NEMO-1 study

dose finding stage

NEonatal Seizure Treatment with **M**edication **O**ff-patent:
Dose-finding for bumetanide

Information leaflet for parents

The NEMO-1 study

Neonatal seizure treatment study

Thank you for reading this sheet about our research study.

Why have you asked that my baby take part in NEMO-1?

Your baby has shown signs of stress after their delivery. The doctors and nurses looking after your baby have noticed that your baby has started to have neonatal seizures (also called fits or convulsions).

Neonatal seizures can be difficult to treat, and the doctors in your hospital are involved in a research study to look at new ways to treat neonatal seizures. This is called the NEMO-1 study. We are asking you to allow your baby to take part in the NEMO-1 study. Approximately 50 babies will take part in the NEMO-1 study in hospitals across Europe, around 24 babies will be included in the dose finding stage. Results of all 50 babies will contribute to finding out the best dose of bumetanide to use in newborn babies and what levels babies have after a certain dose (pharmacokinetic analysis) . This sheet gives you information about NEMO-1, which the doctors involved in the study will also discuss with you later.

You will have a chance to ask questions about the study. Once you understand the study, if you are happy for your baby to take part, we will ask you to sign a consent form. We will give you a copy of this information leaflet and the consent form to keep.

What are the possible benefits of taking part?

We do not know if the study will help your baby, but the new drug may help your baby. The information we get may help us to treat other babies with seizures in the future. We hope also to get important information about the effects of seizures on a baby's brain. We will be able to share this information with other parents in the future.

What are neonatal seizures?

Seizures are caused by to too much electrical activity in the brain. Seizures are sometimes difficult to treat in newborn babies. The drugs, we use to treat seizures in babies do not always work.

The first drug which most doctors use to treat seizures in a newborn baby is called phenobarbitone. This works to stop seizures in about half of babies treated.

New research has found that if a drug called bumetanide is given at the same time as phenobarbitone, it may help phenobarbitone to work better. The NEMO-1 study will find out the best dose of bumetanide to use in newborn babies and what levels babies have after a certain dose (pharmacokinetic studies). After this, another study (NEMO-2), will test bumetanide in a larger group of babies.

What is involved for my baby?

If your baby's seizures do not stop after the first dose of phenobarbitone, we will give them a second dose of phenobarbitone, and at the same time a single dose of bumetanide. We will give your baby four doses of bumetanide in total over 36 hours.

We will monitor your baby during the study using EEG (brainwave) monitoring. We will continue this EEG for up to 48 hours to see if the number of seizures your baby has reduces or if the seizures stop altogether.

To make sure that your baby's body salts stay safe after their treatment with bumetanide we will need to take small blood samples every eight to twelve hours after they have had this drug for up to 48 hours.

Whenever possible we will take these samples from a line already in place in your baby. However, sometimes we will need additional blood samples.

We would like also to keep a small amount (4x0.5ml) of this blood so that we can work out the best dose of bumetanide to give. In total this is about half a teaspoonful that we will take over 60 hours. At the end of the study, we will measure the levels of bumetanide in these samples. We will keep the sample for up to 2 years after the study so we analyse all of the samples at one time. After this the remaining sample will be discarded.

We would be grateful if you would allow us to contact you at a later date to see how your baby is growing and developing.

Will my baby have any side-effects from this drug?

High doses of bumetanide have been shown to put babies at a very small risk of hearing loss. In this study, we will use a low dose of bumetanide. However, we will give all babies involved in the study hearing tests before they leave hospital.

Bumetanide is a type of drug called a diuretic. This may lead to your baby passing more urine and salt. This can sometimes lead to an imbalance in the body's salts, or dehydration. Your baby will be monitored very carefully for salt imbalances and dehydration. If this occurs the medication will be stopped, and the imbalance or dehydration will be corrected with special fluids given through a vein.

Bumetanide is a drug that has been used for many years to help babies with other conditions and is known to be very safe. This new use may be very helpful. Off-patent medicines are no longer under a patent from the pharmaceutical company that developed them.

Will my baby suffer any side-effects from the EEG?

The EEG is safe and painless, with no known side effects. We will have to handle your baby to place the EEG discs on the scalp.

We will attach the discs to your baby's head with a special soft paste and the discs are connected to a machine. It will record the electrical activity in your baby's brain.

As part of the EEG, we may also make a continuous video recording so we can watch your baby's movements.

If at any time we consider it unsafe for your baby to continue in the trial we will withdraw them. You can also remove your baby from the trial at any time. After withdrawal we will give them standard medical care. Unless you tell us otherwise, we will use any data we have collected up to the time your baby is withdrawn.

What will happen to the information collected in the study?

We will make all data collected and stored in the study anonymous. This means we will remove your name and your baby's name, address and other details and store them separately so we can contact you to arrange follow-up. We will give your baby a NEMO-1 study number and we will use this number to look at the data for the study.

Who is organising and funding the research?

The European Commission under Framework Programme 7 is funding the study under a scheme to support the use of off-patent medicines to treat important illnesses. Your local hospital ethics committee approved this protocol.

This trial is insured by Only for Children Pharmaceuticals (O4CP) who will monitor its safety.

Where can I get more Information?

If you have any questions about this study, you can contact us at:

Name of local principal Investigator: Prof. Neil Marlow

Address of local principal investigator: UCL EGA Institute for Women`s Health
74 Huntley Street;
London WC1E 6AU
United Kingdom

Phone number of local principal investigator:+44 (0) 20 7679 6060

Email of local principal investigator: n.marlow@ucl.ac.uk

NEMO-1 patient identification number:

Centre number:

Form version: 1.0

Date_____/_____/_____

If you agree to take part, the doctors involved in the study will talk to you again during the 48 hours that your baby is taking part. They will be available at any stage to discuss concerns or worries that you may have. If you have a concern about your baby's clinical care, please ask to speak to your baby's Consultant Neonatologist who will then meet you to discuss your concerns.

Notes:

_____
_____
_____
_____
_____

NEMO-1 study (dose finding stage)
Consent form

Project title NEMO1: An open label exploratory dose finding and pharmacokinetic clinical trial of bumetanide for the treatment of NEonatal seizure using Medication Off-patent

Name of chief investigator: Dr Ronit Pressler

Name of **local** principal investigator: _____

Address of **local** principal investigator: _____

Phone number of **local** principal investigator: _____

Email address of **local** principal investigator: _____

Please read the information below and then write your initials in the grey boxes.

1. I confirm that I have read and understood the information sheet dated ____/_____/___ (version___) for the above study and that I have had a chance to ask questions.
2. I confirm that I have had enough time to think about whether or not I want my baby to be included in the study.
3. I confirm that I am happy for my baby's anonymised video EEG data to be securely transferred to Cork, Ireland, via encrypted transfer media.
4. I confirm that I am happy for researchers in the NEMO team to have access to the results of my baby's routine hearing test, should that test be done after discharge from hospital.
5. I understand that I do not have to allow my baby to take part in the NEMO study and I can withdraw my baby from the study at any time, without giving any reason, without my baby's medical care or legal rights being affected.
6. I agree that if I choose to withdraw my baby from the study I give NEMO researchers permission to keep and use data or samples collected before this withdrawal. I understand that I can withdraw this permission at any time.
7. I understand that researchers involved in the NEMO study at this hospital_____ (hospital name) or regulatory authorities may look at parts of my baby's medical notes and the records of the labour and delivery of my baby. This will allow them to check that the trial has been run safely. I give permission for these individuals to have access to these records.
8. **I agree to allow my baby to take part in the NEMO study.**
9. I agree to allow small samples of my baby's blood to be retained for up to two years and then discarded after analysis.
10. I agree that the study team may contact me in the future regarding this study.

Name of patient:	Birth date: _____/_____/_____	HN:
Name of parent or guardian	Signature of parent or guardian	Date _____/_____/____
Independent witness	Witness signature	Date _____/_____/____
Investigator (to be contacted if there are any problems)	Signature	Date _____/_____/____