Prevention of acute muscle wasting in critically ill adults using enteral ketogenic feeding: the Alternative Substrates In the Critically Ill Subject II (ASICS –II) trial

PATIENT INFORMATION SHEET

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REC: XXXX

Introduction

We are inviting you to decide if you would like to take part in a clinical study, which we hope will prevent the muscle weakness that many of our patients who are admitted to critical care unit suffer from. This weakness leaves them struggling with doing basic activities like going to the toilet, getting dressed or getting out of bed, leaving them needing a lot of help.

This study will help us understand if giving people a vegan, non-alcoholic feed that makes the body produce ketones naturally, instead of the regular feed given in ICU, will stop patients losing muscle. Before you decide, it is important to understand why we are doing this research and what it involves. Please take time to read the following information and decide whether you would like to take part.

Why are we doing this research?

Increasing numbers of patients are surviving critical illness because of improvements in care on ICUs. Weakness is common after being on an ICU and can last for a very long time - even years - into recovery. We know that patients lose a lot of muscle while on an ICU, and this causes most of the weakness. This weakness makes it harder for patients to return to their normal lives when they leave hospital. Patients struggle to do basic care like going to the toilet, getting dressed or getting out of bed alone, meaning they need a lot of care and support for years. This places a huge burden of patients, families and carers, many of whom also suffer mental ill health and loss of money as a result. We think we might be able to prevent this if we change the way we feed the patients.

Patients on the ICU are often unable to eat food normally due to their illness and the treatment. For this reason, liquid (watery) feed is usually given continuously through a feeding tube which

is passed through the nose and into the stomach. However, we think the contents of the feed might contribute to the patients losing muscle, and that giving a feed which will push the body to produce chemicals naturally called ketones might be better. We would like to find out if this is true.

Why have I been invited?

We have invited you to consider taking part in this study because you have been admitted to our critical care unit and the doctors and nurses treating you have identified you to be considered suitable to be included in the study.

Do I have to take part?

No. It is up to you to decide whether or not you would like to be involved in the study. If you decide to take part in this study. You are free to withdraw from the study at any time, without giving a reason. If you decide that you do not want to take part, or later to withdraw from the study, this will not affect the standard of care you will receive.

What will happen to me if I take part?

If you agree to take part, we will ask you to sign a consent form. Sometimes, we do not know which is the best way of treating patients. To find out if there is a difference in muscle loss when giving a liquid feed that encourages the body to produce ketones, compared with the standard feed. We will put each patient who has agreed to take part in the study into either the experimental group (receiving ketogenic feed) or the standard feed group. A computer programme will randomly assign patients to one of two groups. This makes sure there is an equal chance of being placed in each group. Neither you nor the doctor could choose which feeding group you went into. All other care that you will receive with be the same as you would receive if you weren't taking part in the study. We will place the feed in specially coloured bags, so no-one will know which group you are in until the very end of the study.

For every patient, feeding via the tube will continue for the first 10 days or until the patient is able to eat. It will be slowed or stopped if they can't absorb the feed they are being given. Patients in both groups will be prescribed the amount of food they need, based on weight, height and their clinical condition.

On days 1, 7 and 10 from entering the study, we will measure the size of part of the thigh muscle using an ultrasound machine (it is the same machine used to scan pregnant women). It is a painless and perfectly safe technique that has no known side effects. We will also measure fat and muscle using a technique called "bioimpedance" as is often done in gyms and home

weighing machines. This is also a painless and perfectly safe technique that has no known side effects.

We will take a small sample of blood on days 1, 7 and 10 of being in the study. All samples will be held securely, in access-controlled buildings, with access-controlled laboratories, with temperature-controlled and monitored freezers. Access to samples will be to members of the research team only. All samples will be stores in pseudonymised (this means we replace your name with a code, so your data can't easily be traced back to you) form and therefore, no-one will be identifiable from them. Samples may be sent to other laboratories in the UK. The blood samples will be used to measure ketone levels, changes to the way the body's metabolism works, and how it responds to being critically ill. At the end of the study, if there is no consent for future research, or if there is no further application to a research ethics committee to perform future research, the samples will be destroyed in accordance with the Human Tissue Act.

At around 30 days from being in the study, researchers will ask you to perform a simple physical assessment to see how many times you can stand up from sitting in a chair over 30 seconds. If you are in hospital, this will be done in person. If you are at home, this will be done via video or telephone conference call.

We will also ask you to complete a questionnaire about your quality of life, and function, 30 and 90 days from being in the study. We will contact you by telephone, and the questionnaires will be completed by telephone. This will help us to understand more about the impact of muscle loss from a stay in the ICU.

In either group, you will still be given all the routine treatment that you would receive if not being in the trial. We will partially use results from standard assessments performed when admitted to the hospital, and will therefore, look at your medical records. We would also like to do a telephone follow-up at 1 month, to find out about your health. You will not need to attend any follow-up appointments in person. The data we are collecting will be pseudonymised, therefore you will not be identifiable from it.

We will also tell your GP that you are participating in this study, so that they can add this to your record. We will not share any results of your study tests with them.

What will happen to the samples collected from me?

After we have collected your blood samples, we will transport it to the laboratories located at Queen Marys University of London and to other universities (University College London, University of Nottingham, University of Exeter and Oxford University). Academic and Industry partners may be sought for further analyses but the samples will be stored anonymously (but always linked to this research). All samples will be held securely, in access-controlled buildings

with access-controlled laboratories with temperature-controlled and monitored freezers. Access to samples will be to members of the research team only. All samples will be stores in pseudonymised form and therefore, you will not be identifiable from them.

We will use these blood samples to establish if you were able to make ketones, and if they are being used to prevent muscle wasting, and to see if this helps other parts of the body work well, such as the white cells in the blood. We will also collect some nutritional and biochemical data from your blood sample, in relation to the ketogenic feed and its metabolism.

At the end of the study, if there is no consent for future research, or if there is no further application to a research ethics committee to perform future research, your blood samples will be destroyed in accordance with the Human Tissue Act. If consented for samples to be used in further research, then this will be used in accordance with ethical approval obtained and at the end samples will be destroyed in accordance with the Human Tissue Act

What are the possible risks and benefits of me taking part in the study?

We are not expecting any significant side effects to occur during this study. A ketogenic diet has been used safely in our previous study of critically ill patients, and in other groups, e.g. healthy people and those who have experienced accidents, fits, or heart disease. Minor gut symptoms may occur, e.g. diarrhoea (a lot of loose stools); we would like to collect additional safety information, from close monitoring during the study period to ensure that the feed is safe. Ultrasound of the muscle does not carry any risks. We would only be requiring a small additional volume of blood from tests that would be routinely performed on you while on the ICU. The main disadvantage will be the increased amount of questions you will be asked. We have kept the demands on your time to a minimum.

We cannot promise the study will help you, but the feed that we are using in this trial may prevent muscle wasting in our patients, and help future patients who are in the ICU.

What can my I do and what should I avoid?

There are no restrictions for you with regard to taking part in this study. It will not limit your life or impact your recovery in any way. We will write to your General Practitioner to make sure they are aware of the trial.

What will happen if I don't want to carry on with the study?

You can withdraw from the study at any time. This will not affect the standard of care that you receive. We will stop the intervention (if ongoing). However, we will retain all samples and information collected from you up to this point. If you choose to stop taking part in the study, we

would like to continue collecting information about your recovery from your medical records, which you can accept or decline. We may use this data in study reports or final analyses. If you do not want us to collect any further information from your records, tell us and we will stop. Please do get in touch with the study team if you would like to withdraw from the study.

What if I am not happy about taking part in the study?

We will not make any changes to the way you are cared for in hospital. However, if you have a concern about any aspect of this study, you should ask to speak with someone from the research team, who will do their best to answer your questions. You may also contact the doctors and nurses who lead the study at this hospital on the telephone number at the bottom of this information sheet. You may also contact Patient Advisory Liaison Service (PALS) if you have any concerns regarding the care you received, or as an initial point of contact if you have a complaint. Please telephone xxxxxxx or email xxxxxxx. You can also visit PALS by asking at hospital reception.

Barts Health NHS Trust has agreed that if you are harmed as a result of participation in the study, you will be compensated, via the NHS indemnity scheme provided that, on the balance of probabilities, an injury was caused as a direct result of the procedures you received during the course of the study. These special compensation arrangements apply where an injury is caused to you that would not have occurred if you were not in the study. These arrangements do not affect your right to pursue a claim through legal action.

If you have questions about the research, you may contact Prof Zudin Puthucheary (Chief Investigator) or your local Principal Investigator at this hospital.

What if new information becomes available?

The research doctor will provide you with the details. If you think that at this point you would not want to continue with the study, then please inform the study team.

Confidentiality

Barts Health NHS Trust is the sponsor for this study based in the United Kingdom. We will be using information from you and your medical records in order to undertake this study and will act as the data controller for this study. This means that we are responsible for looking after

your information and using it properly. Barts Health NHS Trust will keep identifiable information about you for 25 years after the study has finished. Your rights to access change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible. You can find out more about how we use your information at http://www.jrmo.org.uk/.

The information we collect about you will remain strictly confidential and nothing that might identify you will be revealed to any third party. Your medical notes will be seen by authorised members of the research team at your hospital so that they can collect information needed for this trial. De-identified data will also be shared with other authenticated researchers for further research and research publications on this topic, but only if they guarantee to preserve the confidentiality of the information requested. Our procedures for handling, processing, storage and destruction of data are compliant with the General Data Protection Regulation 2016/679. Information from national databases will be obtained via strictly confidential communication. Occasionally, some patients lose touch with their hospital following their illness and we will need to collect important basic information from national records. To ensure we identify them correctly, we will need to provide your name, date of birth, postcode and NHS number to the NHS agencies that keep these records. All data will be securely transferred and stored safely on NHS computers in line with strict regulations.

What are your choices about how my information is used?

- You can request to stop being part of the study at any time, without giving a reason, but we will keep information about you that we already have and use it for analyses. This includes the results obtained from the tests done on the sample collected before you withdrew from the study.
- We need to manage your records in specific ways for the research to be reliable. This means that we won't be able to let you see or change the data we hold about you.

Where can you find out more about how your information is used?

You can find out more about how we use your information:

- at www.hra.nhs.uk/information-about-patients/
- by asking one of the research team
- by sending an email to bartshealth.ccpmg@nhs.net or

- by ringing us on 020 7480 4892
- by emailing the Barts Health Data Protection Officer -DPO.bartshealth@nhs.net

Who is organising and funding the research?

The trial is funded by National Institute for Health Research (part of the NHS). Nestle Heath Sciences, a company that has specialised in the manufacturing of nutritional feeds, will be supplying the feed to the sites involved in the study. The trial is sponsored by Barts Health NHS Trust and run by the Critical Care and Perioperative Medicine Research Group at Queen Mary University of London. Your doctor will not receive any payment for including you in the trial. Barts Health NHS Trust has submitted a patent for the feed, and the chief investigator and two of the co-investigators are named inventors on the patent.

Who has reviewed the study?

All research in the NHS is reviewed by an independent Research Ethics Committee, to protect the interests of the patients who take part. This study has been reviewed and granted a favourable opinion by the XXX REC (Date), and has also been approved by NHS Research and Development.

How do I find out about the results of the study?

The results of the study will be published online and made available through Barts Health NHS Trust research reports. We will also contact everyone who has participated to let them know the final trial result if you tell us that you want to know.

Thank You

Thank you for deciding if you can take part in this study and for reading this information sheet, which is yours to keep. If you decide to take part in the study, you will also be given a copy of the declaration form.

Your study doctor is:

Name: Contact phone number:

Your research/specialist nurse is:

Name: Contact phone number: