Trial of Optimal Therapy for Pseudomonas Eradication in Cystic Fibrosis

(www.torpedo-cf.org.uk)

You have been invited to take part in a research study. Before you decide whether or not to take part it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish.

- **Part 1** tells you the purpose of the study and what will happen if you take part
- **Part 2** gives you more detailed information about how the study will be organised

Please 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 to take part.

Part 1

1) What is the purpose of the study?

People with Cystic Fibrosis are at risk of developing infection in their lungs. If this should happen then a common cause of infection can be a bacteria or germ called *Pseudomonas aeruginosa*. Usually when this bacteria is first found in the sputum or cough swab patients are treated with antibiotics to get rid of (eradicate) the bacteria. There is a choice of treatment that can then be used to eradicate the bacteria – either antibiotics taken by mouth (orally) or given directly into the vein usually in the arm or the back of the hand (intravenously, IV). Each is given in association with three months of inhaled antibiotic treatment through a machine called a nebuliser which allows you to inhale the medication as a mist directly into your lungs. It is generally accepted that these treatments are essential to try to get rid of *Pseudomonas* from the lung and your doctor would normally choose one of these methods to treat you if you have *Pseudomonas* in your lungs. However, we do not know for sure which of these two treatments is the best to help to get rid of this type of infection.

The only way to find out which of these two treatments is the most helpful is to compare the two treatments in adults and children with Cystic Fibrosis (CF). This type of study is called a Randomised Controlled Trial (RCT).

We have therefore designed a study to compare the two different antibiotic treatments. If you agree to take part you will be randomly allocated to one of two groups;

Treatment A) 14 days IV ceftazidime and IV tobramycin*
Treatment B) 3 months oral ciprofloxacin*
**Both treatment allocations will be given in conjunction with 3 months inhaled (nebulised) colistin*

2) Why have I been chosen?

This study will recruit 280 patients from CF centres throughout the UK.

You have been asked to take part in this study because your CF centre has recently indentified that you have *Pseudomonas aeruginosa* infection of the lungs.

3) Do I have to take part?

No, taking part is voluntary. It is up to you if you decide whether or not to take part, or drop out at any time, without giving a reason. A decision to leave the study or a decision not to take part will not change the standard of care you receive now or in the future. The study doctor may also ask you to stop taking part in the study at any time if they feel it is necessary.

4) What will happen to me during the study?

The total study duration is up to 24 months, with a minimum follow-up period of 15 months. Study visits will take place every three months and should normally be scheduled to take place at the same time as your normal hospital visit.

Screening

If you are happy to take part, and are satisfied with the explanations from your research team, you will be asked to sign a consent form at the first clinic visit. You will be given a copy of the signed information sheet and consent forms to keep. Once consent has been taken you will be asked some questions about your medical history, and a physical examination will be carried out. This will be performed by your usual CF team and will add approximately 45 minutes to the consultation time.

Treatment Allocation

Half (50%) of the people in the study will be given IV treatment (Treatment A) and the other half will be given Oral treatment (Treatment B), so there is a 50/50 chance of getting either treatment group. You will not be able to choose which treatment you get, the decision of which of the two treatments you receive will be made by chance (this is called 'randomisation')

Treatment A: treatment will be given intravenously over a period of 14 days, with each intravenous treatment lasting no more than 1 hour at a time. Three blood tests will be taken during the course of your treatment to monitor how well your kidneys are working and to check that you are getting the correct amount of tobramycin. These tests are carried out as part of standard care for all patients receiving tobramycin. During the 14 day treatment period, you will usually have to stay in hospital as an inpatient. It is sometimes possible to give some of this treatment at home and you could discuss this with your CF team.

Treatment B: treatment will be given as a tablet which you will need to take twice daily for 3 months.

**Both treatments will be given in conjunction with inhaled colistin for 3 months.*

During your treatment you will be asked to complete a daily treatment diary. The aim of this treatment diary is not to check that you have taken all your medication but will be used to keep an accurate record of when you have taken your medication. You will also be given a short health diary to take home with you at each study visit and will be asked to return the diary when you attend hospital for your next study visit. This diary will allow you to record how many times you have seen your GP or other people involved in your care and will allow the study team to assess how the study treatment impacts on you.

Follow up

After you have stopped receiving treatment you will be required to attend hospital for a follow up visit every 3 months up to a maximum of 24 months after entering the trial. During these visits you will have an examination performed by your usual CF team, perform lung function measurements (spirometry) and will be asked to provide sputum and / or cough samples.

A very important aspect of this study involves assessing how your health or any treatment you receive affects your quality of life so your research nurse will ask you when you consent to enter the study to fill in a questionnaire that asks you about how you are feeling. This questionnaire will then be repeated at 3, 15 & 24 months afterwards. The questionnaires will be completed when you attend for your treatment or follow-up appointments and will take approximately five minutes to complete. It is very important for you to answer all the questions in the questionnaire for us to accurately assess the impact of the treatment upon you.

5) What if I am pregnant, plan to become pregnant or am breastfeeding?

You should not take part in this study if you are pregnant, nor if you plan to become pregnant during the first three months of the study during which time you will be receiving the *Pseudomonas* eradication treatment. There is no reason from the study point of view that you should not become pregnant after this initial three months.

6) What are the alternatives for treatment?

The treatments used for this trial are part of standard NHS care and are both used for the treatment of Pseudomonas infections in the lungs of CF patients. If you decide not to participate in the study, then your doctor will discuss treatment options with you.

7) What are the side effects of the treatment?

There are side effects to all types of medicines:

If you receive Intravenous antibiotics there is a small risk of developing an allergic reaction to the antibiotic, in some rare cases tobramycin can cause kidney problems. However, if you are going to receive IV treatment you will be closely monitored by your clinician. You will have a blood test at the start of treatment to check your kidney function is normal and that you are getting the correct amount of tobramycin. You will also have two further blood tests taken during your treatment to carefully monitor the levels of antibiotic in your body. These are routine tests carried as part of standard care for all patients that receive tobramycin. Tobramcyin can rarely affect your hearing.

Ciprofloxacin can make skin more sensitive to the sun and therefore more prone to sunburn, you should use sun screen when you know you will be in the sun. Other common side effects are feeling sick and development of diarhoea. Ciprofloaxacin can rarely cause joint pain.

Your CF clinician will fully explain the possible side effects for both treatments with you before treatment begins. Should any side effects develop then you should stop taking the study medication and discuss further with your CF team who may feel that it is safe to continue or may wish to give you a different treatment.

8) What are the possible disadvantages and risks of taking part?

Both of these forms of treatment are available to you whether or not you take part in this study. The study will cause you a little added inconvenience because of the additional questions that you will be asked at a maximum of nine clinic visits.

9) What are the possible benefits of taking part?

Both treatments that will be used in the TORPEDO-CF trial have been shown to eradicate Pseudomonas infection from the lungs of CF patients. However, this cannot be guaranteed. The information we get from this study may help us to improve future treatments for CF patients whose lungs have become infected with Pseudomonas aeruginosa.

10) What if there is a problem?

Any complaint about the way you have been dealt with during the study or any possible harm you might suffer will be addressed either by your own CF team or by the study team if necessary. The detailed information on this is given in Part 2.

11) Will my taking part in this study be kept confidential?

Yes. All information which is collected about you during the course of this research will be kept strictly confidential. We will inform your GP and the Medicines for Children Research Network Clinical Trials Unit (CTU) of your participation in the study. Other than this, any information about you that leaves the hospital will have your name and address removed so you cannot be identified from it. The detailed information on this is given in Part 2.

12) Contact for Further Information

Please feel free to ask your doctors any questions about the study or about any of the treatments described above.

This completes Part 1 of the Information Sheet.
If the information in Part 1 has interested you and you are considering participation, please continue to read the additional information in Part 2 before making any decision.

Part 2

13) What if new information becomes available?

Sometimes during the course of a research project, new information becomes available about the treatments/drugs that are being studied. If this happens, your research doctor will tell you about it and discuss with you whether you want to continue participation in the study. If you decide to withdraw your consent the research doctor will make arrangements for your care to continue. If you decide to continue in the study you will be asked to sign an updated consent form.

Also on receiving new information your research doctor might consider it to be in your best interests to withdraw you from the study. Your doctors will explain the reasons and arrange for your care to continue.

If the study is stopped for any other reason, you will be told why and your continuing care arranged.

14) What happens if I change my mind?

If at any point you decide to withdraw from the study you will continue to be treated according to local practice with your usual CF team. If you do withdraw from study treatment, we would like to continue to follow up and collect data as part of your normal clinic visit. However, if you decide to withdraw from the study completely, no more data will be collected about you. All data collected up until the time of withdrawal will be anonymised and included in the study analysis, unless you request that it is removed.

15) What if there is a problem?

If you have a concern about any aspect of this study, you should ask to speak with your CF team who will do their best to answer your questions. If you remain unhappy and wish to complain formally, you can do this through the NHS Complaints Procedure. Details can be obtained from the hospital.

If you are harmed by taking part in this research project, there are no special compensation arrangements. If you are harmed and this is due to someone's negligence, then you may have grounds for a legal action for compensation against the NHS Trust where you are being treated but you may have to pay for your legal costs. The normal National Health Service complaints mechanisms should be available to you (if appropriate).

In the event of defective product then you may have grounds for a legal action for compensation against the manufacturer, but you may have to pay for your legal costs.

16) Will my participation in the study be kept confidential?

All information which is collected about you during this study is considered confidential and giving this information to anyone else (called a third party) is not allowed with the exceptions noted below. The paper files used to record information in this study will be labeled with a unique trial number. Medical information may be given to your doctor or other appropriate medical personnel responsible for your welfare.

In order to confirm that the appropriate informed consent has been taken, copies of your signed consent form will be sent to the Medicines for Children Research Network Clinical Trials Unit (MCRN CTU) in the University of Liverpool. The University of Liverpool is registered as a Data Controller

with the Information Commissioner and will ensure that your confidentiality is preserved.

Your NHS number will be used by the MCRN CTU to request information from your hospital about any microbiology results (cough or sputum samples) generated for the purpose of this study and for a maximum of 12 months prior to you taking part in the study.

If you decide to take part in the study some parts of your medical records and the data collected for the study will be looked at by an authorised person from University Hospitals Bristol NHS Foundation Trust who are sponsoring the study. They may also be looked at by representatives of regulatory authorities or by authorised people from other NHS bodies to check that the study is being carried out correctly. Your medical records will be checked in the hospital and will not be removed. All authorised individuals will have a duty of confidentiality to you and nothing that could reveal your identity will be disclosed outside of the research site. By signing the consent form you will be giving permission for this to happen. In the event of the study results being sent to health authorities, or published, all your records will be kept confidential and your name will not be disclosed to anyone outside the hospital.

All documents and files relating to the study will be stored confidentially either at your local site or at the MCRN CTU or both for up to a maximum of 15 years. Nobody outside of the study will have access to the results of your tests and we will not reveal the information to your family, unless you request it. If you are agreeable, we will notify your GP that you are involved in the study and a copy of this information sheet will be forwarded to them. The results of this study will be published, but it will not be possible to identify individual patients who have participated in the study.

17) Involvement of the General Practitioner?

With your consent, the study doctor will write to your GP to let them know of your involvement in the study. The study doctor may also ask for further medical information from your GP about you if necessary

18) What will happen to any samples I give?

As a part of the main study, sputum and/or cough swab samples will be taken as part of routine clinical care. These samples will be used to screen for a range of bacteria including *Pseudomonas aeruginosa*. If *Pseudomonas aeruginosa* is isolated from your sputum or cough sample, isolates will be collected and transferred to an external laboratory. These isolates will be used only for the purposes of the TORPEDO-CF trial and future Cystic Fibrosis related research. Your isolates will not be used for any commercial purposes. This external laboratory will do some additional testing of the *Pseudomonas* isolates.

The samples will be kept in a secure place until we need them; nobody outside of the study (expect for MCRN CTU staff and your Hospital) will have access to any confidential information that you give to us. Confidential details (such as your name, address and GP details) will be kept locally and not made available to researchers.

Your sample will be coded and the researchers carrying out tests on the samples will not be given information they do not need to carry out the tests and analyse the results. Coded is not the same as anonymous. It will be possible to use the codes to identify that a result is from your sample. However, we do not plan to do this unless there is a good research reason to do so. We will maintain this information so that we can properly manage the samples donated. For instance, sometimes we may need to update our record of your clinical details to help us interpret the results of tests.

19) What will happen to the results of the study?

The results are likely to be published in the six months following completion of the study. Your confidentiality will be ensured at all times and will not be identified in any publication. At the end of the study the results can be made available to you and your GP if you wish.

20) Who is organising and funding the Research?

University Hospitals Bristol NHS Foundation Trust is sponsoring this study; they have assigned the day to day running of the study to the Medicines for Children Research Network Clinical Trials Unit (MCRN CTU) in the University of Liverpool.

This study is funded by the Health Technology Assessment programme of the Department of Health. Each collaborating site has been allocated funds for provision of general office supplies and to support nurse time and pharmacy costs.

21) Who has reviewed the study?

The study has been reviewed for scientific content by expert members of the Health Technology Assessment programme of the Department of Health review committee and a Multi-Centre Research Ethics Committee has reviewed the study for ethical considerations.

THANK YOU FOR READING THIS INFORMATION SHEET.
WE HOPE YOU HAVE FOUND THIS SHEET HELPFUL