**Participant Information Sheet/Consent Form**

**Interventional Study** –*Adult providing their own consent (Consent to continue)*

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| --- | --- |
| **Title** | The Ketones in Neurological Damage (KIND) study |
| **Short Title** | The KIND 1.0 study |
| **Protocol Number****Date**  | 1.013/07/2023 |
| **Project Sponsor/Lead site** | Sir Charles Gairdner Hospital |
| **Co-ordinating Principal Investigator****Site Principal Investigator**  | Dr Matthew AnsteyDr Vanessa Carnegie |
| **Location**  | Sir Charles Gairdner Hospital  |

**Part 1 What does Participation involve?**

**1. Introduction**

You have been enrolled in this research project in accordance with Western Australia Guardianship and Administration Amendment (Medical Research) Act 2020 law which allows the ‘Person Responsible or Medical Treatment Decision Maker’ for a patient to consent to the patient taking part in medical research where the patient is unable to provide consent for themselves. Your ‘Person Responsible or Research Decision Maker’ consented to your taking part in this research at a time when you were unable to consent for yourself. You are now invited to consider whether you wish to continue taking part in this research project.

You have been invited to participate in this research project because you have been / were admitted to the Intensive Care Unit (ICU) in a coma as a result of a severe neurological injury due to either bleeding in the brain or brain injury after out of hospital cardiac arrest.

Usually we treat this by supporting your brain and other organs with sedative drugs, artificial ventilation, and other medications to optimize blood flow and oxygen to the brain, in conjunction with brain operations in certain circumstances.

The aim of the research project is to find out whether giving you ketone esters (an alternative energy fuel for the brain), combined with the usual treatments, is feasible and if so, this will inform future studies that can look at the possible benefits of giving ketone bodies to reduce brain damage and disability.

**2. About this Information Sheet and Consent Form**

This Participant Information and Consent Form tells you about the research project. It explains the procedures involved. Knowing what is involved will help you decide if you want to participate in the research project.

Please read this information carefully. Ask questions about anything that you don’t understand or want to know more about. Before deciding whether or not to take part, you might want to talk about it with a relative, friend or healthcare worker.

Participation in this research is voluntary. If you don’t wish to continue, you don’t have to. You may also refuse to answer any questions you do not want to answer. Even if you volunteer to continue to be in this research, you may withdraw from it any time. If you withdraw, any data collected from you up to your withdrawal will still be used for the study.

If you decide you want to continue in the research project, you will be asked to sign the Consent Form. By signing it you are telling us that you:

* Understand what you have read;
* Consent to continue to take part in the research project;
* Consent to have the tests and treatments that are described in this information sheet;
* Consent to the use of your personal and health information as described in this information sheet;

You will be given a signed copy of this Participant Information and Consent Form to keep.

**3. What is the purpose of this research project?**

There are a wide range of diseases that lead to brain injury in patients admitted to the intensive care unit. These diseases include bleeding in the brain due to a variety of causes as well as diseases that lead to a loss of adequate blood supply to the brain and death of brain cells. The patients who suffer from this spectrum of diseases and acute brain injury are often young and, if they survive, have a high burden of disability and the impacts of this on their own lives as well as the lives of their loved ones and the community.

Current therapies in ICU to support these patients focus on ways to increase oxygen and blood supply to damaged parts of the brain but little research to date has been done looking at how we can increase the energy supply to the brain.

Previous research also indicates that the acutely injured brain may struggle to use glucose – the brain’s usual energy supply – adequately and that this can worsen the damage that has already occurred to brain cells. Therefore, it is important to find alternative fuels the brain can use instead in periods of stress and disease.

Ketone bodies are by-products of the body’s metabolism of fat and are a known alternative fuel for many tissues in the body in times of stress. Previous research has also shown that ketone bodies may be useful in other neurological conditions such as epilepsy, and animal as well as human models of brain disease have suggested that they may be a useful energy source in times of stress including acute brain injury.

Traditionally, humans have increased ketones in the bloodstream by way of a specialized diet called the ketogenic diet, though this process can often take up to many days. There is increasingly interest in the use of dietary supplementation of ketones as a faster way to achieve increased ketone levels in the body.

The aim of this study is to determine the feasibility of giving ketone bodies in the form of dietary supplementation to patients with acute neurological injury admitted to ICU in order to improve neurological outcomes.

**4. What does participation in this research project involve?**

The KIND study team assessed that you were suitable to participate in this research project. Your Next-of-Kin received similar information to this and agreed on your behalf for you to take part. You were randomly assigned (like the toss of a coin) according to an allocated pre-sealed envelope to receive either ketone esters or placebo in the form of a watery solution placed down your feeding tube.

You had a 1 in 2 chance of receiving ketone esters or placebo. A placebo is an inactive and harmless ‘treatment’ given to the patients in the study who are randomised not to receive the active medication. The study is ‘blinded’. This means that you, your Next-of-Kin, the researchers and the clinical staff caring for you did not know whether you received ketone esters or placebo. The blinding and the placebo are used to ensure that the results are a true reflection of the effect of ketone esters. For this study, ‘blinding’ was conducted by administering the study medication in similar syringes. If the doctors treating you need to know which treatment you have received, the researchers will tell the doctors. The techniques of blinding and use of placebo are standard in medical trials.

You will be randomised to receive either 40 grams of ketone ester solution followed by a 10gram per hour infusion for 12 hours or similarly looking placebo within eight hours of admission to ICU.

The research team will collect the following data from your medical records and treatment flowsheet:

* demographic information including weight, height, and gender
* past medical/surgical history
* coma score on admission
* pressures within the brain
* medical diagnosis

The research team will order several sets of blood tests including your acid levels, blood sugar, and blood lactate levels at four, eight and 24 hours after ketone ester administration. They will also order blood test markers of brain injury (S100B) on admission and also 24 hours after the ketone ester or placebo is administered. They will also order several tests on the cerebrospinal fluid from your brain drain (if you already have one inserted as part of your standard care) including ketone and lactate levels at four, eight, and 24 hours after ketone ester administration.

At 3 months after participation, a research team member will make a follow-up phone call to ask you some questions about your health over the phone.

**5. What are the possible benefits?**

We cannot guarantee or promise that you will receive any benefits from this research.

Information gathered from this study will help researchers determine if ketone ester administration is feasible, and if it is, will inform future studies looking at whether they may be of benefit in improving disability and other outcomes in survivors of severe brain injury.

**6. What are the possible risks?**

The most common side effects of ketone esters reported in previous studies include changes to acid and base levels in the blood, changes in blood glucose levels, and some abdominal upset including nausea and diarrhoea. You are assessed daily by study personnel and all efforts are made to minimise discomfort from these side effects.

There is also the potential you may feel anxious by being asked to participate in a research study. We will minimize this risk by assuring you that the study is entirely voluntary, you may withdraw your continued participation and have standard of care at any time, and that the decision of whether or not to continue participation will in no way affect your care.

**7. What if new information arises during this research project?**

During the research project, new information about the risks and benefits of the project may become known to the researchers. If this occurs, you will be told about this new information and the researcher will discuss whether this new information affects you.

**8. Are there alternatives to participation?**

Participation in this research is not your only option. If you do not choose to participate in this study, you will receive standard medical treatment for severe brain injury. You can discuss this with your healthcare worker before deciding whether or not you should continue to take part in this research project.

**9. Do I have to take part in this research project?**

Participation in any research project is voluntary. If you do not wish to take part, you do not have to. If you decide to participate and later change your mind, you are free to withdraw from the project at any stage. Your decision whether you participate or not, or to take part and then withdraw, will not affect your routine treatment or your relationship with those treating you or your relationship with Sir Charles Gairdner Hospital.

**10. What if I withdraw from this research project?**

If you decide to withdraw from the project, please notify a member of the research team before you withdraw. This notice will allow that person or the research investigator to inform you if there are any special requirements to withdrawing. The researchers would like to keep the personal and health information about you that have already been collected. This is to help them make sure that the results of the research can be measured properly.

**11. Could this research project be stopped unexpectedly?**

This research project may be stopped for a variety of reasons. These may include reasons such as unacceptable side effects, the treatment being shown not to be effective or the treatment being shown to work and not need further investigation.

**12. How will I be informed of the results of this research project?**

Once the project has been completed, a summary of the results will be available from the chief investigator, Dr Matthew Anstey, on request.

**13 What happens when the research project ends?**

A follow-up phone call at 3 months following discharge will be planned to assess your quality of life using a standardised survey called the Glasgow Outcome Score Extended (GOSE). After this, your active participation in this project will end.

***14. Action If An Adverse Event Arises During The Trial***

In the event that you suffer an adverse event or a medical accident during this study that arises from your participation in the study, you will be offered all full and necessary treatment by [institution name]. The Sir Charles Gairdner Group Human Research Ethics Committee has approved this study on the basis (amongst others) that the reported risk of such an event is either small or acceptable in terms of the risk you face as a result of your current illness or the benefit that is possible with the new treatment being tested. No provisions have been made in this trial to offer trial participants who suffer an adverse reaction monetary compensation, but the absence of such a provision does not remove your rights to seek compensation under common law.

**Part 2 How is the research project being conducted?**

**15 What will happen to information about the participant?**

The information gathered about you by the investigator and the research team will be held by the investigator in strict confidence. Your trial records **without your name attached** will be made available to the study management committee and through publication in the peer-reviewed medical literature to government regulatory bodies in Australia and overseas. All the people who handle your information will adhere to traditional standards of confidentiality and will also comply with all relevant privacy legislation. In Australia this is the Privacy Act 1988. If the results of the trial are published in a medical journal, as is intended, no reader will be able to identify individual patients.

*How can I access my information?*

In accordance with relevant WA laws, you have the right to access the information collected and stored by the researchers about you. You also have the right to request that any information, with which you disagree, be corrected. Please contact one of the researchers named below if you would like to access your information.

**16 Complaints and compensation**

If the participant suffers any injuries or complications as a result of this research project, you should contact the study team as soon as possible and you will be assisted with arranging appropriate medical treatment for the participant. If you are eligible for Medicare, you can receive any medical treatment required to treat the injury or complication, free of charge, as a public patient in any Australian public hospital. Please see section 19 for the contact details of the institution for any complaints.

**17 Who is organising and funding the research?**

This research has been initiated by a Dr Matthew Anstey, ICU consultant.

The study has not received any funding and clinician’s support to the study is in-kind.

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No member of the research team will receive a personal financial benefit from the participant’s involvement in this research project (other than their ordinary wages).

**18 Who has reviewed the research project?**

All research in Australia involving humans is reviewed by an independent group of people called a Human Research Ethics Committee (HREC). The ethical aspects of this research project have been approved by the Sir Charles Gairdner and Osborne Park Health care Group ethics committee. Approval for this study has been given by [institution name], where the research will be carried out.

This project will be carried out according to the *National Statement on Ethical Conduct in Human Research (2007)-Updated 2018*. This statement has been developed to protect the interests of people who agree to participate in human research studies.

**19 Further information and who to contact**

The person you may need to contact will depend on the nature of your query.

If you want any further information concerning this project or if the participant has any medical problems which may be related to their involvement in the project (for example, any side effects), you can contact the Coordinating principal investigator Dr Matthew Anstey on *0864570076* or any of the following people:

 **Clinical contact person/s**

|  |  |
| --- | --- |
| Name | *Dr* |
| Position |  |
| Telephone |  |
| Email |  |

For matters relating to research at the site at which the participant is participating, the details of the local site complaints person are:

**Complaints contact person**

|  |  |
| --- | --- |
| Name |  |
| Position |  |
| Telephone |  |
| Email |  |

If you have any complaints about any aspect of the project, the way it is being conducted or any questions about the research participant in general, then you may contact:

|  |  |
| --- | --- |
| Reviewing HREC name |  |
| HREC Executive Officer |  |
| Telephone |  |
| Email |  |

**Reviewing HREC approving this research** **and HREC Executive Officer details**

**Local HREC Office contact (Single Site - Research Governance Officer)**

|  |  |
| --- | --- |
| Name |  |
| Position |  |
| Telephone |   |
| Email |  |

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| **Short Title** | The KIND 1.0 study |
| **Protocol Number****Date** | 1.013/07/2023 |
| **Project Sponsor/Lead site** | Sir Charles Gairdner Hospital |
| **Co-ordinating Principal Investigator****Site Principal Investigator**  | Dr Matthew AnsteyDr Vanessa Carnegie |
| **Location**  | Intensive care unit, G Block, Sir Charles Gairdner Hospital |

**Participant Consent Form**

**Interventional Study** –*Adult providing their own consent (Consent to continue)*

I have read or have had read to me in a language that I understand, the Participant Information Sheet and I understand the purposes, procedures and risks of this research project as described within it.

I have had an opportunity to ask questions and I am satisfied with the answers I have received.

I freely agree to participate in this research project as described and understand that I am free to withdraw at any time during the project without affecting my future health care.

I give permission for my doctors, other health professionals, hospitals or laboratories outside this hospital to release information to Sir Charles Gairdner Hospital concerning my disease and treatment that is needed for this project. I understand that such information will remain confidential.

I understand that the investigator and [institution name] will adhere to usual standards of confidentiality in the collection and handling of my personal information and that the standards of the Privacy Act 1988 will apply to the way my information is handled. I understand that I will be given a signed copy of this document to keep.

I understand that I will be given a signed copy of this document to keep.

**Declaration by Participant – for participants who have read the information**

|  |
| --- |
| Name of Participant (please print) \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_Signature \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Date \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ |

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| **Declaration - for participants unable to read the information and consent form**Witness to the informed consent process:Name (please print) \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_Signature \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Date \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ \* Witness is not to be the Investigator, a member of the study team or their delegate. Witness must be 18 years or older. |

**Declaration by Study Doctor/Senior Researcher†**

I have given a verbal explanation of the research project; its procedures and risks and I believe that the participant has understood that explanation.

|  |
| --- |
|  |
|  | Name of Study Doctor/Senior Researcher† (please print) |  |  |
|  |  |
|  | Signature |  |  Date |  |  |
|  |

† A senior member of the research team must provide the explanation of, and information concerning, the research project.

Note: All parties signing the consent section must date their own signature.

**Form for Withdrawal of Participation**

**Interventional Study** –*Adult providing their own consent (Consent to continue)*

|  |  |
| --- | --- |
| **Title** | The Ketones in Neurological Damage (KIND) study |
| **Short Title** | The KIND 1.0 trial |
| **Protocol Number****Date** | 1.013/07/2023 |
| **Project Sponsor/Lead site** | Sir Charles Gairdner Hospital |
| **Co-ordinating Principal Investigator****Site Principal Investigator**  | Dr Matthew AnsteyDr Vanessa Carnegie |
| **Location**  | Intensive care unit, G Block, Sir Charles Gairdner Hospital |

**Declaration by Participant**

I wish to withdraw from participation in the above research project and understand that such withdrawal will not affect my routine treatment, my relationship with those treating me or my relationship with Sir Charles Gairdner Hospital.

|  |
| --- |
|  |
|  | Name of Participant (please print) |  |  |  |  |
|  |
|  | Signature |  |  Date |  |  |
|  |

*In the event that the participant’s decision to withdraw is communicated verbally, the Study Doctor/Senior Researcher will need to provide a description of the circumstances below.*

**Declaration by Study Doctor/Senior Researcher†**

I have given a verbal explanation of the implications of withdrawal from the research project and I believe that the participant has understood that explanation.

|  |
| --- |
|  |
|  | Name of Study Doctor/Senior Researcher† (please print) |  |  |
|  |  |
|  | Signature |  |  Date |  |  |
|  |

† A senior member of the research team must provide the explanation of and information concerning withdrawal from the research project.

Note: All parties signing the consent section must date their own signature.