TO BE PRINTED ON HEADED PAPER

MAST-DURATION

MAST trial: Anti-epileptic drug use following brain injury
https://masttrial.org/

We are inviting adults who have suffered from a seizure following a head injury to join this research study, comparing a short course and a long course of anti-epileptic treatment.

This document gives information about the study including the aims, risks and benefits of taking part.

In this information sheet, we use the words “I” and “you” referring to the study participant. Some people in this study may be unable to read this document themselves or complete the consent form. In that case, a relative/friend can complete the form on their behalf, however the words “I” and “you” still refer to the study participant and not the person completing the form.

Please let us know who will complete this consent form:

☐ The patient

☐ A relative or friend (Personal Legal Representative)

☐ An independent healthcare professional

Participant information sheet & informed consent form

You are being invited to take part in a research trial. Before deciding whether to take part, you need to understand why this research is being done and what it involves. Please take time to read the following information carefully and talk to others about the trial if you wish. Please ask us if anything is not clear or if you would like more information. Please take time to decide whether or not you wish to take part.

Section 1 tells you the purpose of this trial and what will happen to you if you take part.
Section 2 gives you more detailed information about the conduct of the trial.

Section 1: Purpose of the trial and what will happen

1. What is the purpose of the trial?

You are being invited to participate in this study because you have suffered from a seizure following a head injury and are now being treated with anti-epileptic medication. Patients who experience seizures after brain injury are typically started on a course of anti-epileptic drugs to prevent further seizures. Some doctors favour a short course of medication, whereas others favour a longer course. We wish to assess if one approach is better than the other, in order to guide best practice in the future. In this trial we will be testing a short course (up to 3 months) of medication versus a longer course (at least 6 months) of medication.

What is a traumatic brain injury?

It is a brain injury that occurs when an external force causes damage to the head. These injuries are common and are usually caused by falls, assaults, road traffic accidents and mishaps at home etc. Symptoms following a head injury differ according to which part of the brain is damaged and how severe the damage is. Seizures which occur after brain injury can result in additional brain damage, longer hospital stays and increase the risk of more seizures in the future.

What is a seizure and how is it treated?

Seizures are bursts of electrical activity in the brain that temporarily affect how it works. A seizure may happen in the early days after a head injury, while your brain is still healing, or it may happen months later. Seizures can affect people in different ways, depending on which part of the brain is involved. Symptoms can include uncontrollable jerking and shaking (called a "fit"), losing awareness and staring blankly into space, becoming stiff, strange sensations, (such as a "rising" feeling in the tummy, unusual smells or tastes, and a tingling feeling in your arms or legs) or collapsing. These symptoms can last anywhere between a few seconds and two minutes. Following a seizure you may feel weak or confused.

2. What is the drug being tested?

Phenytoin and levetiracetam are part of a group of medicines called “anti-epileptic drugs”; these medicines are both used for the treatment of seizures and epilepsy.

3. Why have I been invited?

You have been invited to participate in this trial because you have been prescribed with phenytoin or levetiracetam following a post traumatic seizure. We plan to include 428 participants who have had a post traumatic seizure from 29 hospitals across the UK.

4. Do I have to take part?

Participating in this trial is completely voluntary. If you decide to participate you will be asked to sign an Informed Consent Form, however you are still free to change your mind and leave the trial at any time without giving a reason. If you chose not to participate or to leave the trial, your future medical treatment and normal standard of care will not be affected in any way.

5. What will happen to me if I take part?

If you agree to participate in the trial, you will sign the Informed Consent Form at the end of this document and be given a copy of this to take away and refer to later. If you were not able to give informed consent when you arrived in hospital, we may have invited a legal representative to consent on your behalf, until you were able to do so. This person would be either:

- A relative or friend
- A court appointed deputy who has a personal relationship with you
- An Independent Healthcare Professional nominated by the researcher, in the absence of one of the above, and suitably independent of the research project

As we sometimes don't know which way of treating patients is best, we need to compare different treatment regimens. We put people into groups and give each group a different treatment. You will be allocated one of the treatment duration groups for this trial in a random way (by chance), much like flipping a coin. You will have a 50% chance of receiving your medication for up to a maximum of 3 months or for a minimum of 6 months.

Duration

The treatment will start in hospital and will last for either up to **3 months** or at least **6 months** (longer if your doctor thinks necessary). Your doctor will decide which medication you should receive. Your medication may initially be administered into a vein through a drip, and then be administered by mouth usually with tablets or capsules. The dose will be decided by your doctor in line with normal prescribing practices. It is important that the medicine is taken correctly and must not be stopped or changed, without consulting your doctor or the study team first. When you are discharged you will be able to receive your medication, if required, either from your GP or by post/courier from the hospital. It is important that you continue to take your study medication regularly as directed by your study doctor. Please be aware that your medication will need to be stopped gradually, according to a set schedule, and you will be provided details of this nearer the time.

If you experience any seizures during the trial, you will receive the standard care for your condition. Your doctor may decide that it is in your best interest to change your treatment, including changing your medication, at any time. **We will ask you to report any potential seizures you experience over the next 24 months to your neurosurgical team, GP and a member of our research team.**

Assessments

To assess your recovery the study team will contact you after you leave the neurosurgical unit, but there will not be any extra visits to the hospital because of the trial. Your doctor will contact you to tell you when to start reducing your medication. We will ask you to fill in a short questionnaire pack at 6, 12, 18 and 24 months after your initial injury asking about your current state of health. You may complete the questionnaires either by yourself or with the assistance of a relative/friend. If we do not receive a completed questionnaire by post, we may email or telephone you, or your

relative, to complete them over the phone. We will contact you by phone at 6 months to ask you about your current health and any potential side effects of the trial drug. We may also contact your GP, local hospital or rehabilitation centre for information regarding your recovery. If you would prefer to answer the questionnaire over the phone or you require the questionnaire in another format (e.g. different language, large print), please let us know.

The trial team will collect additional healthcare information such as admission to hospital, by using your NHS/CHI number to access data from NHS Digital. This involves collecting, processing, and transferring your personal data (name, gender, date of birth, postcode, and NHS/CHI number) for medical research purposes. Once the data has been linked and collected, your personal identification details will be removed for the analysis.

Equivalent national health record organisations exist in Wales (Secure Anonymised Information Linkage, Public Health Wales), Scotland (electronic Data Research and Innovation Service, Public Health Scotland) and Northern Ireland (Belfast Health and Social Care Trust). If you live in these areas, the same central healthcare records' will be obtained from these sources.

6. What will I have to do?

You will not be asked to undertake any interventions in addition to the standard care you would normally receive from your doctor. You will need to take the study medication as directed by your doctor for either up to 3 months or at least 6 months. You will need to stop taking the study medication when advised by your doctor and you will need to follow the tapering schedule in order to minimise any side effects. It is important that you fill in the questionnaires when these are sent to you. You will be asked to complete the questionnaires either when you come to the hospital for a routine outpatient appointment or we will contact you by post, email or telephone.

Some medicines and herbal products can affect the way your study medication works, and your study medication can also reduce the effectiveness of other medicines taken at the same time. Please talk to your doctor before you start taking any other medicines or herbal products.

Prenatal exposure to trial medicines may increase the risks for birth defects. So if you are a woman of childbearing potential, and are planning pregnancy, please avoid becoming pregnant for the entire duration of treatment and for 1 month after your last treatment with the trial drug

Trial medicines could also reduce the effectiveness of hormonal contraceptives. The following types of planned contraception that may not work well for you, which means you could become pregnant are:

- progestogen-only pill
- combined oral contraceptive pill
- contraceptive implant
- contraceptive patch
- vaginal ring

If you use any of these methods of contraception, please take extra precautions for the entire duration of treatment and for 1 month after your last treatment with the trial drug. The following types of planned contraception that may work well for you to stop you getting pregnant are:

- Intrauterine device (IUD, coil or intrauterine system)
- Condom
- Diaphragm

- Female condom
- Contraceptive injection.

You do not need to use contraception if:

- you have only one partner, and the man has had an operation to cut the tubes that carry sperm (vasectomy)
- you are a woman who cannot become pregnant
- you practice true abstinence as part of your usual and preferred lifestyle (no sexual activity from 7 days before the first dose until 14 days after the last dose of trial medication). If you become sexually active, you must use one of the methods listed above

If you become pregnant during the trial or within 1 month of stopping treatment, you should inform your trial doctor immediately. Your trial doctor will discuss all the options available to you. The outcome and progress of any pregnancy would be followed and you would be asked questions about the pregnancy and baby, if appropriate.

You should tell the trial team if you feel unwell or different in any way. If you have any major concerns or are feeling very unwell please contact your trial doctor immediately using the contact numbers at the end of this information sheet.

You should discuss your participation in this trial with any insurance provider you have (e.g. travel insurance, protection insurance, life insurance, income protection, critical illness cover and private medical insurance) and seek advice if necessary, as failure to notify them may affect or invalidate your cover.

7. What are the side effects of the drug being tested?

The most frequently reported side effects associated with Phenytoin are:

- problems with eye movement
- abnormal muscle movements, speech changes, loss of coordination, mental confusion
- dizziness, sleep problems, pins and needles
- nausea, vomiting, constipation, change in taste
- skin rash, increase in body hair
- liver problems
- decreased bone mineral density
- changes in facial features
- gum overgrowth
- vitamin D deficiency

If possible phenytoin will be given orally, as a tablet or capsule, however if your doctor does not think that this is clinically appropriate, then phenytoin can be given intravenously (i.e. directly into a vein). Your doctor will monitor this very closely and watch out for any possible side effects, which could include:

- abnormal heart beats
- low blood pressure
- skin irritation

The most frequently reported side effects associated with Levetiracetam:

- common cold, cough
- sleepiness, headache
- loss of appetite, nausea, vomiting, diarrhoea, abdominal pain
- sleep problems, mood changes
- dizziness, tremor, vertigo
- rash
- fatigue

In the unlikely event of any serious unforeseen reactions, or if any concerns arise, the drug will be stopped immediately. Your doctor will carefully monitor all of your medicines to check for any possible interactions.

If you withdraw from the trial due to side effects of the trial medication, your doctor will decide which alternative treatment is best for you. You will still be able to continue with the follow-up questionnaires if you wish to.

8. What are the possible disadvantages and risks of taking part?

Apart from the potential side effects from the study drug, there are no additional risks or disadvantages involved with taking part in this study. You will continue to receive the standard care for your condition. You will be asked to complete the questionnaires at 6, 12 18 and 24 months, but we will endeavour to coincide this with a routine clinical appointment if possible.

9. What are the possible benefits of taking part?

The study drug you will be provided with is a standard anti-epileptic drug, used to control seizures. We expect your seizures to be reduced as a result of taking the study drug. Information collected as part of your participation in this trial will help patients with a traumatic brain injury in the future.

10. What are the alternatives for treatment?

The alternatives for treatment are routine standard care at this hospital. Current practice regarding the duration of treatment with anti-epilepsy drugs in patients with brain injury varies across hospitals.

11. What happens when the trial stops?

Once treatment with the study drug has finished, you will continue to be treated and managed as per the routine standard of care at your hospital.

12. Expenses & Payment?

You will be monitored whilst in hospital. Thereafter we will contact you by post, telephone or at a routine outpatient visit. If we ask you to complete a postal questionnaire we will send a pre-stamped addressed envelope for the reply. You will not receive any payment for participating in this study and we do not anticipate you will incur any expenses by participating in this study. If you need to collect a prescription for your trial medication post-discharge you will be reimbursed for any direct prescription charges.

Section 2: Trial Conduct

13. What if new information becomes available?

Sometimes during the course of a trial, new information becomes available which might affect your decision to continue participating in this trial. Your trial doctor will contact you to discuss the new information and whether you wish to continue participating in the trial. If you still wish to continue on the trial, you will be asked to sign a new Informed Consent Form. The trial sponsor, the regulatory authority or the trial doctor may decide to stop the trial at any time. If that happens we will tell you why the trial has been stopped and arrange for appropriate care and treatment for you.

14. What if I decide I no longer wish to participate in the trial?

You are free to withdraw from this trial at any time without giving a reason and without affecting your future care or medical treatment. If you decide not to participate any further, you will no longer receive the trial treatment. Any data already collected will continue to be used in the trial analysis.

The trial doctor may also choose to withdraw you from the trial if they feel it is in your best interests or if you have been unable to comply with the requirements of the trial. Reasons for trial withdrawal could include:

- You have experienced a serious side effect
- You are unable to complete the visits, medication or trial documentation as required
- You become pregnant or plan to become pregnant
- The trial doctor feels you no longer appear to benefit from the treatment.

If you have experienced any serious side effects during the course of the trial which require you to withdraw from the trial, your trial doctor will follow-up with you regarding your progress until the side effect has stabilised or resolved.

15. What if there is a problem?

Any complaint about the way you have been dealt with during the trial or any possible harm you might suffer will be addressed. If you have any concerns about any aspect of this trial you should speak to your trial doctor who will do their best to answer your questions.

In the event that something does go wrong and you are harmed by taking part in the research and this is due to someone's negligence then you may have grounds for a legal action for compensation against Cambridge University Hospitals NHS Foundation Trust or the University of Cambridge. The normal National Health Service complaints mechanisms will still be available to you (if appropriate).The University has obtained insurance which provides no-fault compensation i.e. for non-negligent harm, you may be entitled to make a claim for this.

If you wish to complain or have any concerns about any aspect of the way you have been approached or treated during this trial, you can do this through the NHS complaints procedure. In the first instance it may be helpful to contact the *(to be completed locally as appropriate – in England this will refer to the Patient Advice and Liaison Service (PALS))* at your hospital.

16. Will my taking part in this trial be kept confidential?

Cambridge University Hospitals NHS Foundation Trust (CUH) and The University of Cambridge are the Sponsors for this clinical trial based in *the United Kingdom.* They will be using information from you and your medical records in order to undertake this trial and will act as the data controller for this trial. This means that they are responsible for looking after your information and using it properly. The Sponsor organisations will keep identifiable information about you for a maximum

of 12 years after the trial has finished ensuring your safety and allowing the trial to be reviewed by the authorities after it is finished.

Your rights to access, change or move your information are limited, as the Sponsor organisations need to manage your information in specific ways in order for the research to be reliable and accurate. To safeguard your rights, we will use the minimum personally-identifiable information possible.

You can find out more about how the Sponsors use your information using the information below:

- For Cambridge University Hospitals NHS Foundation Trust, please visit: https://www.cuh.nhs.uk/corporate-information/about-us/our-responsibilities/looking-after-your-information, or email the Data Protection Officer at: gdpr.enquiries@addenbrookes.nhs.uk
- For University of Cambridge, please visit: https://www.medschl.cam.ac.uk/research/information-governance/ or email the Information Governance team at: researchgovernance@medschl.cam.ac.uk

[For participants recruited at CUH (where the Sponsor is also the site). Delete paragraph when localising document at other sites]

Cambridge University Hospitals will collect your name, (NHS number, contact details, gender and date of birth) to send you follow up questionnaires, contact you by telephone, access your health records, make sure that relevant information about the trial is recorded for your care, and to oversee the quality of the trial. Individuals from the Sponsors and regulatory organisations may look at your medical and research records to check the accuracy of this trial. Cambridge University Hospitals will pass these details to the Sponsors along with the information collected from and/or your medical records. The only people in the Sponsor organisations who will have access to information that identifies you will be people who need to contact you in relation to this trial and to audit the data collection process. Cambridge University Hospitals will keep identifiable information about you from this trial for a maximum of 12 years after the trial has finished.

[For participants recruited at other participating sites. Delete paragraph when localising document at CUH]

We will pass personal information about you (your name, NHS number, contact details, gender and date of birth) to the Sponsor organisation to send you follow up questionnaires, contact you by telephone, and access your health records. Patient identifiable information will be stored securely and the only people in the Sponsor organisations who will have access to information that identifies you will be people who need to contact you in relation to this trial and to audit the data collection process. We may also pass your name and address to a courier if we need to send you any medication.

(Add site name) will keep identifiable information about you from this study for ### years after the study has finished.

All information collected about you as a result of your participation in the trial will be kept strictly confidential. Your personal and medical information will be kept in a secured file and be treated in the strictest confidence.

Once you have agreed to participate in this trial you will be allocated a Trial ID Number. This is a unique trial number which will be used on all your trial documentation along with your initials and month/year of birth. Your initials and partial date of birth are considered to be personal information. We collect this personal information on trial documentation to help ensure that the data we receive as part of your trial participation is correctly allocated to you. By cross checking these unique references we can ensure the integrity of the data.

The people who analyse the information will not be able to identify you and will not be able to find out your name, NHS number or contact details. Only anonymous trial data, without any personal information will be published at the end of the trial.

Cambridge University Hospitals will also collect information about you for this trial from the national health record organisations mentioned in point 5. This information will include your name, gender, date of birth, postcode, and NHS number and health information, which is regarded as a special category of information. We will use this information to follow any hospital admissions you have during the trial.

We will need to inform your GP of your participation in this trial so that any medical decisions made by your GP account for any treatment you are receiving as part of this trial. We may also ask your GP to continue to prescribe your trial medication after you are discharged home. If you are transferred to a local hospital or rehabilitation centre, your doctors may contact the trial team to let us know where you are.

17. What will happen to the results of the trial?

The results of the trial will be anonymous and you will not be able to be identified from any of the data produced. When the results of this trial are available they may be published in peer reviewed medical journals and used for medical presentations and conferences. They will also be published on the EU Clinical Trials Register website, a central registry for all clinical trials conducted in the EU.

Anonymous datasets from the trial may also be made available to other researchers in line with national and international data transparency initiatives.

If you would like to obtain a copy of the published results please contact your trial doctor directly who will be able to arrange this for you.

18. Who is funding the trial?

The trial is being funded by the National Institute for Health Research Health Technology Assessment Programme.

19. Who has reviewed this trial?

All research within the NHS is reviewed by an independent group of people called a Research Ethics Committee, to protect your interests. This trial has been reviewed and given favourable opinion by Cambridge East Research Ethics Committee. The Medicines and Healthcare Products Regulatory Agency (MHRA) who are responsible for regulating medicines in the UK have also reviewed this trial.

20. Further information and contact details

If you would like more information or wish to discuss any aspect of this study then please call one of the research team at any time, …….. or ……. on the numbers below.

If you have any concerns about the study you may approach your local Patient Advice and Liaison Services (or equivalent) for independent advice [details to be provided locally].

In the event of an emergency please contact:

[Details to be added for local contacts]

INFORMED CONSENT FORM - DURATION
ADULT PATIENT

Trial Title: MAST trial: Anti-epileptic drug use following brain injury
Principal Investigator: [Printed name to be inserted] **Participant Number:** _____

If you agree with each sentence below, please initial the box		**INITIALS**
1	I have read and understood the Participant Information Sheet version ##, dated #### for the above trial and I confirm that the trial procedures and information have been explained to me. I have had the opportunity to ask questions and I am satisfied with the answers and explanations provided.	
2	I understand that my participation in this trial is voluntary and that I am free to withdraw at any time, without giving a reason and without my medical care or legal rights being affected.	
3	I understand that personal information about me will be collected and used in accordance with this information sheet. This information will be kept in the strictest confidence and none of my personal data will be published.	
4	I understand that sections of my medical notes or information related directly to my participation in this trial may be looked at by responsible individuals from the sponsor, regulatory authorities and research personnel where it is relevant to my taking part in research and that they will keep my personal information confidential. I give permission for these individuals to have access to my records.	
5	I understand that my GP will be informed of my participation in this trial and sent details of the MAST trial.	
6	II understand that my name, gender, date of birth, postcode, and NHS/CHI number will be used to access my central healthcare data that are held and maintained by the national health record organisations described in point 5 (Assessments) on page 4 to provide information about my health status as part of this trial. I understand that, if I live in Wales, Scotland, or Northern Ireland, this information will be obtained from the equivalent sources described	
7	I understand that my personal data might be transferred between the trial team at different trial sites in relation to my participation in this trial. I understand that any personal data will be sent using (secure/encrypted mail servers etc.).	
8	I have read and understood the compensation arrangements for this trial as specified in the Participant Information Sheet.	
9	I understand that the doctors in charge of this trial may close the trial, or stop my participation in it at any time without my consent.	
10	I have read and understood my responsibilities for the trial including using appropriate contraception as listed in points 5 & 6.	

OPTIONAL		**YES**	**NO**
11	I agree to long term follow up of my data (beyond the end of the treatment study) using routinely collected data and appropriate linkage to allow my research data to be used.		

I agree to participate in this trial:

_____	_____	_____
Name of patient	Signature	Date
_____	_____	_____
Name of person taking consent	Signature	Date

Time of Consent (24hr clock) _____:_____

1 copy for the patient, 1 copy for the trial team, 1 copy to be retained in the hospital notes.

Patient Legal Representative
INFORMED CONSENT FORM - DURATION –
ADULT RELATIVE/FRIEND

Trial Title: MAST trial: Anti-epileptic drug use following brain injury
Principal Investigator: [Printed name to be inserted] **Participant Number:** _____

If you agree with each sentence below, please initial the box		**INITIALS**
1	I have read and understood the Participant Information Sheet version ##, dated #### for the above trial and I confirm that the trial procedures and information have been explained to me. I have had the opportunity to ask questions and I am satisfied with the answers and explanations provided.	
2	I understand that my relative/friend/'s participation in this trial is voluntary and that they are free to withdraw at any time, without giving a reason and without their medical care or legal rights being affected.	
3	I understand that personal information about my relative/friend/'s will be collected and used in accordance with this information sheet. This information will be kept in the strictest confidence and none of their personal data will be published.	
4	I understand that sections of my relative/friend/'s medical notes or information related directly to their participation in this trial may be looked at by responsible individuals from the sponsor, regulatory authorities and research personnel where it is relevant to their taking part in research and that they will keep their personal information confidential. I give permission for these individuals to have access to their records.	
5	I understand that my relative/friend/'s GP will be informed of their participation in this trial and sent details of the MAST trial.	
6	I understand that my relative/friend/'s name, gender, date of birth, postcode, and NHS/CHI number will be used to access their central healthcare data that are held and maintained by the national health record organisations described in point 5 (Assessments) on page 4 to provide information about their health status as part of this trial. I understand that, if they live in Wales, Scotland, or Northern Ireland, this information will be obtained from the equivalent sources described.	
7	I understand that my relative/friend/'s personal data might be transferred between the trial team at different trial sites in relation to their participation in this trial. I understand that any personal data will be sent using (secure/encrypted mail servers etc.).	
8	I have read and understood the compensation arrangements for this trial as specified in the Participant Information Sheet.	
9	I understand that the doctors in charge of this trial may close the trial, or stop my relative/friend/'s participation in it at any time without my consent.	
10	I have read and understood my relative/friend/'s responsibilities for the trial including using appropriate contraception as listed in points 5 & 6.	

OPTIONAL		**YES**	**NO**
11	I agree to long term follow up of my friend/relative's data (beyond the end of the treatment study) using routinely collected data and appropriate linkage to allow my friend/relative's research data to be used.		

I agree to my relative/friend participating in this trial:

_____	_____	_____
Name of friend/relative	Signature	Date
_____	_____	_____
Name of person taking consent	Signature	Date

Time of Consent (24hr clock) _____:_____

1 copy for the relative/friend, 1 copy for the trial team, 1 copy to be retained in the hospital notes.

Independent Healthcare Provider (IHP) Enrolment form - DURATION

Trial Title *MAST trial:* Anti-epileptic drug use following brain injury.

Principal Investigator: [Printed name to be inserted] **Participant Number:** _____

ALL 5 Questions must be initialled (and the 4 ticks marked) and the form signed to authorise enrolment		Initial Box
1) I confirm that the patient's next of kin is not available for discussion		
2) I confirm that I am independent, defined for this study as: **A person who is NOT connected with the conduct of the trial**, specifically:	Please also tick boxes	
a) NOT the sponsor of the trial;	❑	
b) NOT a person who undertakes activities connected with the management of the trial;	❑	
c) NOT an investigator of the trial, or;	❑	
d) NOT a health care professional who is a member of the investigators team for the purposes of the trial (Not on delegation log)	❑	
3) I confirm that I have been fully informed of the MAST trial, its objectives and study procedures and that enrolment of the patient mentioned above in the MAST trial is appropriate according to my professional medical judgment.		
4) As far as I am aware, the patient would not object to being involved in this trial.		
5) I understand that a member of the research team will provide the next of kin, and the patient (if they regain capacity), with information about the trial as soon as possible and I understand that their agreement will be sought in order to continue.		

Name of researcher	Signature	Date
Name of IHP	Signature	Date

Time of Authorisation (24hr clock): _____:_____

1 copy for the IHP, 1 copy for the trial team, 1 copy to be retained in the hospital notes.