RCT Legal Representative Information Sheet
Version 5.0, 25 May 2018

DexEnceph: A study of dexamethasone in adults with Herpes Simplex Virus (HSV) encephalitis
Brain Infections Group, University of Liverpool

We understand this is a difficult and stressful time for you, so we firstly want to thank you for taking the time to read this leaflet.

Your relative/friend is being invited to take part in a research study on HSV encephalitis. This condition is extremely rare and is probably something you had never heard about before. Your relative/friend is too unwell to decide whether they wish to take part in the study. We are asking you to decide on their behalf. We appreciate this decision can be very difficult. This is why a team member will go through this leaflet with you, explaining what taking part in the study would involve and answering any questions.

Important things you need to know

- This is a study for patients with encephalitis (swelling of the brain) caused by a virus called herpes simplex virus (HSV).
- Encephalitis can make you confused and drowsy, behave out of character, affect your sleep and memory, change your mood or may cause you to have fits.
- We want to find out if reducing the swelling with a drug called dexamethasone is of benefit to patient's memory in the longer term.
- In the study there will be two groups of patients, one that receives dexamethasone and one that does not.
- If your relative/friend is in the group that receives dexamethasone this will be for 4 days in hospital.
- Both groups will have the same investigations to see if dexamethasone has been of benefit.
- Dexamethasone is a commonly used drug in brain swelling and many other conditions. Like all medicines, dexamethasone has side-effects. We will explain what these can be later.

We would like invite your relative/friend to take part in a research study

- We feel your relative/friend is not able to decide for themselves whether to take part. We would like to ask you to decide on their behalf.
- Before you decide please think about what would have been their wishes and feelings. Any known advance decisions they have made should take precedence.
- The information in this form is the same as we would have given to them.
- We understand if you do not feel able to take on this responsibility. If this is the case please let us know.
- Your decision will not affect their care.
- You can discuss with friends, family and other clinical staff before making a decision.
- Please let us know if there is anything in this leaflet that is not clear or if you would like more information. A member of our team will answer your questions.

HSV encephalitis

1. What is HSV encephalitis?

Encephalitis means swelling of the brain and has many different causes. It is often caused by a virus. Herpes Simplex Virus (HSV) is the most common virus that causes encephalitis in the UK.

HSV encephalitis is very rare. It is diagnosed by finding the virus in fluid around the brain and spinal cord. This fluid is called CSF (cerebrospinal fluid). The CSF is obtained by the doctor who performs a lumbar puncture (LP).

HSV encephalitis is treated with the drug aciclovir. Despite treatment, some people are left with significant loss of memory. About 2 out of every 3 people will have memory difficulties long term.

The study

2. Why are we doing this study?

We know dexamethasone can reduce swelling. Reduction in swelling of the brain may improve the recovery of patients with HSV encephalitis.

This study, called DexEnceph, will allow us to compare the recovery of patients that received a short course of dexamethasone and those that did not.

3. Why has your friend/relative been invited to take part?

There are two reasons why they may have been invited to take part:

A. Their doctors have diagnosed him/her with having HSV encephalitis.

OR

B. You may have been invited to take part before the diagnosis is made. This is because the doctors think there is a chance they may have HSV encephalitis. This will mean you have more time to think about taking part.

4. What will happen during the study?

All patients in the study will receive aciclovir. This is standard treatment for HSV encephalitis.

In addition, if you decide to take part in the study, your relative/friend may be offered a short course of dexamethasone. This will be decided at random by a computer. This is to be fair, so neither you, the doctor, nor the research team, can choose whether they receive dexamethasone or not. Half of the people in the study will receive dexamethasone and half will not.

If your relative/friend receives dexamethasone this will be given 4 times a day for 4 days. It is given in a line they already have for clinical care.

What taking part involves

5. What tests will be done?

When you sign up to the study:
Blood sample
CSF sample
MRI scan

↓

After 2 weeks:
MRI scan
Blood sample
CSF sample

↓

After 1 month (or when you are discharged from hospital):
Review of activities daily living
Short memory test only

↓

After 6 months:
Memory test
MRI scan
Blood sample
Review of activities daily living
Health questionnaires

↓

After 18 months:
Memory test
MRI scan
Review of activities daily living
Health questionnaires

All the tests done when signing up to the study and the CSF tests after 2 weeks will be done as part of your relative's/friend's care whether they take part in the study or not.

6. What do the memory tests involve?

These tests are the most important in this study as they will help us find out if dexamethasone improves memory problems from HSV encephalitis. These tests are sometimes called Neuropsychology tests. They are completed after six months of the illness.

The key part of this test takes about 35 minutes. If your relative/friend is not too tired we can continue with further tests that will provide useful information. These can take up to 2 hours.

They are not pass or fail tests. They provide information about your relative/friend's memory and thinking processes.

They can be done in one day or divided over a few short visits. If your friend/relative has left hospital we can travel to see them in a convenient place for them. The test will be arranged on a day(s) which suits them.

The results can be added to their hospital notes for future reference if you wish or kept confidential within the trial.

7. What does the MRI scan involve?

As part of your relative/friend's care their doctor will organise an MRI scan when they are in hospital. If they take part in the study we will ask them to have another 3 scans later on.

MRI scans allow us to assess if the brain has been affected by the infection and, if so, which parts.

Each scan takes about 20 minutes. The scan can be noisy but they will be offered headphones.

The extra 3 scans are planned for:

- 2 weeks after the first one (when they are still in hospital)
- After 6 months
- After 18 months

We will check that you are still happy for them to have the scan each time.

Sometimes scans may find something not related to this illness. If this happens the doctors looking at the scans will tell your relative/friend's hospital doctors who will look into this further.

None of the research scans are compulsory so if they do not wish to have them they can still be part of the study.

8. Are there risks to having an MRI scan?

There are no known risks from an MRI scan. They do not use radiation. MRI scans are done routinely in patients with HSV encephalitis.

Because MRI scans use strong magnets your relative/friend will not have the scan if they have any metal implants or fragments in their body.

Where you lie is quite enclosed and some people may find this unsettling. If your relative/friend has a fear of confined spaces you should discuss this with your doctor before the scan.

If you think your relative/friend may be pregnant let your local research team know. We will not ask pregnant women to have MRI scans due to possible risks to the foetus.

9. What samples are collected? What does this involve?

We will collect blood and CSF samples during the study.

All patients with HSV encephalitis need a lumbar puncture (LP) when they come to hospital to find out why they are unwell. The doctor uses a small needle to

take a sample from the lower part of the back. This is repeated after 2 weeks of treatment to see if all the virus has gone. Both lumbar punctures are part of the standard care in all patients with this condition.

We will take a little extra fluid at this time for the research tests. The amount of fluid we ask for each time is about 1 teaspoon, 5.5mls.

If your relative/friend has already had a lumbar puncture before you were told about the study, we will take stored CSF that is leftover for research tests.

Blood tests are done at 3 different times spread over 6 months. We take between 1 to 4 teaspoons of blood, this is 5 to 25mls.

With these blood and CSF tests we will be able to better understand how the infection affects the body and how the body tries to defend itself against it.

10. What will happen to the samples that will be collected? Will any genetic tests be done?

All samples will be taken at the hospital and then transported to the University of Liverpool or other laboratories working in the study. The samples will not have any personal information written on them. In the University they will be stored in a secure building.

There is an option for the blood and CSF collected to have tests looking at DNA. DNA is found in all cells of the body and contains the genetic information for the working of all human. This study collects DNA samples to find out why some people get HSV encephalitis and others do not, and why some people have severe problems due to HSV and others do not. The information we learn from DNA may benefit others with this condition in the future but will not influence your relative/friend's treatment or their future health.

Some of their samples may be left over. We will ask you if they can be used for this and future studies run by the University of Liverpool.

11. How do you review activities of daily living?

We will find out how the illness has affected your relative/friend's day-to-day life.

The research team will look at their hospital notes. They may also contact you. This will happen when they are in hospital and when they have gone home.

We will compare patients who received dexamethasone to those that did not and see if it made a difference.

12. What are the health questionnaires?

Two questionnaires will sent through the post. They will ask your views about your their health and quality of life. Please send them back in a pre-paid envelope.

Dexamethasone

13. What are the side effects of dexamethasone?

Dexamethasone is used widely in patients and the side-effects are well known as this medicine has been prescribed for a long time. A short course of dexamethasone will be prescribed in this study. Side effects are less common when dexamethasone is given for shorter periods.

It is important you know about the possible side-effects before deciding to take part. These are:

- Stomach pain, indigestion, having more appetite than usual, feeling or being sick.
- Feeling tired or fatigued
- Mood and behaviour changes, especially at the beginning.
- Higher blood sugars

Other possible risks can include:

- Stomach ulcers and bleeding of ulcers.
- Decreased response to infections.

Your relative/friend will be in hospital when they take dexamethasone so you can tell doctors immediately if they have any problem.

If they suffer side effects you or the doctors can decide to stop the dexamethasone at any point.

Dexamethasone is prescribed to women who are pregnant or breast feeding as there are no known risks to the foetus.

Other things to consider

14. Does my friend/relative have to take part?

No, taking part is voluntary. If you agree, we will ask you to sign a consent form.

If you agree to take part you are free to change your mind at any time, without giving a reason. You may decide your relative/friend only has some tests in the study without having to drop out of the study altogether. This will not affect the standard of care they receive.

If you withdraw your relative/friend from the study we will stop collecting data. We will ask you if we can use the information and samples we have gathered up to the point that they are withdrawn.

15. What happens if there is a problem?

If you have any concerns about any part of this study, please speak with the hospital doctor (consultant) or one of your research team.

If you remain unhappy and wish to complain formally you can do this using the NHS Complaints Procedure. You can get information on how to do this from the Patients Advice Liaison department (PALS) in the hospital.

If your relative/friend suffers harm from taking part in this study, there are no special compensation arrangements. If harm occurs to them and it is due to someone's negligence, they may have grounds for legal action for compensation against the NHS hospital where they are being treated but they may have to pay the legal costs.

16. Who will know my friend/relative has taken part in this study?

Only people in your relative/friend's clinical care team and people involved in the study will have access to personal data. With your consent we will tell their GP that they are taking part.

All information collected during this study will be confidential and anonymised. It will be handled, stored and destroyed in accordance with the General Data Protection Regulation.

University of Liverpool is the sponsor for this study based in the United Kingdom. We will be using information from you and your medical records in order to undertake this study and will act as the data controller for this study. This means that we are responsible for looking after your information and using it properly. University of Liverpool will keep identifiable information about you for 15 years after the study has finished

Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that

we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible.

You can find out more about how we use your information http://www.dexenceph.org.uk/. Our Data Protection Officer is Victoria Heath and you can contact them at V.Heath@liverpool.ac.uk.

Benefits and risks

17. What are the benefits of taking part?

Your relative/friend may benefit from receiving dexamethasone, however we will not know this until the end of the study. They may also benefit from the increased monitoring of having extra scans and memory tests.

The information we get from this study may benefit patients in the future.

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

The disadvantage in taking part in this study may be the risk of having the side-effects of dexamethasone listed in question 13 (this will not be the case if they are in the group that does not have dexamethasone).

There is the inconvenience of having the dexamethasone through the drip when they are in hospital. Once they leave hospital there is the inconvenience of travelling to hospital for 2 scans, having the memory tests and completing questionnaires.

Contact details

If you have any questions about this study, then please contact the study team members:

Principal Investigator (Doctor leading this study in your hospital):
Name: _____

_____

Telephone:_____

Research Nurse:
Name: _____

_____

Telephone:_____

Name of Hospital: _____

_____

Further information

This study is being run at your hospital and many other NHS hospitals throughout the UK. It aims to recruit 90 patients over 4 years.

It is organised by the University of Liverpool and is funded by the National Institute for Health Research (NIHR), the public body in charge of research in the UK.

Our study team includes The Encephalitis Society, a charity that supports patients and families (www.encephalitis.info).

The study has been reviewed for scientific content by expert members of NIHR. The National Research Ethics Service Committee Liverpool Central has reviewed the study and given approval for it to take place.

DexEnceph
BrainInfectionsUK.org

RCT Legal Representative Consent Form
Version 5.0, Dated: 25/May/2018
EudraCT Number: 2015-001609-16

Centre Name: Centre Code:
Name of Principal Investigator:
Study Number:

Please complete this form. When completed give one copy to the participant to keep, send one to CTU [fax/encrypted email/post], and keep one in the participant's medical notes. Please put the original in the site file

For legal representative: once you have understood each statement please initial the YES OR NO box	**YES**	**NO**
1. I confirm I have read and understand the Information Leaflet (dated DD/MMM/YYYY) for the above study, and have had the opportunity to ask questions and have these answered satisfactorily.	INITIAL IF YES	INITIAL IF NO
2. I agree for my relative/friend/patient to take part in this study.	INITIAL IF YES	INITIAL IF NO
3. I understand that participation is voluntary and that I am free to withdraw my relative/friend/patient from the study at any time without giving a reason and without their care or our legal rights being affected.	INITIAL IF YES	INITIAL IF NO
4. I agree for this consent form and our contact details to be passed to the University of Liverpool for the administration of the study.	INITIAL IF YES	INITIAL IF NO
5. I understand that relevant sections of my relative/friend/patient's medical notes and any data collected during the study may be looked at by authorised individuals from the research and clinical team and Regulatory Authorities where it is relevant to them taking part in this research. I give permission for these individuals to have access to their records.	INITIAL IF YES	INITIAL IF NO

6. I agree for genetic tests to be done on blood and CSF collected. I understand these genetic tests will not be of any individual significance to my relative/friend/patient.	INITIAL IF YES	INITIAL IF NO
7. I agree for my relative/friend/relative to have MRI scans as part of the trial.	INITIAL IF YES	INITIAL IF NO
8. I agree to gift the remainder of any blood or CSF sample to the University of Liverpool where it will be stored for use in future research. This may include genetic tests.	INITIAL IF YES	INITIAL IF NO
9. I agree to any images or scans that are taken to be used for teaching, education and publication (in scientific journals, books or internet).	INITIAL IF YES	INITIAL IF NO
10. I agree for my relative/friend/patient's GP to be informed they are taking part in this study.	INITIAL IF YES	INITIAL IF NO

Name of Legal Representative (Please print)	Relationship to Participant	Signature	Date (DD/MM/YYYY)

Researcher*	Signature	Date (DD/MM/YYYY)

*** Important:** Prior to signing please ensure local research contact details are complete on page 6.

Information to Research Team:

Once a Consent Form has been signed, please copy three times: One for the participant, one to file in the medical notes and fax/ post /encrypted email one to CTU. Please place original in the site file.

Please fax/email/post this consent form to CTU **separately** to other anonymised trial documents (e.g. CRF).