*To be printed on hospital headed paper*

**PARENT INFORMATION SHEET**

rEECur

**International Randomised Controlled Trial of Chemotherapy for the Treatment of Recurrent and Primary Refractory Ewing Sarcoma**

Dear Parent/Guardian,

We would like to invite your child to take part in a non-commercial clinical trial, run by the University of Birmingham, called rEECur that concerns the treatment of his/her disease. Before you decide whether you want your child to take part, it is important that you understand why the research is being done and what it involves. Please take time to read the following information sheet carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish for your child to take part. Taking part in this trial is voluntary and will not affect the standard of care your child receives.

This document is provided to help you understand what treatment will be given to your child, and will provide answers to the following questions:

* **Section 1 – What is the standard treatment for Ewing sarcoma that has not responded to treatment or has recurred?**

This section explains what the standard treatment for Ewing sarcoma in these situations involves.

* **Section 2 – What are clinical trials and what is the rEECur trial?**

This section explains why the research is being done, and what it involves.

* **Section 3 – What else do I need to know about taking part in the trial?**

This section answers any additional questions you may have about taking part in this trial.

# Section 1: What is the standard treatment for Ewing sarcoma that has not responded to treatment or has recurred?

There is no standard treatment for Ewing sarcoma that has not responded to initial treatment or has recurred. In these situations doctors take into account factors such as how long has passed since initial treatment of the Ewing sarcoma, how widespread the disease is when it becomes clear that it has not responded or has recurred and how well the child or young person is. If treatment is given with the intention of cure, treatment can include chemotherapy, radiotherapy, surgery or any combination of these. For some children and young people, treatment is not given with the intention of cure, but to improve symptoms. In this situation, treatment may still involve any combination of chemotherapy, radiotherapy or surgery or may not involve any of these.

# Section 2: What are clinical trials and what is the rEECur trial?

**What are clinical trials?**

Clinical trials are research studies that compare different types of treatment to help find more effective and safer ways of treating participants with a specific disease. Each trial is aimed at improving survival rates and/or reducing side effects. It is largely because of clinical trials that such progress has been made in the treatment of children’s and young people’s cancers over the last few decades.

**What is the rEECur trial?**

The aim of the rEECur trial is to compare different chemotherapy regimens to find out which is most effective and/or has fewest side effects. The best way of testing this is through a randomised trial. In a randomised trial, participants are selected on a random basis by computer and allocated to receive one of a small number of different treatments (known as treatment arms). This method means that neither the participant/parents, nor the doctor will be able to influence which treatment arm is given to each participant. Equal numbers of participants are treated in each arm and at the end of the trial the results are compared.

If you agree for your child to take part in the trial you will be asked to sign a consent form before treatment starts. If you give your consent your child will be allocated to one of the available chemotherapy regimens (or treatment arms). Each regimen is already in widespread use across Europe in participants with recurrent Ewing sarcoma. The chemotherapy regimens have never been compared in a clinical trial so we do not yet know which one is the best at treating recurrent Ewing sarcoma or which has fewest side effects. A randomised study will allow us to compare the regimens to help us work out which is best.

**Why has my child been invited to take part?**

Your child has been invited to participate in this trial because he/she has recently been diagnosed with Ewing sarcoma that has either not responded to initial treatment (this is sometimes called ‘refractory’ disease) or has recurred after the end of treatment. About 500 children and adults in the UK and around the world will take part in this study.

**Does my child have to take part?**

No. You may decide whether or not you want your child to take part in this trial. If your child does take part, we will ask you to sign a consent form. You are free to withdraw your child from the study at any time, without giving a reason and your child will continue treatment at the same hospital with the same medical team. If your child is of an age to be able to give his/her opinion, your child may express a wish not to take part in the trial. If this is the case, his/her views must be taken into consideration. If you decide for your child not to participate, the doctor will discuss with you the treatment options available.

**What will happen to my child if he/she takes part?**

If you agree for your child to participate, the doctor will review your child’s diagnostic tests and medical notes to confirm that he/she is eligible for the study. .

Your child will then be entered into the trial and randomly allocated to one of the available treatment arms:

|  |  |
| --- | --- |
| **IFOS** | Four cycles of chemotherapy with a drug called  **ifosfamide**  Each cycle will involve 5 consecutive days of chemotherapy and will be given at 3 week intervals |

OR

|  |  |
| --- | --- |
| **CE** | Six cycles of chemotherapy with two drugs called  **carboplatin** and **etoposide**.  Each cycle will involve 3 consecutive days of chemotherapy and will be given at 3 week intervals |

**Expenses and payments**

Neither you nor your child will receive any money or travel expenses for taking part in this trial.

**What will my child and I have to do?**

*Before treatment starts*

Before your child starts treatment, his/her doctor will perform the following routine tests:

* Physical check-up including measuring height and weight
* Blood tests +/- urine tests
* Assessment of your child’s kidneys called a GFR.
* Scans (which may include CT, PET-CT, MRI, bone scan, x-ray). The doctor will decide which type of scans your child needs depending on where the tumour is located.

Your child may also have additional tests such as a bone marrow aspirate and biopsy. This is a test to see if the disease has spread to the bone marrow. The doctor will explain how this will be done.

If you agree, your child’s doctor may also organise an extra scan called a PET-CT scan. PET-CT scans are sometimes used in Ewing sarcoma to see how widespread the disease is but they are not always a routine scan. The study will investigate whether PET-CT is better than routine scans at measuring how widespread disease is before and after treatment.

You and your child will also be asked to complete a questionnaire called a ‘Quality of Life’ questionnaire, to look at how his/her Ewing sarcoma is affecting their ability to carry out normal activities. Your child’s questionnaire will be at a level appropriate for their age and understanding and will take up to 10 minutes to complete. You may be asked to read the questionnaire to your child.

In order to receive chemotherapy, your child may need a central line, like the central line they had during their initial treatment for Ewing sarcoma. Your child’s doctor will discuss this with you. The central line enables the doctors to give drugs directly into the bloodstream (intravenously) and to take blood samples without using any extra needles.

*During trial treatment*

While your child is having chemotherapy treatment they will be carefully monitored using the same routine tests that would be used if they were having chemotherapy but were not in the rEECur trial. These routine tests will include blood +/- urine tests, scans and GFR. These tests are to ensure that your child is fit to continue chemotherapy. In addition, if your child has had a PET-CT scan before treatment, they will have another PET-CT scan after 4 cycles of chemotherapy.

You and your child will be asked to complete two more quality of life questionnaires, one on completion of cycle 2 and one on completion of cycle 4.

*Other Treatment*

Your child may have additional treatments including surgery, radiotherapy and high dose chemotherapy (sometimes known as ‘myeloablative therapy’ or a ‘stem cell transplant’). These treatments are not part of the trial. Your doctor will decide if your child should have them and will discuss them with you.

**How will the doctor know if things are going well?**

During treatment, your child will have routine tests to monitor progress such as physical examinations, blood tests and scans.

**What are the side effects of standard chemotherapy?**

Chemotherapy is used in all arms of this clinical trial. Chemotherapy destroys tumour cells, but can also damage normal healthy cells in the body. Side effects occur when healthy cells become damaged. Common side effects of chemotherapy drugs include:

* Hair loss, but it will grow back after the chemotherapy has finished
* Nausea (feeling sick) and vomiting
* Reduced bone marrow function

The bone marrow makes red blood cells, white blood cells and platelets.

* + Red blood cells carry oxygen. If these are low, your child may be tired or pale and need a blood transfusion.
  + White blood cells fight infection. If these are low, your child will be at risk of developing an infection. If he/she develops a fever, admission to hospital will be necessary for intravenous antibiotics (through a drip).
  + Platelets help stop bleeding and bruising. If these are low, a platelet transfusion can be given.

The effect on the bone marrow is temporary. Before each cycle of chemotherapy, blood tests will be done to check that your child’s bone marrow function has recovered enough to continue.

Other side effects include a sore mouth, dry skin, constipation and diarrhoea. These are temporary. Your child’s doctor or a dietician will be able to advise you if necessary. Medication is available to help manage some of the side effects.

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Ifosfamide can affect the central nervous system leading to drowsiness, confusion, disorientation, restlessness and hallucinations. Ifosfamide can also cause kidney problems.

Carboplatin sometimes affects the nerves, causing neuropathy which may lead to numbness, pins and needles and occasionally weakness. Some people develop kidney problems and sometimes carboplatin causes deafness. Occasionally, people become allergic to carboplatin.

Etoposide can cause kidney and liver problems.

There are other side effects of chemotherapy, some of which can be serious or life-threatening, and your child’s doctor will be available to discuss these with you.

Chemotherapy can also have long-term effects such as a reduction in fertility and an increased risk of developing a second cancer after the completion of treatment. Your child’s doctor will discuss these side effects with you.

*Radiation risk*

As part of this study, your child may have bone scans, PET-CT scans and up to five CT scans. They may also have assessments of their kidneys called GFRs. All of these tests are to look at the extent of disease and how your child is responding to treatment. Most of the tests that your child will undergo are the same as if they were not taking part in this trial, as they form part of standard practice.  However, in some centres PET-CT scans would not routinely be performed as part of standard practice, but they may provide useful information about the extent of disease.  Your child would only have these scans if the doctor feels that they may be useful, and with your agreement.

All of these tests use ionising radiation, which is thought to be associated with a very small increased risk of developing a second cancer in the future. At present, there are no better ways of imaging the body which avoids this radiation, and the tests are only performed to inform your child’s treatment and management.

*Harm to the unborn child*

It is important that pregnancy does not occur during treatment because chemotherapy can damage an unborn baby. If your child has reached the age of puberty, we shall need to discuss matters concerning contraception or pregnancy with him/her. This may or may not be in your presence as your child can request that this discussion takes place confidentially.

If your child is sexually active, he/she must agree to use an effective form of contraception during the time that he/she is receiving trial treatment. Both girls and boys must continue to use contraception for 12 months after the end of treatment.

If your child is female and of child-bearing age, she will have a pregnancy test before treatment starts. If your daughter becomes pregnant whilst on the study, the pregnancy will need to be monitored. Information about the outcome of the pregnancy will be collected from the mother’s and baby’s medical notes. If your son’s partner becomes pregnant during the study, the outcome of the pregnancy will also be monitored. Females must not breastfeed during chemotherapy.

**What will my child and I have to do?**

If you agree to your child taking part in the trial, you and your child will be asked to:

* Attend all scheduled clinic appointments
* Tell the study doctor about any medications your child takes, even if it is medicine you buy without a prescription or is a natural or herbal remedy
* Tell the doctor about any side effect, injury, symptom or complaint your child experiences, including any unplanned hospital admissions
* If your child is sexually active, ensure that they use an adequate method of birth control while receiving treatment. Both girls and boys must continue to do so for 12 months after the end of treatment.
* Complete the questionnaires when asked to do so

**Will any additional samples be taken from my child?**

With your consent, we would like to collect some additional tumour, bone marrow and blood samples at times when we are collecting samples for diagnosis and monitoring of treatment. These samples will be used in ethically approved research studies designed to further improve treatment for future patients with Ewing sarcoma. Samples may be sent to and analysed at laboratories in Europe. You will be offered the chance to consent to this.

**What are the alternative treatments?**

In the UK, several chemotherapy regimens are used in Ewing sarcoma that has not responded to initial treatment or has recurred. The chemotherapy regimens being studied in this trial are among the most commonly used regimens. However, other chemotherapy regimens are also used. Your doctor may discuss these other regimens with you.

**What are the possible disadvantages and risks of taking part?**

As this is a randomised trial, there is a risk that your child may not be assigned to the treatment arm that you or your child would prefer. Neither you, your child, nor your doctor can choose a particular chemotherapy regimen as part of this trial. Although all of the chemotherapy regimens in this trial are already used to treat people with recurrent or refractory Ewing sarcoma, there is no guarantee that they will benefit your child.

**What are the possible benefits of taking part?**

We cannot promise that your child will benefit from taking part in this study. It is possible that the treatment arm that your child is allocated to will be the most effective or have the fewest side effects. We will not know this until the results of the trial are available. The information gained from this study will help improve treatment for other children and adults with Ewing sarcoma in the future.

**How long will my child be involved in the trial?**

After treatment has finished, the study team will continue to collect data about your child’s health for at least 5 years. Your child will only need to attend routine clinic appointments for this information to be collected.

# Section 3: What else do I need to know about taking part in the trial?

**What if relevant new information becomes available?**

Sometimes during the course of a trial we get new information about the treatment being studied. If this happens, the study doctor will tell you and discuss whether your child should continue in the trial. If you decide you do not want your child to carry on, the doctor will make arrangements for his/her care to continue. If you decide for your child to continue in the trial, the doctor may ask you to sign an updated consent form. If new information becomes available, the doctor might consider it to be in your child’s best interests to change your child’s treatment. The doctor will explain the reasons and arrange for your child’s care to continue.

**What will happen if I don’t want my child to carry on with the study?**

You are free to withdraw your child from trial treatment at any time without giving a reason and this will not affect his/her standard of care. If this happens, you will be asked to allow the continued collection of follow-up data (your child will not need to attend more clinic appointments than normal for his/her condition), though you are also free to withdraw consent for further data collection if you wish.

**What if there is a problem?**

If you have a concern about any aspect of this trial, you should contact the local medical team who will do their best to answer your questions. You can use the contact number at the end of this sheet. If you remain unhappy and wish to complain formally, you can do this through the National Health Service (NHS) Complaints Procedure. Details can be obtained from your hospital.

In the event that something does go wrong and your child is harmed during the trial, there are no special compensation arrangements. The Cancer Research UK Clinical Trials Unit (the Trial Office) does not hold insurance against claims for compensation for injury caused by participation in this trial and they cannot offer any indemnity. If your child is harmed and this is due to someone’s negligence, then you may have grounds for legal action for compensation against the sponsor of the trial (University of Birmingham) or the NHS Trust but you may have to pay your legal costs. NHS Trust hospitals have a duty of care to participants treated, whether or not the participant is taking part in a clinical trial and the normal NHS complaints mechanisms will still be available to you (if appropriate).

**Will my child’s taking part in this trial be kept confidential?**

All information collected about your child for this trial will be subject to the General Data Protection Regulation and equivalent European Legislation and will be kept strictly confidential. All information will be securely stored at the Cancer Research UK Clinical Trials Unit at the University of Birmingham (the Trial Office) on paper and electronically and will only be accessible by authorised personnel.

With your permission, your child’s GP will be notified that your child intends to participate in the trial. A copy of your child’s consent form will be sent in the post to the Trial Office. We may also share information with other hospitals involved in the care of your child and with the national cancer registry for the country where your child lives. We would also like to collect your child’s NHS number or national equivalent. This will help us combine it with information held about your child by other health or government organisations. Doing this makes maximum use of the information you have provided and allows researchers to discover more.

In the Trial Office, your child will be identified by a unique trial number, their initials, date of birth and hospital number; we may also collect their histopathology (tissue sample) number. In routine communication between the hospital and the Trial Office, your child will only be identified by their trial number. Information about your child, including medical data, may be provided to the Trial Office on paper, over the phone, or electronically.

By allowing your child to take part in the trial, you will be agreeing to allow research staff from the Trial Office to look at the trial records, including your child’s medical records. It may be necessary to allow authorised personnel from government regulatory agencies (e.g. the Medicines and Healthcare products Regulatory Agency (MHRA)), sponsors and/or NHS bodies to have access to information about your child. This is to ensure that the trial is being conducted to the highest possible standards.

In addition, linked-anonymised (this means identified by a unique reference number only) data from the trial may be provided to other third parties (e.g. other academic institutions) for research and safety monitoring.

Copies of your child’s Informed Consent Form may be forwarded onto other healthcare professionals to prove that they are taking part in the trial (for example this may be your child’s GP if we are asking them to provide information for your child).

In addition, copies of your child’s scans may be sent to the Trial Office or to another hospital to be reviewed by an independent group of specialist doctors. Some personal details, which may include your child’s full name, and date of birth, may be sent with the scans to ensure that they are correctly identified.

All individuals who have access to your child’s information have a duty of confidentiality.Under no circumstances will your child be identified in any way in any report, presentation or publication arising from this trial.

If you choose to withdraw your child from the trial treatment, we would still like to collect relevant information about his/her health, as this will be invaluable to our research. If you have any objection to this please let your child’s doctor know.

You can withdraw your consent to our processing of your child’s data at any time. Under the provisions of the General Data Protection Regulation you have the right to know what information the Trial Office have recorded about your child. If you wish to view this information please contact Legal Services at the address below.

Legal Services

University of Birmingham

Edgbaston

BIRMINGHAM

B15 2TT

**General Data Protection Regulation (GDPR) Information**

The University of Birmingham is the sponsor for this study based in the United Kingdom. We will be using information from your child and/or their 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 child’s information and using it properly. The University of Birmingham will keep identifiable information about your child for up to 25 years after the study has finished.

Your child’s rights to access, change, or move their information is limited, as we need to manage their information in specific ways in order for the research to be reliable and accurate. If your child withdraws from the study, we will keep the information about them that we have already obtained. To safeguard your child’s rights, we will use the minimum personally-identifiable information possible.

You can find out more about how we use your child’s information in our Privacy Policy on our website (www.birmingham.ac.uk/crctu).

The NHS via your child’s hospital(s) will collect information from your child’s medical records for this research study in accordance with our instructions. Your child’s hospital(s) will use their 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 child’s care, and to oversee the quality of the study.

The NHS will keep identifiable information about your child from this study for up to 25 years after the study has finished.

**What will happen to any samples taken from my child?**

Samples taken from your child for trial and research purposes will be stored at an approved laboratory. After the samples have been used for research associated with this trial, there may be spare material left over. With your consent, this may be stored and used for other ethically approved research.

**Will any genetic tests be done?**

Genetic tests may be done on samples taken from your child in order to confirm diagnosis, and with your consent, for research purposes. No testing for inherited diseases or paternity will be carried out.

**What will happen to the results of the trial?**

When the trial is complete the results will be published in a medical journal but no individual participants will be identified. If you would like to obtain a copy of the published results, please ask your study doctor or nurse.

**Who is organising and funding the trial?**

rEECur is a non-commercial clinical trial. The idea for the trial came from doctors who work in hospitals and universities in the UK and other European countries, and these doctors lead this research study.

This trial is being sponsored by the University of Birmingham, run by the Cancer Research UK Clinical Trials Unit based at the University, and is funded by the European Commission through their FP7 funding programme and Cancer Research UK. <http://www.cancerresearchuk.org/>.

**Who has reviewed the trial?**

This clinical trial has been reviewed by the European Commission FP7 Funding Committee, Cancer Research UK and also by an independent Research Ethics Committee. Research Ethics Committees review all research to protect the safety, rights, wellbeing and dignity of participants.

**Further information and contact details**

If you have any questions or concerns about your child’s disease or this clinical trial, please discuss them with your child’s doctor. You may also find it helpful to contact CancerHelp, an information service about cancer Freephone: **0808 800 40 40, website:** [www.cancerhelp.org.uk](http://www.cancerhelp.org.uk)**.**

**Contact Details**

Study Doctor: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Research Nurse: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

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*Thank you for reading this information sheet.*