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Comparing anti-epileptic treatments for seizures following traumatic brain injury

Submission date
19/10/2020

Recruitment status
No longer recruiting

Registration date
20/10/2020

Overall study status
Ongoing

Last Edited
09/03/2021

Condition category
Nervous System Diseases

[X] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
The majority of patients who suffer a traumatic brain injury (TBI) do not need to stay in hospital overnight. However, some require admission to a specialist hospital, as their injury is more serious. Seizures can be harmful or even fatal, if not treated appropriately. Medications that reduce the risk of seizures are called anti-epileptic drugs (AEDs). However, AEDs have side effects, which can affect patients' quality of life, memory, concentration and general health. Patients with seizures after TBI are typically prescribed an AED to prevent further seizures, most commonly phenytoin or levetiracetam. Some doctors favour a short course, whereas others favour a longer course. The first part of the study aims to answer if one approach is better than the other (MAST-DURATION). The second part of the study aims to answer if a 7-day course of either phenytoin or levetiracetam should be used for patients with a serious TBI to prevent seizures from happening (MAST- PROPHYLAXIS).

Who can participate?
MAST-DURATION:
Patients aged 10 and over, with a traumatic brain injury, managed in a neurosurgical unit, who have started on phenytoin or levetiracetam due to an acute symptomatic seizure during acute hospitalisation.
MAST-PROPHYLAXIS:
Patients aged 10 and over, with a traumatic brain injury, managed in a neurosurgical unit, without an acute symptomatic seizure.

What does the study involve?
MAST-DURATION:
Patients will be randomly allocated to receive to a maximum of 3 months or a minimum of 6 months course of phenytoin or levetiracetam.
MAST-PROPHYLAXIS:
Patients will be randomly allocated to receive either phenytoin, levetiracetam or no anti-epileptic drug for a period of 7 days.
Current international guidelines for traumatic brain injury recommend the use of phenytoin for the prevention of early post-traumatic seizures, when the benefits are thought to outweigh the risks. In practice, alternative anti-epileptic drugs such as levetiracetam are being used clinically

as they are associated with fewer risks.
Patients will be assessed for seizures during hospital admission and will also be asked to complete follow-up questionnaires at 6,12, 18 and 24 months.

What are the possible benefits and risks of participating?
MAST-DURATION:
The study drugs patients will be provided with are standard anti-epileptic drugs, used to control seizures. The researchers expect seizures to be reduced as a result of taking the study drug.
MAST-PROPHYLAXIS:
There is no guarantee that patients will benefit from taking part in this trial.
Apart from the potential side effects from the study drugs, there are no additional risks or disadvantages involved with taking part in this study. Patients will continue to receive the standard care for their condition.

Where is the study run from?
Addenbrookes Hospital (UK)

When is the study starting and how long is it expected to run for?
January 2020 to March 2026

Who is funding the study?
National Institute for Health Research (NIHR) (UK)

Who is the main contact?
1. Prof. Peter Hutchinson
pjah2@cam.ac.uk
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Study website
https://masttrial.org/

Contact information

Type(s)
Scientific

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Type(s)
Public

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Additional identifiers

EudraCT/CTIS number
2020-000282-16

IRAS number
276415

ClinicalTrials.gov number
NCT04573803

Secondary identifying numbers
CCTU0235, IRAS 276415, HTA - NIHR128226, CTA 24551/0044/001-0001

Study information

Scientific Title
Pharmacological management of seizures post traumatic brain injury (MAST trial)

Acronym
MAST

Study objectives
MAST-DURATION: There will be a significant difference in the rate of late post-traumatic seizures (PTS) within 24 months post-traumatic brain injury between a longer course of phenytoin or levetiracetam (at least 6 months) and a shorter course (up to 3 months) in traumatic brain injury patients with early seizures.

MAST-PROPHYLAXIS: There will be a significant difference in the rate of post-traumatic seizures within the first 2 weeks post-traumatic brain injury between a 7-day course of phenytoin, levetiracetam or no anti-epileptic drug.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 11/01/2021, Cambridge East (East of England - Cambridge East Research Ethics Committee, The Fulbourn Centre, Home End, Fulbourn, Cambridgeshire, CB21 5BS, UK; +44 (0) 207 104 8102; cambridgeeast.rec@hra.nhs.uk), ref: 20/EE/0252

Study design
MAST-DURATION: Phase III randomized multicentre pragmatic parallel-group trial
MAST-PROPHYLAXIS: Phase III randomized multicentre pragmatic parallel-group trial

Primary study design
Interventional

Secondary study design
Randomised parallel trial

Study setting(s)
Hospital

Study type(s)
Prevention

Participant information sheet
The PIS will be made available on the website https://masttrial.org/

Health condition(s) or problem(s) studied
Post-traumatic seizures in traumatic brain injury patients

Interventions
MAST-DURATION: Patients will be randomized 1:1 to a maximum of 3 months OR a minimum of 6 months duration of a clinically prescribed AED (phenytoin or levetiracetam).

MAST-PROPHYLAXIS: Patients will be randomized 1:1:1 to phenytoin, levetiracetam or no AED for a period of 7 days.

Dosing for both parts of the trial will be as clinically prescribed and administered as per routine practice.

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Phenytoin, levetiracetam

Primary outcome measure
MAST-DURATION: Occurrence of late PTS measured using self-report questionnaire within 24 months after TBI
MAST-PROPHYLAXIS: Occurrence of PTS measured using clinical observation/self-report questionnaire within 2 weeks after TBI

Secondary outcome measures
1. Occurrence of PTS measured using self-report questionnaire up to 2 years (MAST-PROPHYLAXIS only)
2. Levels of disability measured using Extended Glasgow Outcome Scale at 6, 12, 18 and 24 months
3. Cognitive function measured using Neurobehavioural Symptom Inventory at 6, 12, 18 and 24 months
4. Quality of life measured using EQ-5D-5L at 6, 12, 18 and 24 months
5. Adverse events measured using Liverpool Adverse Events Profile at 6, 12, 18 and 24 months
6. Economic evaluation using the EQ-5D-5L questionnaire at 6, 12, 18 and 24 months
7. Frequency of PTS measured using self-report questionnaire within 24 months post traumatic brain injury
8. Mortality measured using data from the Spine for patients in England, nurse telephone calls outside England at 6, 12, 18 and 24 months
9. Adverse events of special interest measured using reports from sites and self-report during treatment

Overall study start date
05/01/2020

Completion date
01/03/2026

Eligibility

Key inclusion criteria
MAST-DURATION:
1. Patients aged ≥10 years with TBI managed in an NSU who have started on phenytoin or levetiracetam due to an acute symptomatic seizure during acute hospitalisation
2. Patient or Legal Representative is willing and able to provide informed consent or in the absence of a legal representative, an Independent Healthcare Professional provides authorisation for patient enrolment

MAST-PROPHYLAXIS:
1. Patients aged ≥10 years, with TBI managed in an NSU without an acute symptomatic seizure
2. Patient or Legal Representative is willing and able to provide informed consent or in the absence of a legal representative, an Independent Healthcare Professional provides authorisation for patient enrolment

Participant type(s)
Patient

Age group
Mixed

Lower age limit
10 Years

Sex
Both

Target number of participants
MAST-DURATION: 428 patients; MAST-PROPHYLAXIS: 1221 patients

Key exclusion criteria
MAST-DURATION:
1. Un-survivable injury
2. Previous history of epilepsy
3. Patients who are on an AED pre-TBI
4. Patient who has been clinically prescribed an AED to treat PTS (other than phenytoin or levetiracetam) since current admission
5. Any hypersensitivity to study drug selected or any of its excipients

MAST-PROPHYLAXIS:
1. Post-traumatic seizures
2. Unsurvivable injury
3. Previous history of epilepsy
4. Patients who are on an AED pre-TBI
5. Pregnancy or breastfeeding
6. Any hypersensitivity to study drug (or hydantoins or pyrrolidone derivatives) or any of its excipients
7. Time interval from the time of admission to NSU to randomisation exceeds 48 hours

Date of first enrolment
05/03/2021

Date of final enrolment
01/03/2024

Locations

Countries of recruitment
England

Northern Ireland

Scotland

United Kingdom

Wales

Study participating centre
Addenbrookes Hospital
Cambridge University Hospitals NHS Foundation Trust
Hills Road
Cambridge
United Kingdom
CB2 0QQ

Study participating centre
Freeman Hospital
Freeman Road
High Heaton
Newcastle Upon Tyne
United Kingdom
NE7 7DN

Study participating centre
Derriford Hospital
Derriford Road
Plymouth
United Kingdom
PL6 8DH

Study participating centre
Royal Preston Hospital
Sharoe Green Lane
Fulwood
Preston
United Kingdom
PR2 9HT

Study participating centre
Southampton General Hospital
Tremona Road
Southampton
United Kingdom
SO16 6YD

Study participating centre

Queen Elizabeth Hospital
Mindelsohn Way
Edgbaston
Birmingham
United Kingdom
B15 2GW

Study participating centre
Walsgrave General Hospital
Clifford Bridge Road
Coventry
United Kingdom
CV2 2DX

Study participating centre
Queens Medical Centre
Derby Road
Nottingham
United Kingdom
NG7 2UH

Study participating centre
St. Mary's Hospital
The Bays
South Wharf Road
London
United Kingdom
W2 1BL

Study participating centre
James Cook University Hospital
Marton Road
Middlesbrough
United Kingdom
TS4 3BW

Study participating centre
Northern General Hospital
Herries Road

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United Kingdom
S5 7AU

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University Hospital Aintree
Lower Lane
Liverpool
United Kingdom
L9 7AL

Study participating centre
St. James's University Hospital
Beckett Street
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LS9 7TF

Study participating centre
Royal Sussex County Hospital
Eastern Road
Brighton
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BN2 5BE

Study participating centre
NHS Grampian
Summerfield House
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AB15 6RE

Study participating centre
NHS Lothian
Waverley Gate
2-4 Waterloo Place
Edinburgh
United Kingdom
EH1 3EG

Study participating centre
NHS Greater Glasgow and Clyde
1055 Great Western Road
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United Kingdom
G12 0XH

Study participating centre
Southmead Hospital
Southmead Road
Westbury-On-Trym
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BS10 5NB

Study participating centre
Cardiff & Vale University LHB
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CF14 4XW

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Blackshaw Road
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Study participating centre
The Royal London Hospital
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Study participating centre

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Anlaby Road
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HU3 2JZ

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Study participating centre
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Study participating centre
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Study participating centre
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Study participating centre
Queens Hospital
Rom Valley Way
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RM7 0AG

Study participating centre
Belfast City Hospital
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Sponsor information

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Cambridge University Hospitals NHS Foundation Trust

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cctu@addenbrookes.nhs.uk

Sponsor type
Hospital/treatment centre

Website
http://www.cuh.org.uk/

Organisation
University of Cambridge

Sponsor details
Trinity Lane
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CB2 1TN
+44 (0)1223 337733
researchgovernance@medschl.cam.ac.uk

Sponsor type
University/education

Website
http://www.cam.ac.uk/

Funder(s)

Funder type
Government

Funder Name
National Institute for Health Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
The protocol will be made available on the website https://masttrial.org/

The findings of the MAST trial will be disseminated via peer-reviewed journals and presentations at national and international meetings. In addition to meetings orientated around neurosurgery, conferences organised for the different health professionals who care for patients post traumatic brain injury will be targeted.

Research findings will be disseminated to relevant service user groups and charities through newsletters, website posts and public presentations. The MAST trial website will also include dedicated pages for members of the public. The trial will be presented in open days organised by hospitals participating in the trial where members of the public are invited to find out about ongoing research. Talks/presentations will also be given at meetings of local/regional relevant service user groups and charities.

Intention to publish date
01/03/2029

Individual participant data (IPD) sharing plan
The data-sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			26/07/2023	No	No