PATIENT INFORMATION SHEET (RCT)
(Patient Info RCT V18 10Oct2011)

CONSTRUCT: COmparison of iNfliximab and ciclosporin in STeroid Resistant Ulcerative Colitis; a Trial (CONSTRUCT)

About 150,000 people in the UK have ulcerative colitis and it is one of the most important diseases seen by gastroenterologists. CONSTRUCT is an important study set up to improve the treatment of ulcerative colitis.

We would like to invite you to take part in this research study. We appreciate that you are not feeling well at the moment but before you decide you need to understand why the research is being done and what your involvement would be. This leaflet gives you information about the study - please take time to read it carefully to decide whether or not you wish to take part. Your consultant or specialist nurse will talk to you about the study. Please talk to others, such as your family about it if you wish. Please ask if there is anything that is not clear or if you would like more information.

What is the purpose of the study?
Patients with ulcerative colitis that is resistant to steroid treatment may need to change to a different treatment or require surgery. Two treatments are available for treatment in these circumstances infliximab (which would be prescribed as Remicade) and ciclosporin (which would be prescribed as Sandimmun/Neoral). These drugs are often an effective treatment in the short term but we don't know which is best and there is little information about their longer term effects on health and quality of life.

To help doctors recommend the best drug treatment for patients we want to find out how effective these drugs are for patients in the long term and understand if one drug is more effective than the other. By taking part in this study, you will be helping doctors to decide which drug they should recommend.

Why have I been invited?
You have been diagnosed with ulcerative colitis and are being treated as an inpatient in a hospital that is taking part in this study of people with your condition. Your ulcerative colitis has not responded adequately to steroids and you now need additional treatment.

Do I have to take part?
No. Your participation in this study is entirely voluntary. It is up to you to decide whether to take part. If you decide to take part, you are free to leave the study at any time and without giving a reason. This will not affect your medical care in any way. If you decide to participate you will be given this information sheet to keep and be asked to sign a consent form.

What will happen to me if I take part?

- If you agree to take part, we will first ask you to sign a consent form which is your indication that you understand the study and agree to take part.
- You will be treated with either infliximab or ciclosporin. The treatment will be chosen randomly (by chance) by a computer
- You will have an equal chance of receiving either infliximab or ciclosporin. You will know which drug you are being given. Whichever drug is chosen for you, it will be given to you in the same way that it would be given if you were not taking part in the study.
- If you are given infliximab this will be given into a vein via a drip. If you are given ciclosporin, the initial treatment is given into a vein, with further doses given in capsule form.
- Infliximab will be given at 0, 2 and 6 weeks, unless there is any problem. Because it is an antibody it normally stays in the body for 6-8 weeks. Ciclosporin will be given for 12 weeks, unless there is any problem. Because it is not long-lasting in the body, it is given every day.
- No normal treatment will be withheld whilst you take part in the study.

- It is important that you realise that treatment is not always effective. If the trial treatment doesn't make you better, you are likely to need surgery. There are no other medical treatments that have been shown to be effective in this situation.
- If you agree to take part we will ask you to complete a questionnaire, if you have not already done so. This needs to be done before you receive the trial drug treatment. The questionnaires will include questions about your health, feelings and quality of life and use of health services and take around 30 minutes to complete.

- We will ask you to complete further questionnaires at three, six, 12. 18 and 24 months after your treatment followed by one questionnaire a year over the next eight years. The questionnaires take around 30 minutes to complete. These questionnaires may be completed on a computer with the help of a nurse when you attend for follow up appointments so you will not be required to make additional visits to the hospital.
- If a questionnaire cannot be completed at the hospital, we will telephone you to make arrangements to complete it, possibly over the phone.
- If you agree to take part and then require an operation on your bowel, we will also ask you to complete questionnaires when you are discharged from hospital after your operation and then monthly for 3 months.
- In addition, we will follow your progress over 10 years, using hospital information about any investigations, treatment or surgery you may have.
- You will also be giving permission for us to have copies of the results of the blood tests you will have done as part of your normal care. This includes the tests done while you are an inpatient and the tests that will be done after you have been discharged from hospital at three, six, 12, 18 and 24 months after your treatment. These tests should be done at your routine follow up appointments so we will not be asking you to make additional hospital visits or have additional blood tests. The blood tests over the two years will show us how inactive or active your ulcerative colitis is and the questionnaires will allow us to see how your quality of life and general health changes following the drug treatment

- A sample of patients will be asked to take part in a telephone interview with a researcher three months and twelve months after treatment to find out their views about the treatment and progress. These interviews will be recorded and typed up but will be stored under a number so it will not be possible to identify you. You will be given the opportunity to indicate whether you agree to this when you complete the consent form.

What will I have to do?
You will be expected to take the medication as directed by your doctors and they will advise you on whether you can continue to take other medication or other prescribed or over-the-counter drugs and whether you will need to make any changes to your diet.

You might already be or have recently been involved in another drug study. If this is the case, you cannot participate in this study.

When you are discharged from hospital, you will be attending for outpatient appointments as part of your normal clinical care and we are not asking you to make additional visits but would urge you to keep your scheduled hospital appointments.

An important part of this study is the information we gain from the questionnaires that you complete so we do ask that you complete all the questionnaires so that we have a complete set of data for you.

What is the drug that is being tested?
The two drugs that are being studied are infliximab and ciclosporin. These are not new drugs. The drugs are already used to treat patients with your condition but we do not yet know which is better, or the long term effects of either drug.

The drugs will be given to you in the same way as they would if you were not taking part in the study. Both drugs will initially be given via a drip into one of your veins. Sometimes further doses of the drugs will be given.

What are the alternatives for treatment?
For patients with ulcerative colitis who have become resistant to treatment with steroids, advanced medical therapies are required and the two drugs that we are studying are available for the treatment of this condition. The only other treatment available is surgery and this is usually only undertaken if patients fail to respond to the advanced medical therapies.

What are the possible disadvantages and risks of taking part?
There are no additional risks associated with taking part in this trial as you would be prescribed one of the two drugs whether or not you take part in the trial.

What are the side effects of any treatment received when taking part?
Like all medicines infliximab and ciclosporin sometimes cause side effects in some people. Please remember that when you first receive the treatment you will be an inpatient and will be monitored closely by the specialist team looking after you.

You should be aware that the following side effects have been reported:

Infliximab
Most side effects are mild to moderate. However some may be serious and may require treatment. Side effects may appear up to six months after the last treatment.

Up to 10% (one in 10) people have experienced: Headache, dizziness, nausea, abdominal symptoms, allergic reactions, rash, urticaria, viral infections (for example herpes), respiratory infections (cold, sinus infections, bronchitis, pneumonia).

Up to 1% (one in 100) people have experienced: Depression, agitation, sleep disturbances, impaired wound heeling, bacterial infections, (for example tuberculosis, urinary tract infections, deep skin infections, sepsis), fungal infections, asthma, abnormal liver function, low blood cell counts including anemia, worsening of demyelinating nerve disease, autoimmune disease activation (SLE, lupus), worsening of heart failure, hair loss, bleedings, allergic anaphylactic reactions, injection site reactions.

Less than 0.1% (one in 1000) people have experienced: Gastrointestinal bleedings or perforation, circulatory failure, multiple sclerosis, lymphoma.

Ciclosporin
Most side effects are mild to moderate. However some may be serious and may require treatment.

More than 10% of people have experienced: Kidney problems, high blood pressure, headache, tremor and increased levels of lipids (for example cholesterol) in the blood.

Up to 10% of (one in 10) people have experienced: Numbness or tingling, loss of appetite, feeling or being sick, stomach pain, diarrhoea, swollen gums, liver problems, high level of uric acid or potassium in the blood, low levels of magnesium in the blood, muscle pain or cramp, increased hair growth on the body and tiredness.

Up to 1% of people (one in 100) have experienced: Seizures, confusion, disorientation, decreased responsiveness, agitation, sleeplessness, visual disturbances, blindness, coma, partial paralysis, loss of co-ordination, changes in blood (for example anaemia), allergic rash, water retention which may cause swelling and weight increase.

Up to 0.1% of people (one in 1000) have experienced: Problems with the nerves that control muscles, inflammation of the pancreas, high levels of glucose in the blood, muscle weakness, wasting of muscles, destruction of red blood cells which may be associated with kidney problems, changes in the menstrual cycle in women and slight enlarging of the breasts in men.

Up to 1 in 10,000 people have experienced: Swelling at the back of the eye which may be associated with an increase in pressure inside the head (benign intracranial hypertension) and visual disturbances.

Like other medicines that dampen down the immune system ciclosporin may cause tumours or other malignancies, particularly of the skin. It may also make you more likely to get infections which may be serious.

What are the possible benefits of taking part?
You will be receiving one of the two drugs as part of your treatment and by taking part in the trial you will be helping to identify which of the two drugs is the most effective treatment for people with your condition. This means that if you need this type of treatment in the future, your doctors will be better informed about which of the two drugs to give you.

What happens when the research study stops?
As a patient with ulcerative colitis you will continue to be reviewed in the gastroenterology clinic so your follow up will be as normal.

What if relevant new information becomes available?
Sometimes we get new information about the treatment being studied. If this happens, your research doctor will tell you and discuss whether you should continue in the study. If you decide not to carry on, your research doctor will make arrangements for your care to continue. If you decide to continue in the study he may ask you to sign an updated consent form.

If the study is stopped for any other reason, we will tell you and arrange your continuing care.

What will happen if I don't want to carry on with the study?

You may withdraw your consent and discontinue your participation in this study at any time without the need to give us a reason. This would not in any way affect the normal standard of care you receive.

What if there is a problem?

Complaints
If you have a concern about any aspect of this study, you should ask to speak to the local research team who will do their best to answer your questions. Alternatively you may wish to contact the coordination team in Swansea (Trial Manager Anne Seagrove, XXXX or Professor John G Williams, XXXX Trial Secretary, Emma Riordan, XXXX).

If you remain unhappy and wish to complain formally, you can do this through the NHS Complaints Procedure. Details can be obtained from [details]

Harm

Non-negligent harm: As sponsor of this trial, Swansea University have insurance should you suffer non-negligent harm.
Negligent harm: As sponsor of this trial, Swansea University have insurance should you suffer negligent harm.

NHS based research
In the event that something does go wrong and you are harmed during the research and this is due to someone's negligence then you may have grounds for a legal action for compensation but you may have to pay your legal costs. The normal National Health Service complaints mechanisms will still be available to you (if appropriate).

Will my taking part in this study be kept confidential?
Yes. All information which is collected about you during the course of the research will be kept strictly confidential in accordance with ethical and legal practice and the Data Protection Act.

You will have a unique trial number and any data will be collected and stored with this number. Any personal identification will be stored separately from the data. The clinical team looking after you and the research team are the only people who will know specific personally identifiable information that would allow someone to identify you and contact you.

If you agree to take part your GP will be informed. If you do not want your GP to be informed you can indicate this on the consent form.

What will happen to any samples I give?
Any samples you give will be part of your routine clinical care and will therefore be dealt with as normal in the hospital. We will be given copies of the results by your hospital doctor.

Will any genetic tests be done?
No genetic tests will be done as part of this study.

What will happen to the results of the research study?
The results of the study will be used to help doctors choose the best treatment for patients with steroid resistant ulcerative colitis. Your personal information (name, date of birth, home postcode and NHS number) will not be revealed in any audit, study report or publication, at any time.

You will be asked if you would like to receive a summary of the results of the research.

Who has reviewed the study?
All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee to protect your safety, rights, wellbeing and dignity. This study has been reviewed approved by Wales Research Ethics Committee.

The study has also been given Clinical Trial Authorisation by the Medicine and Healthcare Products Regulatory Agency (MHRA) and permission from the hospital's Local Research Ethics Committee and Research and Development Office.

Who is organising and funding research?
The study is being run by the College of Medicine at Swansea University in collaboration with the University of Glamorgan and Bangor University. The study is funded by the National Institute for Health Research Health Technology Assessment Programme.

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