lactam antibiotic via the study administration method you were randomised to, or if during the study there is evidence to suggest beyond reasonable doubt that one administration method is more beneficial than the other, then your involvement in the study may be stopped.

Although we do not know whether continuous or intermittently giving antibiotics is best, you may or may not benefit directly from participating in this study. The research staff will be reviewing your laboratory results and antibiotic therapy each day that you are in the study. Your participation may or may not help other people with infections in the future but by participating in this research, you may contribute to the knowledge and development of new treatment strategies for infections in the future. We hope the information learned from this study will help other people with similar infections in the future.

WHO PAYS FOR THE STUDY?

This study is funded by the National Health and Medical Research Council of Australia.

There is no cost to participating in this study and there is no payment for participation.

WHAT IF SOMETHING GOES WRONG?

If you are injured in this study, which is unlikely, you may be eligible for compensation from ACC just as you would be if you were injured in an accident at work or at home. This does not mean that your claim will automatically be accepted. A claim would have to be lodged with ACC, which may take some time to assess. If the claim is accepted, you may receive funding to assist in their recovery.

WHAT ARE MY RIGHTS?

Participation in this research study is voluntary. You can change your mind about participating without giving a reason, and, if you do you will continue to receive the best possible care.

Participants have the right to privacy. All information that is collected during this study is confidential to the extent permitted by the applicable laws and regulations. Study participants will be assigned a unique number and will be identified only by this number. The medical information collected during this study will be transferred into the study database and processed to allow the results of this study to be analysed and reported or published for scientific purposes. The data collected in New Zealand is being shared with Australia via a secure server, and all data analysis will be undertaken in Australia. Study results will be published in a form that will not allow the identification of individual study participants.

The identity of participants will be kept confidential at all times. The data collected for the study may be viewed by members of the Ethics Committee. The data will be shared with the BLING III study management committee or their approved representative to check that the study is being carried out correctly. All staff have a duty of confidentiality to research participants and nothing that could reveal your identity will be disclosed by these persons.

Study data will be stored in a secure location for a period of 15 years after the study is complete.

WHO DO I CONTACT FOR MORE INFORMATION OR IF I HAVE CONCERNS?

A description of this clinical trial will be available on http://www.clinicaltrials.gov This website will not include information that can identify you. You can search this website at any time. The study identifier is NCT03212990.

If you have any questions, concerns or complaints about the study at any stage, you can contact:

Dr. Colin McArthur or Study (Research) Coordinators on ph: 09 3074949 ext. 24800

If you want to talk to someone who isn't involved with the study, you can contact an independent health and disability advocate on:

Phone: 0800 555 050
Fax: 0800 2 SUPPORT (0800 2787 7678)
Email: advocacy@hdc.org.nz

For Maori health support please contact :

1. For support, talk to your whānau in the first instance.
2. Alternatively you may contact the administrator for He Kamaka Waiora Māori Health Team on 09 486 8324 ext 2324.
3. If you have any questions or complaints about the study, you may contact the Auckland and Waitematā District Health Boards' Māori Research Committee or Māori Research Advisor by phoning 09 486 8920 ext 3204

You can also contact the health and disability ethics committee (HDEC) that approved this study on:

Phone: 0800 4 38442 (0800 4 ETHIC)

Email: hdecs@moh.govt.nz

If you agree to participate in the study you will be asked to sign the Consent Form and you will be given a copy to keep for your own reference.

Thank you in advance for your help in this study