AH 443.21

Participant Information Sheet/Consent Form

Interventional Study - *Adult providing own consent*

Alfred Health

Title	An evaluation of the efficacy of eptinezumab in the inpatient management of status migrainosus in comparison to intravenous lignocaine in patients who have failed other therapies
Short Title	SMITE: Status Migrainosus Inpatient Treatment with Eptinezumab
Protocol Number	1.0
Project Sponsor	Alfred Health
Principal Investigator	Dr. Jason Ray/Dr. Elspeth Hutton
Associate Investigator(s)	Dr. Mahima Kapoor Dr Emma Foster
HREC Reference	HREC/77323/Alfred-2021
Location	The Alfred Hospital

Part 1 What does my participation involve?

1 Introduction

You are invited to take part in this research project. This is because you are currently suffering from a migraine, and have presented to hospital with status migrainosus (a migraine attack that has lasted more than three days). The research project is testing a new treatment for status migrainosus. The new treatment is called eptinezumab.

This Participant Information Sheet/Consent Form tells you about the research project. It explains the tests and treatments involved. Knowing what is involved will help you decide if you want to take part in the research.

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 your treating doctor.

Participation in this research is voluntary. If you don't wish to take part, you don't have to. You will receive the best possible care whether or not you take part.

If you decide you want to take part in the research project, you will be asked to sign the consent section. By signing it you are telling us that you:
• Understand what you have read
• Consent to take part in the research project

• Consent to have the tests and treatments that are described
• Consent to the use of your personal and health information as described.

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

2 What is the purpose of this research?

The aim of this study is to determine the safety and efficacy of eptinezumab in treating status migrainosus, compared to usual treatment for this condition (intravenous lignocaine). Currently, there are only limited options in treating status migrainosus, and no high-quality research into its treatment. This study will provide doctors with evidence on how to best treat patients who present to hospital with status migrainosus in the future.

Eptinezumab is an intravenous medication which targets calcitonin gene-related peptide (CGRP). Eptinezumab is approved by the Therapeutic Goods Administration (TGA) for the prevention of migraine, and has been shown in clinical trials to reduce the frequency of migraine attacks. It has not previously been studied to see if it stops an acute attack of status migrainosus in migraine patients. Therefore, it is an experimental treatment for status migrainosus. This means that it must be tested to see if it is an effective treatment. It is an infusion which takes 30 minutes. The most commonly reported side effects are nasopharyngitis (cold-like symptoms) (8%) or sensitivity reactions (flushing, hot flush, itching, allergic reaction) in 2% of people.

Lignocaine is an intravenous medication which is currently used as the standard care in treating status migrainosus. It is an anaesthetic medication which is given for up to five days to treat status migrainosus.

This research has been initiated by the study doctors, Dr Elspeth Hutton and Dr Jason Ray. It has received funding from Lundbeck Australia Pty Ltd, the company that produces eptinezumab.

3 What does participation in this research involve?

You will be invited to participate in this research if you are between the ages of 18 and 65, have a diagnosis of migraine for more than one year, and are admitted to hospital for treatment of status migrainosus that has not responded to, or have a contraindication to, standard treatment (triptans and chlorpromazine). You will be given this information to read, and have time to answer any questions you may have related to the trial. If you agree to participate, you will be asked to sign the consent form prior to any study assessments being performed.

If you consent, you will be participating in a randomised controlled clinical trial. Sometimes we do not know which treatment is best for treating a condition. To find out we need to compare different treatments. We put people into groups and give each group a different treatment. The results are compared to see if one is better. To try to make sure the groups are the same, each participant is put into a group by chance (random). This is a double-blind study. This means that neither you nor your study doctor will know which treatment you are receiving. However, in certain circumstances your study doctor can find out which treatment you are receiving.

Screening

Initially, you will undergo screening with the study doctor to ensure that you are eligible for the study. This is to ensure that this is an appropriate study for you, and that you do not have a condition that would make either treatment unsafe. This will involve:

- Asking questions related to your medical history and presentation to hospital,
- A physical examination, (including height and weight)
- Undergoing blood tests, including a pregnancy test (if applicable)
- Having an electrocardiogram (ECG).

After screening, you will be randomised to receive one of two treatments.

Study Procedures

You will receive either:

- A 30-minute intravenous infusion of 300mg of eptinezumab (the trial medication) followed by up to five days of a placebo intravenous infusion

OR

- A 30-minute placebo intravenous infusion, followed by up to five days of a lignocaine intravenous infusion (the current standard treatment, 2mg/min)

Throughout the study, you will be able to receive other pain relief medication if required.

A placebo is a medication with no active ingredients or a procedure without any medical benefit. It looks like the real thing but is not. This research project has been designed to make sure the researchers interpret the results in a fair and appropriate way.

On the first day of treatment, you will also be asked to complete four (4) questionnaires on the effect that migraine has on your life, this takes approximately 15 minutes to complete. While you are in hospital receiving the five-day infusions we will:

- Perform daily blood tests (including full blood count, kidney function, electrolytes, magnesium and liver function) and daily ECGs
- Ask you to rate your pain scale on a scale from 1-10 every three hours while you are awake
- We will document your medical history, vital signs, and physical examination throughout your admission

You will be discharged from hospital after five days, or once your pain score has reduced to less than two on two consecutive occasions, whichever occurs first. If after the five-day infusion you still have ongoing pain, your ongoing care will be determined by your treating doctor. You will be asked to keep a headache diary for the next 3 months, and asked to record how many times you present to either your local doctor or an emergency department for your migraine.

You will be contacted by the study doctor by phone 30 (thirty) days after going to hospital to check whether you have any adverse events, how often you saw a doctor for your migraine, and how many migraines you have had. You will then have a final visit after 90 (ninety) days to complete the same four surveys you did in hospital, and assess your migraine frequency. You will have a final phone call 20 (twenty) weeks after your first visit to hospital to ensure that you have not developed any side effects of the treatment.

Your involvement in this research project will be the length of your hospital admission for status migrainosus (up to five days), two phone calls and then one study visit, over a total of 20 weeks. There are no additional costs associated with participating in this research project, nor will you be paid. All medication, tests and medical care required as part of the research project will be provided to you free of charge. You will be reimbursed for any reasonable travel, parking, meals and other expenses associated with the research project visits.

If you decide to participate in this research project, the study doctor will inform your local doctor.

4 What do I have to do?

If you agree to take part in this study, you will receive medication to treat status migrainosus. You will not need to stay in hospital longer then is required to treat your pain. While in hospital, your doctors will continue your regular medication, which will be given by the nursing staff as usual.

You should not donate blood or fall pregnant for six months after participating in this study. There are no other lifestyle restrictions from participation in this study. It is important that you continue a headache diary and complete the follow-up reviews after you leave hospital. There will be two phone calls scheduled to discuss your health and collect information about any potential side effects from the treatment you received during the trial. There will be one in-person study visit when safety assessments will be conducted.

5 Other relevant information about the research project

This study is being undertaken at the Alfred Hospital. A total of forty people will take part in this study, and divided randomly and equally into two groups:

- Twenty people will receive eptinezumab and then a placebo infusion for up to five days
- Twenty people will receive a placebo infusion and then a lignocaine infusion for up to five days

This study is the first of its kind to assess either the treatment of status migrainosus in a controlled manner, or the use of eptinezumab as a treatment of status migrainosus.

6 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 take part and later change your mind, you are free to withdraw from the project at any stage.

If you do decide to take part, you will be given this Participant Information and Consent Form to sign and you will be given a copy to keep.

Your decision whether to take part or not to take part, or to take part and then withdraw, will not affect your routine treatment, your relationship with those treating you or your relationship with Alfred Health.

7 What are the alternatives to participation?

You do not have to take part in this research project to receive treatment at this hospital. Other options are available; these include intravenous lignocaine infusion, the standard treatment for status migranosus. Your study doctor will discuss these options with you before you decide whether or not to take part in this research project. You can also discuss the options with your treating doctor.

8 What are the possible benefits of taking part?

We cannot guarantee or promise that you will receive any benefits from this research; however, possible benefits may include:

- Treatment of your current presentation with status migrainosus
- A reduced length in hospital
- Fewer migraine days in the next three months

9 What are the possible risks and disadvantages of taking part?

9.1 Possible side effects

Medical treatments often cause side effects. You may have none, some or all of the effects listed below, and they may be mild, moderate or severe. If you have any of these side effects, or are worried about them, talk with your study doctor. Your study doctor will also be looking out for side effects.

There may be side effects that the researchers do not expect or do not know about and that may be serious. Tell your study doctor immediately about any new or unusual symptoms that you get.

Many side effects go away shortly after treatment ends. However, sometimes side effects can be serious, long lasting or permanent. If a severe side effect or reaction occurs, your study doctor may need to stop your treatment. Your study doctor will discuss the best way of managing any side effects with you.

Having a drug injected or blood taken may cause some discomfort, bruising, minor infection or bleeding. If this happens, it can be easily treated.

Possible side effects of eptinezumab include:

Side Effect	How often is it likely to occur?	How severe might it be?	How long might it last?
Nasopharyngitis	Eight in every hundred patients	Mild	A couple of days
Hypersensitivity reaction*	two in every hundred patients	Mild	During infusion

* hypersensitivity reactions included itching, flushing, or allergic reaction on the day of infusion

9.2 Issues relating to pregnancy, breast-feeding or planned parenthood

The effects of eptinezumab on the unborn child and on the newborn baby are not known. Because of this, it is important that research project participants are not pregnant or breast-feeding and do not become pregnant during the course of the research project. You must not participate in the research if you are pregnant or trying to become pregnant, or breast-feeding. If you are female and child-bearing is a possibility, you will be required to undergo a pregnancy test prior to commencing the research project. If you are male, you should not father a child or donate sperm for at least six months after the last dose of study medication.
Both male and female participants are strongly advised to use effective contraception during the course of the research and for a period of six months after enrolment in the research project. You should discuss methods of effective contraception with your study doctor.

If you do become pregnant or father a child whilst participating in the research project, you should advise your study doctor immediately.
Your study doctor will advise on medical attention for you or your partner should this be necessary. In the event you become pregnant or father a child during the course of this study, the study sponsor would like to collect information on your/your partner's pregnancy and its outcome. You will be provided with a separate Participant Information Sheet/Consent Form to read and consider.

9.3 Psychological distress

If you become upset or distressed as a result of your participation in this project, or as a result of completing the questionnaires the researchers will be able to help arrange appropriate support. We anticipate that any symptoms of distress or anxiety will be addressed by your clinician in the consultation, and we will guide you to appropriate resources for further evaluation or treatment as needed.

10 What will happen to my test samples?

You will be asked to provide additional consent for the collection of your blood during the research project. This is a necessary part of the project to ensure the safety of your clinical care.

Samples of your blood obtained for the purpose of this research project will be processed at Alfred Health. Your blood will only be used for tests that directly relate to your clinical care, and not for any other research purpose.

If we detect a significant or abnormal test result, we will inform you as part of your routine clinical care.

11 What if new information arises during this research project?

Sometimes during the course of a research project, new information becomes available about the treatment that is being studied. If this happens, your study doctor will tell you about it and discuss with you whether you want to continue in the research project. If you decide to withdraw, your study doctor will make arrangements for your regular health care to continue. If you decide to continue in the research project you will be asked to sign an updated consent form.

Also, on receiving new information, your study doctor might consider it to be in your best interests to withdraw you from the research project. If this happens, he/ she will explain the reasons and arrange for your regular health care to continue.

12 Can I have other treatments during this research project?

Whilst you are participating in this research project, you may not be able to take some or all of the medications or treatments you have been taking for your condition or for other reasons. It is important to tell your study doctor and the study staff about any treatments or medications you may be taking, including over-the-counter medications, vitamins or herbal remedies, acupuncture or other alternative treatments. You should also tell your study doctor about any changes to these during your participation in the research project. Your study doctor should also explain to you which treatments or medications need to be stopped for the time you are involved in the research project.

During this research project you would not be able to start a new (or different) medication which is designed to reduce the frequency of migraine attacks.

13 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 supervisor to discuss any health risks or special requirements linked to withdrawing. If you withdraw from the project, you will be invited to continue to attend the follow up visits. This is to ensure that we have as much information about the safety of the medication as possible.

If you do withdraw your consent during the research project, the study doctor and relevant study staff will not collect additional personal information from you, although personal information already collected will be retained to ensure that the results of the research project can be measured properly and to comply with law. You should be aware that data collected by Alfred Health up to the time you withdraw will form part of the research project results. If you do not want them to do this, you must tell them before you join the research project.

14 Could this research project be stopped unexpectedly?

This research project may be stopped unexpectedly for a variety of reasons. These may include reasons such as:
• Unacceptable side effects
• The drug/treatment/device being shown not to be effective
• The drug/treatment/device being shown to work and not need further testing
• Decisions made in the commercial interests of the sponsor or by local regulatory/health authorities.

15 What happens when the research project ends?

Following the end of your participation in the study, you will be invited to attend and continue to follow-up the management of migraine at the headache clinic of Alfred Health. Eptinezumab is not available on the pharmaceutical benefit scheme, so you would not be able to continue the medication after the end of the trial, however the clinic specialists will be able to discuss with you other options in managing your migraine.

The results of the study will be published following its conclusion in a peer-reviewed medical journal. We would be happy to write you a letter sharing a summary of the results of the study with you once it has been completed. This will include information about the overall results of the study, not specific information about your individual results. If you would like to receive a copy of the results, please indicate below:

Part 2 How is the research project being conducted?

16 What will happen to information about me?

By signing the consent form you consent to the study doctor and relevant research staff collecting and using personal information about you for the research project. Any information obtained in connection with this research project that can identify you will remain confidential. It will be treated as all other confidential medical information, stored on a secure REDCap password protected server at Alfred Health. Only researchers involved in the study will be able to access this information. Your information will only be used for the purpose of this research project and it will only be disclosed with your permission, except as required by law.

Information about you may be obtained from your health records held at this health service for the purpose of this research. By signing the consent form you agree to the study team accessing health records if they are relevant to your participation in this research project.

Your health records and any information obtained during the research project are subject to inspection (for the purpose of verifying the procedures and the data) by the relevant authorities and authorised representatives of the Sponsor, Alfred Health, the institution relevant to this Participant Information Sheet, Alfred Health, or as required by law. By signing the Consent Form, you authorise release of, or access to, this confidential information to the relevant study personnel and regulatory authorities as noted above.

It is anticipated that the results of this research project will be published and/or presented in a variety of forums. In any publication and/or presentation, information will be provided in such a way that you cannot be identified, except with your permission. Results will only be presented in a non-identifiable, generalised form.

Information about your participation in this research project may be recorded in your health records. In accordance with relevant Australian and Victorian privacy and other relevant laws, you have the right to request access to your information collected and stored by the research team. You also have the right to request that any information with which you disagree be corrected. Please contact the study team member named at the end of this document if you would like to access your information.

Any information obtained for the purpose of this research that can identify you will be treated as confidential and securely stored. It will be disclosed only with your permission, or as required by law.

17 Complaints and compensation

If you suffer 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. 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.

18 Who is organising and funding the research?

This research project is being conducted by Dr. Elspeth Hutton and Dr. Jason Ray, and sponsored by Alfred Health. This study is being conducted with the support of Lundbeck Australia Pty Ltd, a company that produces eptinezumab under the trademark Vyepti.

Lundbeck may benefit financially from this research project if, for example, the project assists Lundbeck to obtain approval for a new indication for eptinezumab.

You will not benefit financially from your involvement in this research project..

In addition, if knowledge acquired through this research leads to discoveries that are of commercial value to Lundbeck, the study doctors or their institutions, there will be no financial benefit to you or your family from these discoveries.

Alfred Health will receive a payment from Lundbeck for undertaking this research project.

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

Dr. Hutton has received an honorarium for sitting on the Lundbeck medical advisory board. No other members of the research team have declarations of interest.

19 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 HREC of Alfred Health, the institution where both the research and standard care will be carried out.

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

20 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 you have any medical problems which may be related to your involvement in the project (for example, any side effects), you can contact the principal study doctor on 03 9074 2470 or any of the following people:

Clinical contact person

Name	Georgia Ramsay
Position	Study Coordinator
Telephone	03 9074 2470
Email	g.ramsay@alfred.org.au

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

Complaints contact person

Position	Complaints Officer
Telephone	03 90763619
Email	research@alfred.org.au

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

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

Name	Alfred Health HREC
Position	HREC Executive Officer
Telephone	03 9076 3618
Email	research@alfred.org.au

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Consent Form - *Adult providing own consent*

Title	An evaluation of the efficacy of eptinezumab in the inpatient management of status migrainosus in comparison to intravenous lignocaine in patients who have failed other therapies
Short Title	SMITE: Status Migrainosus Inpatient Treatment with Eptinezumab
Protocol Number	1.0
Project Sponsor	Alfred Health
Coordinating Principal Investigator/ Principal Investigator	Dr. Jason Ray/Dr. Elspeth Hutton
Associate Investigator(s)	Dr. Mahima Kapoor Dr. Emma Foster
HREC Reference	HREC/77323/Alfred-2021
Location	The Alfred Hospital

Consent Agreement

I have read the Participant Information Sheet or someone has read it to me in a language that I understand.

I understand the purposes, procedures and risks of the research described in the project.

I give permission for my doctors, other health professionals, hospitals or laboratories outside this hospital to release information to Alfred Health concerning my disease and treatment for the purposes of this project. I understand that such information will remain confidential.

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 study without affecting my future health care.

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

I would like to receive a summary of the research results. ☐ Yes ☐ No

Declaration by Participant – for participants who have read the information

Name of Participant (please print) _____

Signature _____ Date _____

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.

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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.

I understand that, if I decide to discontinue the study treatment, I may be asked to attend follow-up visits to allow collection of information regarding my health status. Alternatively, a member of the research team may request my permission to obtain access to my medical records for collection of follow-up information for the purposes of research and analysis.

Name of Participant (please print) _____

Signature _____ Date _____

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.

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.

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Form for Withdrawal of Participation - *Adult providing own consent*

Title	An evaluation of the efficacy of eptinezumab in the inpatient management of status migrainosus in comparison to intravenous lignocaine in patients who have failed other therapies
Short Title	SMITE: Status Migrainosus Inpatient Treatment with Eptinezumab
Protocol Number	1.0
Project Sponsor	Alfred Health
Coordinating Principal Investigator/ Principal Investigator	Dr. Jason Ray/Dr. Elspeth Hutton
Associate Investigator(s)	Dr. Mahima Kapoor Dr. Emma Foster
HREC Reference	HREC/77323/Alfred-2021
Location	The Alfred 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 Alfred Health.

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.