PARENT INFORMATION LEAFLET

Cooling in Mild Neonatal Encephalopathy Trial

(THE COMET Trial)

Cohort 2

VERSION 2.1, 20/09/2019

IRAS ID: 241031
Sponsor Reference: 18HH4385

Information leaflet for parents

We understand that this may be a difficult time for you. However, we think it is important for you to know about this particular study, taking place in our neonatal unit. This leaflet explains why the research is being done and what it will involve. Please take time to read the information carefully. One of our team members will go through the information sheet with you and answer any questions you have.

What is neonatal encephalopathy?
Neonatal encephalopathy is also known as 'birth asphyxia related brain injury' and happens when the brain does not receive enough oxygen or blood flow around the time of birth. It is not always known what causes this, but we do know that it can lead to brain injury. How well your baby recovers depend on how severe this brain injury is.

Why are we doing this study?
We know that babies with moderate or severe encephalopathy benefit from being cooled for the first 3 days after birth. However, we do not know whether this is an effective treatment for babies with mild encephalopathy. Although most babies with mild encephalopathy tend to rapidly recover on their own, it is difficult to say which babies will do well without any treatment and which will babies will progress to more moderate or severe encephalopathy after six hours of age.

Therefore, most hospitals in the UK, now provide the standard 3 day cooling therapy to all babies with encephalopathy, irrespective of the severity of brain injury. While cooling therapy is a relatively safe treatment, it does involve separating the baby from parents and keeping the baby in the intensive care unit and sedating with morphine (opioids). Cooling therapy may also cause transient problems with blood clotting (low platelets) and blood pressure. Moreover, recent data from laboratory studies suggests that a shorter period of cooling, may be equally neuroprotective as cooling for full 3 days in mild encephalopathy, while minimising the adverse effects of cooling.

The aim of this study is to examine if cooling therapy for 2 days is as good (neuroprotective) as cooling therapy for 3 days in babies with mild encephalopathy.

What does whole body cooling involve?
The normal core body temperature of babies is around 36.5°C. During cooling, each baby's core body temperature is reduced to 33.5°C using a special cooling mattress. After the completion of cooling, babies are slowly re-warmed to their normal body temperature. Cooling therapy is effective only if started within six hours of birth. Babies will also receive sedation with morphine or other opioids during cooling to make sure that they are not stressed. The rest of their clinical care, including feeding, will be exactly the same as for any other baby with neonatal encephalopathy.

Why is my baby suitable for this study?
We are recruiting babies who have mild neonatal encephalopathy following birth asphyxia who were started on started on cooling therapy within six hours of birth, but do not meet the established criteria (i.e. moderate or severe encephalopathy) for cooling. Your baby has suffered from birth asphyxia and was started cooling therapy by your doctors within six hours of birth. This is primarily because a small number of babies with mild encephalopathy may develop seizures between 6 to 24 hours of age, which require cooling therapy.

However, you baby has recovered rapidly over the first 24 hours after birth, and the electrical activity of the brain (aEEG) has remained normal, without any seizures. A detailed clinical examination now suggests that your baby has mild or no encephalopathy, and hence is likely to do well without any treatment. We are recruiting such babies to our study to examine if cooling therapy can be

discontinued after 2 days, instead of the standard 3 days required for babies with more severe brain injury.

What is involved in participating in this study?
If you agree to participate, your baby will be randomly allocated by a computer to one of the two groups.

Group 1: Cooling therapy for 3 days
Group 2: Cooling therapy for 2 days

As part of their routine clinical care, your baby will have an MRI scan before 2 weeks of age to see if they have any visible brain injury, so that we can make a prediction of the long-term implications on their health. Your baby's doctor will discuss the results of the MRI scan with you, including any incidental findings on the MRI.

The MRI takes approximately one hour, and neonatal nurses and/or doctors will closely monitor your baby during the scan. We often give babies an oral sedative for MRI scanning, which they usually tolerate very well. Most babies will sleep through the scan with this sedation and wake up soon after the scan for a feed. In most babies, the MRI scan is performed before the baby is discharged home. Occasionally, your baby may be discharged prior to the MRI scan, and the scan will be performed as an outpatient appointment. In this case, your baby will continue to be monitored for a few hours after the scan, to make sure that they are fully awake, and have had a good feed before going home.

We will also collect the data from your baby's clinical records, and the results of other tests they may receive as a part of their routine care. This may include an aEEG/EEG (brain activity recording), a brain ultrasound scan, an ECG (heart activity recording), and blood tests. We will collect the ECG data by attaching three small ECG leads to your baby for the first three days. We will also use 1 ml (quarter teaspoon) of blood collected soon after birth, and again three days later, to find out if cooling therapy is improving the activity of genes. These results will not be available before the entire study is completed, and so will not change the care given to your baby, but may influence the care given to similar babies in the future. Whenever possible, we will co-ordinate the time of these samples with your baby's routine clinical blood tests. Your baby may also have a detailed neurological assessment at two years of age as part of their routine clinical care, to see how they are developing. We will collect the data from this assessment for the purpose of this study.

We will also collect information from the mother's medical notes at the time of birth, to find details of any antenatal medical problems and the results of any important tests.

What are the risks of cooling and MRI scans?
Although cooling is remarkably safe, it may lower the platelet (blood clotting) levels in your baby's blood. We will monitor the platelet levels of all babies with neonatal encephalopathy, and will administer platelet transfusions if required. Some babies may develop small bumps on their skin, which will eventually disappear without any consequence. It is also possible that cooling may increase the hospital stay of your baby by a day or two.

MRI does not use x-rays or any harmful ionising radiation. According to expert authorities, there is no clear evidence of any adverse long-term effects following MRI scans. MRI scans are noisy, and require babies to be still. Hence, we will provide adequate ear protection for your baby and may give them some light oral sedation.

Does my baby have to take part?
Your baby does not have to take part in this study if you do not want them to be involved. If you do agree for your baby to take part, you will be given this information sheet to keep and will be asked to sign a consent form. You will be given a copy of the signed consent form for your records.

Whether or not you agree for your baby to take part, this will not affect the standard of care you and your baby receive in any way. If you choose not to take part, the care usually received by babies at your hospital will vary depending upon their guidelines, and this may or may not include cooling. Depending on your hospital's policy, your baby may still have the MRI scan and neurological assessment at two years of age.

What happens when the research study ends?
The final assessment for this study is at the time of the MRI scan (before two weeks of age). We are hoping to obtain further funding to perform a detailed neurological assessment of all babies at school age as well. We may contact you and your GP at a later stage, requesting your permission to undertake these assessments.

What if relevant new information becomes available?
It is possible that new information may become available during the course of the study (2-3 years). It is unlikely that this will affect your baby's involvement with this study. If the study is stopped early because of new information, you will be informed about this.

What will happen if I do not want to carry on with the study?
Your baby's participation in this study is entirely voluntary. You are free to decline for your baby to enter or for your baby to withdraw from the study at any time without having to provide a reason. If you choose to do this, it will in no way affect your baby's future medical care. We may ask you for your consent to use the information already collected so far, or as a part of standard clinical care, for research purposes.

What if there is a problem?
Imperial College London holds insurance policies which apply to this study. If you experience harm or injury as a result of taking part in this study, you will be eligible to claim compensation without having to prove that Imperial College London is at fault. This does not affect your legal rights to seek compensation.

If you are harmed due to someone's negligence, then you may have grounds for legal action. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been treated during the course of this study then you should immediately inform the local Principal Investigator (Name xx, Tel: xxx). The normal National Health Service complaints services are also available to you. If you are still not satisfied with the response, you may contact the Imperial AHSC Joint Research Compliance Office.

Will my taking part in this study be kept confidential?
All information collected about your baby (or other family members) during the course of this research will be kept strictly confidential. We may inform your baby's GP about him or her taking part in this research, and will seek your permission to do so. Once your baby reaches two years of age we may also collect any additional information from your GP or from any other hospital where your baby might have received clinical care. All babies who receive NHS care also have their clinical data stored at the National Neonatal Research Database at Imperial College London. We will seek your permission to access these data for research purposes.

General data protection transparency statement
Imperial College London is the sponsor for this study based in the United Kingdom. We will be using information from you and your baby's 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. Imperial College London will keep identifiable information about you for 10 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 on the link below. http://www.imperial.ac.uk/joint-research-compliance-office/standard-operating-procedures/

[NHS/other site] will use your name, NHS number and contact details to contact you about the research study, and make sure that relevant information about the study is recorded for your care, and to oversee the quality of the study. Individuals from Imperial College London and regulatory organisations may look at your medical and research records to check the accuracy of the research study. [NHS site] will pass these details to Imperial College London along with the information collected from you and your baby's medical records. The only people in Imperial College London who will have access to information that identifies you will be people who need to contact you to neurodevelopmental follow up of your baby or audit the data collection process. 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. [NHS/ other site] will keep identifiable information about you from this study for 10 years after the study has finished.

Imperial College London will also collect information about your baby for research from the national neonatal database, based at Imperial College London. This information will include your baby's name, NHS number, contact details and health information, which is regarded as a special category of information. We will use this information to the purpose of the current research.

The information about your baby could be used for research in any aspect of health or care and could be combined with information about you from other sources held by researchers, the NHS or government, in future. Where this information could identify you or your baby, the information will be held securely with strict arrangements about who can access the information. The information will only be used for the purpose of health and care research, or to contact you about future opportunities to participate in research. It will not be used to make decisions about future services available to you, such as insurance. Where there is a risk that you can be identified your data will only be used in research that has been independently reviewed by an ethics committee.

Who will have access to my case/research records?
All the data and images collected as part of this study will be stored both on a secure computer locally, and centrally at Imperial College London. Only the researchers involved in this study will have access to the data collected during the course of this study. A representative of the hospital's Research Ethics Committee will also have access to data. The 1998 Data Protection Act safeguards the use of some types of personal information. This places an obligation on those who record or use personal information, but also gives rights to people about whom information is held. If you have any questions about data protection, please contact a member of the research team or PALS (patient advice and liaison service) or the Data Protection Officer. The results from our project will be published as papers in medical journals. No data will be published that allows for individuals to be identified in any way. If requested, we will be able to send you copies of any papers published when we have completed the study. The study may also form part of a postgraduate research project (MD or PhD).

Who do I speak to if I have further questions or worries or complaints?
In the first instance please contact the Principal Investigator locally. If you wish to speak to someone not directly involved in the study, please contact PALS at the local hospital.

What will happen to the results of the study?
This study will run for three years. The results of the study will be made available to doctors and nurses caring for babies like yours across the world. You and your baby will by no means be identified in any report or publications about the study. We can send you a summary of the final results, if requested.

Who is organising and funding the research?
The study will be run at several national and international sites. It is funded by the National Institute for Health Research. Imperial College London is the main sponsor. Doctors will not be paid for including you in the study, nor do participants receive payment.

Who has reviewed/ approved the study?
All research in the NHS is looked at by an independent group of people called a Research Ethics Committee, to protect your interests. This study has been reviewed and approved by West of Scotland Research Ethics (REC 5) Committee.

Please do not hesitate to ask if you have more questions.

Local Principal Investigator

Dr Gaurav Atreja MD DCH FRCPCH
Consultant Neonatologist
Imperial Hospitals NHS Foundation Trust
Du Cane Road, London W12 0HS
Phone 02033131134
Sec: Marion Smith 02033135369
Email: gatreja@nhs.net

Maria Moreno Morales, BSc
Neonatal Neurology Research Nurse
Centre for Perinatal Neuroscience
Imperial College London, Du Cane Road, London, W12 0HS
Mobile:07454308089
Email: m.moreno-morales@imperial.ac.uk

Sudhin Thayyil MD, DCH,FRCPCH, PhD
Reader on Hon Consultant Neonatologist
Head of Academic Neonatology
Director Centre for Perinatal Neuroscience
Imperial College London and Imperial Neonatal Service
Du Cane Road, London, W12 0HS
Mobile: 07912888700
Email: s.thayyil@imperial.ac.uk