PATIENT INFORMATION SHEET
BILCAP: A RESEARCH TRIAL EVALUATING CHEMOTHERAPY IN PATIENTS FOLLOWING SURGERY FOR BILIARY TRACT CANCER

Introduction

You have had an operation to completely remove a cancer of the biliary tract, that is, a cancer of the bile duct or gall bladder. We would like to invite you to take part in a research study to see whether chemotherapy following surgery is beneficial. About 360 patients who have had an operation for bile duct or gall bladder cancer like yourself will take part in this research study over three years. This leaflet gives you some information about the study, why it is being done, and what the potential benefits and risks of taking part in this research may be. Please take time to read the following information carefully and discuss it with relatives, friends or your GP if you wish, before you decide whether or not to take part. If you have any questions about this study, please feel free to ask your doctor.

What is the purpose of the study?

You have had an operation to remove a cancer of the biliary tract. This means cancers of the gall bladder and bile ducts (or cholangiocarcinomas). Although it is possible that you may be cured by this operation, there is a chance that the cancer may return. Chemotherapy is used to reduce the likelihood of the return of other types of cancer but it is not known whether it works for biliary tract cancers. Therefore we are conducting a study to determine whether chemotherapy can help. The medical team at this hospital are taking part in the study.

The aim of this study is to see how effective chemotherapy is in treating your disease after surgery. The drug being used in this study is capecitabine (also known as Xeloda®). This drug is given in tablet form to be taken orally (by mouth). Capecitabine is used to reduce the likelihood of return of other types of cancer (such as colon cancer), but it is not currently used to treat biliary tract cancer. We would like to know whether or not treating patients like yourself with capecitabine helps reduce the risk of the cancer returning.

We are also interested in how this treatment might affect patients' quality of life and well-being. We think it is very important to find out how people taking part in the study feel, both emotionally and physically. We would also like to study any side effects . This information will be used to examine the possible advantages and disadvantages of the treatment. The results from this study will make it easier to advise future patients about whether chemotherapy treatment would be helpful.

Why have I been chosen?

360 people who have had a curative operation for biliary tract cancer will be invited to take part in the study. Other hospitals in the UK will also be involved in the study.

Do I have to take part?

No. It is up to you to decide whether or not to take part. If you decide to take part you will be given this information sheet to keep and be asked to sign a consent form. You will be given a copy of the consent form to keep. You may choose not to take part in the study, or you may withdraw from the study at any time. You do not have to give any reason for your decision. If you choose not to take part in the study or to withdraw from the study, your doctor will continue to treat you with the best means available and your standard of care will not be affected.

If you choose to take part in the study but later choose to withdraw, we would still like to collect information about your treatment as this will be invaluable to our research. If you have any objection to this please let your doctor know when you decide to withdraw from the study. Data already collected prior to withdrawal will be kept and analysed.

What will happen if I take part?

You will already have had an operation to remove the cancer. Before you enter into the study, the study team will review tests that you have had such as blood samples. If these tests indicate that you are suitable and you have given your consent, then you will be entered into the study. Sometimes, as in this situation, we do not know which way of treating patients is best, so we need to make comparisons. In this study people will be put into two groups and then compared.

A computer will decide whether you:

Receive chemotherapy with capecitabine and then undergo regular follow up

Or Do not receive chemotherapy and undergo regular follow up (observation)

Neither you nor your doctor will be able to choose which of the two groups you are put into. Your treatment will be chosen at random by the computer, based at the BILCAP Study Office. This procedure called "Randomisation" means that everyone has an equal chance of being put into each group. It also ensures that the two groups will be comparable and that the trial is as fair a test of the treatment as possible.

In this study, you will have a one in two chance of receiving chemotherapy with capecitabine. To find out your treatment group, one of your medical team will contact the Cancer Research UK Cancer Trials Centre in Birmingham.

What will the study treatment involve?

Chemotherapy group:

- You will be given capecitabine in tablet form, to take at home orally (by mouth). These tablets are given twice a day, for two weeks out of three, for a maximum of 24 weeks. During the treatment period you will attend outpatient appointments at your hospital/clinic at the beginning of each cycle of treatment (every 3 weeks). At these visits a physical examination and blood tests will be carried out. During treatment you will be asked to fill out a diary sheet to keep a record of the capecitabine you have taken. We would also like you to report any side effects you have to the medical team.
- During treatment and after treatment has ended you will be seen at the hospital for regular follow-up visits (see below).

Observation group:

- After your surgery you will not be scheduled to receive chemotherapy, but will be seen at the hospital for regular follow-up visits (see below).

Travel expenses will not be paid, however hospital transport can be arranged. The trial centre will continue to collect information from your doctor on your health status for several years.

What will the study follow-up visits involve?

The study follow-up visits will include blood tests and scans to monitor your disease. You will be asked to attend the hospital for these follow-up visits every 3 months for the first year, and every 6 months for the second year. After this you will be asked to come to hospital for follow up on a 12-monthly basis.

By taking part in this clinical trial your disease will be assessed by CT scans at regular intervals. The number of scans that you receive may be higher than the total you would receive if you are not taking part in the clinical trial. Any potential health risk associated with these scans is considered to be low for a patient with your medical condition.

How long will the study treatment continue for?

If you are selected for chemotherapy, the amount of treatment you receive will depend on how well you tolerate the treatment and on any side effects you experience. You will be on the study treatment for up to six months. Your treatment may be stopped sooner if:

- Your cancer returns
- Your side effects are too severe
- Your doctor decides that the treatment you are getting is no longer in your best interest.
- New information is discovered showing that the treatment given is not in your best interest.
- You decide to discontinue treatment for any reason.

If your treatment is stopped, your doctor will continue to treat you with the best means available.

Whether you are in the chemotherapy or observation group, the follow-up period for the study will last for 5 years. During this time you will continue to be seen by your doctor in outpatient clinics and may be offered other treatment as appropriate.

What happens when the research study stops?

At the end of the research study, or if you withdraw from the research study for any reason, you will continue to be treated with the best means available and may be offered other treatment as appropriate.

What are the alternatives to study treatment?

If you do not choose to go into the study, you are likely to be placed on observation, but this will vary and depends on the centre where you are being treated. Your doctor will discuss any possible alternative treatments with you. One of the aims of this study is to establish a standard treatment across the UK.

Are there any reasons why I should not take capecitabine?

You should not take capecitabine if you pregnant or are breastfeeding a baby, as the drug may pass to your baby in the milk. You should also not take capecitabine if you know you lack the enzyme DPD (dihydropyrimidine dehydrogenase). Lack of this enzyme, which disposes of capecitabine, is rare. You should tell your doctor if you have known kidney or liver problems, or if you are taking a blood thinner (such as warfarin), if you are taking phenytoin, or if you take the vitamin folic acid. Capecitabine has a minor or moderate influence on the ability to drive and use machines. If you feel this may affect you, please feel free to discuss this point further with your doctor.

What are the side effects of treatment?

Chemotherapy drugs attack cancer cells but may also damage normal cells. This can cause side-effects, although these are usually temporary. Capecitabine is commonly used in other cancers and so its side-effects are well known. These side-effects will not affect everyone, as each person's reaction to this drug is different, and you may experience none or several of the side effects listed below. You will be monitored carefully and given medicines to reduce any side effects.

***Common side effects from capecitabine*.**

- Diarrhoea. If this happens please consult your doctor immediately. About one in 5 people will get diarrhoea more than 4 times a day for several days at a time. Diarrhoea can usually be controlled with loperamide or Imodium (supplies of which you will be given to take home). However if the diarrhoea is severe, you must stop taking the chemotherapy tablets until the diarrheoa is completely better.
- Hand-and-foot syndrome (a rash where the palms of the hands or soles of the feet become painful, swollen and red). If this happens you should consult your doctor immediately and if it is serious you will be advised to stop the chemotherapy until the rash is completely better.
- Temporary decrease in blood cell counts. The number of red blood cells, white blood cells and platelets in your blood (blood counts) may drop. Platelets are the cells which help the blood to clot, white blood cells help fight infection and red blood cells carry oxygen around your body. Fewer of these cells may lead to a slightly increased risk of bruising or bleeding, getting infections or becoming anaemic. The effect is usually temporary and your blood cell count will be checked regularly throughout treatment. In order to test your blood, about a teaspoon will be taken. As with all chemotherapy, infections because of a low white blood cell count can rarely be life-threatening so you must contact your doctor immediately if you develop a fever and feel unwell.
- Sore mouth and taste change (stomatitis). You may have a sore mouth and notice small mouth ulcers during treatment. Your food may taste different, however normal taste will return after the treatment ends.
- Nausea and vomiting. There are now very effective anti-sickness drugs to prevent or greatly reduce nausea and vomiting, which your doctor will give you if necessary.
- Abdominal pain and constipation. It may help you to drink plenty of fluids, eat a high fibre diet and take gentle exercise. Sometimes you may need to take medicines to stimulate your bowel. These can be prescribed by your doctor.
- Hair loss. This will affect around 1 in 5 people to any noticeable degree. It is very unlikely to fall out altogether. It is temporary and the hair will regrow once the treatment is finished
- Changes with nails. Your nails may become darker. White lines may appear on them. These changes usually grow out over a few months once treatment has finished.
- Tiredness and a general feeling of weakness. Allow yourself plenty of time to rest.
- Sensitivity to the sun. This may occur during treatment and for several months afterwards. Wear a high protection factor sun cream and protective clothing.
- Chest Pain. You may experience pain in the middle of your chest especially during exercise. If you do experience chest pain please consult your doctor urgently and stop taking the capecitabine tablets.

What should I do if I experience any side effects?

It is important you inform your medical team of any changes in your health, whether or not you think it is related to the medication. The risk of side effects decreases at lower doses of capecitabine, and your doctor may decide to reduce your dose. Your doctor may also ask you to stop treatment or might reduce the dose of the drug if you have any unexpected side effects or other illnesses which occur as a result of treatment. Remember you are free to stop having treatment at any time.

If you are receiving chemotherapy and become unwell suddenly, especially if you develop a high temperature or shivering fits, **please seek advice immediately from your hospital team** (contact information given at the end of this sheet).

You should contact your hospital team right away if you have any of the following:

- Diarrhoea: if you have more than 4 bowel movements per day or any diarrhoea at night.
- Vomiting: if you vomit more than once in a 24 hour period.
- Nausea: if you lose your appetite and the amount of food you eat each day is much less than usual.
- Severe abdominal pain: If you experience severe pain in the abdominal (stomach) area.
- Stomatis: if you have pain, redness, swelling or sores in your mouth.
- Fever or infection: If you have a temperature of 100.5°F/38°C or greater, or any other signs of infection.
- Hand-and-foot syndrome: if you have pain and swelling or redness of your hands or feet that prevents normal activity.
- Chest pain, particularly following exercise.

If caught early, most of these side effects usually improve after you stop taking capecitabine. After side effects have improved your doctor will tell you whether to start taking capecitabine again and what dose to take. If you have any questions about these side effects, please contact one of the medical team (contact information given at the end of this sheet).

What if I become, or am likely to become, pregnant, or father a child?

Women must not become pregnant and men must not father a child while taking capecitabine, as it may harm the developing foetus. It is therefore very important to avoid pregnancy during chemotherapy and for several months afterwards in case the drugs affect an unborn baby. **Men and women taking capecitabine must use a reliable method of contraception whilst taking this drug, and for at least 3 months afterwards.** Capecitabine should not be taken by breastfeeding women, as it is possible that the drug may be present in breast milk.

Women taking the contraceptive pill should check with your doctor whether it is all right for you to continue. If you can use it, this is the most reliable form of contraception. It is also a good idea to use a 'barrier' method of contraception, for example condoms or the cap, This is especially important if you have suffered from diarrhoea or vomiting, as this can stop the contraceptive pill from working properly.

We do not think that the chemotherapy will affect your partner, but we do not know for certain about this. There is a small chance that the drug could find its way into your body fluids. This is another good reason for using barrier contraception during chemotherapy treatment. This applies whether it is the man or the woman being treated. If you or your partner does become pregnant during the trial, you will receive counselling from your doctor about the possible risks to you and your unborn baby. A pregnancy test may need to be done before starting this study to exclude the possibility of pregnancy.

IMPORTANT: Your ability to become pregnant or father a child may be affected by taking this drug. It is important to discuss fertility with your doctor before starting treatment.

What is involved in the Quality of Life study?

We are very interested in how your treatment might affect your quality of life and well-being. The information we gain will be important, as it will enable us to compare the possible advantages and disadvantages of giving chemotherapy from the patient's point of view. To get reliable information about quality of life, we need as many people as possible to tell us about their treatment experience. However if you do not want to take part please tell us on your consent form, **as this is not compulsory.**

If you decide to take part, you will be asked to complete a questionnaire before you enter into the study and at each of the follow-up visits during the first two years. The questions will be about your general health, and how you feel physically and emotionally. They should take about 15-20 minutes to complete. The purpose of these questionnaires is to compare the well-being of patients in the chemotherapy and observation groups, and to evaluate any side effects of the treatment. Even if you do not wish to complete the questionnaires we would still like you to report any side effects you have with your treatment to the medical team.

How important is it to provide all of this information? You are not obliged to complete all questions in the questionnaires, however it is important we get as complete a picture as possible for the quality of life research. These are standard questionnaires and some of the questions may seem repetitive. If you do take part in this sub-study, please try to complete all of the questions as best you can.

What is involved in the Trans-BILCAP study?

When you have surgery for your biliary tract cancer, specimens are routinely saved in the hospital pathology laboratory. If you choose to participate in Trans-BILCAP, we would like to ask your permission to use both these specimens and other fresh tissue collected routinely during surgery for future scientific studies.

In addition, we would like to also ask you for one 20 ml blood sample specifically for research purposes which will be collected at the time you are randomised. Each person's genetic make up influences the way they respond to any medical treatment – how well it works and what side effects occur. We plan to test a range of genes and proteins from your blood and from your cancer which may influence this. We would also like to test for biological markers which might have given you an increased risk of getting cancer. These studies will involve extracting DNA or other material from the tumour and blood to see whether, in the future, it may be possible to predict which patients will benefit from which treatment. This research is based in UK Universities but may involve collaboration with commercial companies or other institutions.

All tissue specimens and blood samples will be stored indefinitely at the Cancer Sciences Tissue Bank, Southampton which holds a Human Tissue Act licence. There are no plans to destroy any tissue.

These additional studies will not affect your treatment in any way and you can choose to participate in the main trial but not this additional study if you wish.

What are the possible benefits of taking part?

If you take part in this study and are selected to receive chemotherapy, it is possible that the treatment may help to prevent your cancer from returning, but this cannot be guaranteed. The information we get from this study will help us to treat patients with biliary tract cancers better in the future.

What are the possible disadvantages of taking part?

The disadvantages of taking part in the study are mostly associated with the side effects of chemotherapy explained above. Having chemotherapy also means that you will have to attend hospital once every 3 weeks during the treatment period to receive the oral medication. Travel expenses will not be paid, although hospital transport can be arranged.

What if something goes wrong?

Every care will be taken in the course of this study, however if you are harmed by taking part in this research project, there are no special compensation arrangements. If you are harmed due to someone's negligence, then you may have grounds for a legal action but you may have to pay for

it. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been approached or treated during the course of this study, the normal National Health Service complaint mechanisms are available to you. Your doctor will give you further information if necessary.

What if new information becomes available?

Sometimes during a research project new information becomes available about the treatment that is being studied. If this happens your doctor will tell you about it and discuss with you whether or not it is still in your best interests to continue. If you, or your doctor, decide to withdraw from the study, your doctor will ensure that your care will continue. If you decide to continue in the study, you may be asked to sign a new consent form if the design of the trial is slightly changed due to this new information.

Will this study affect any life/private medical insurance that I may have?

If you have any private medical or life insurance you should check with the company before agreeing to take part in the trial to ensure that your insurance will not be affected.

Will I be paid for taking part?

You will not be paid for taking part in this study.

Will my taking part in the study be kept confidential?

If you agree to take part in this study you will need to sign and date the informed consent form attached. Your medical notes will need to be seen by authorised members of our research team so they can collect information needed for this research study and also to check that it is correct. Your doctor with your permission will supply your name, date of birth, hospital number and NHS number when s/he registers you on the study. With your consent, your GP will also be informed that you wish to take part in a clinical study. Your GP may be asked to provide information from your records, which are required for the study.

The BILCAP Trial Office will collect a copy of your signed consent form to confirm you have read and understood this information. Other than this consent form, once you are randomised into the study all other information which leaves the hospital will refer to you only by a unique trial number allocated to you, your initials, date of birth and hospital number to preserve your confidentiality. All information that is collected about you during the course of the research will be treated as strictly confidential. The confidentiality of your medical records will be respected at all times.

Occasionally we may need to check your medical records to make sure that the information provided about you was accurate. This will be done by clinical staff or designated Trials Unit personnel. A government body called the Medicines and Healthcare products Regulatory Agency (MHRA) may also require access to your medical records to ensure that the trial is being run in accordance with UK law. Under no circumstances will you be identified in any way in any report arising from the study.

After your treatment we will continue to contact your hospital to find out how you are. We know that it is possible for patients to lose touch with their hospital. If this happens we still need to be able to collect important basic details on how you are for the full duration of your life. The Office of National Statistics (ONS) keeps records that can easily provide the information we need. With your consent ONS will pass on this information to the BILCAP Study Office if required. Any information received in this way remains confidential and is used only for the purpose of this trial.

What will happen to the results of the study?

At the end of the study the information collected will be analysed and published in recognised medical journals so that the information will be available to all. This is likely to be 1 or 2 years after the study has been completed, and the study is expected to last for 5 years. The identity of the patients who took part in the study will remain confidential. Your doctor and study nurse will be informed of any results throughout the duration of the study. Please tell your doctor if you wish to see a copy of the published report.

Who is organising and funding the research?

BILCAP is a study initiated and led by clinicians. The National Cancer Research Institute (NCRI) Upper Gastrointestinal Cancer Studies Group is overseeing the study with funding from the Cancer Research UK charity. The study is being organised and run by the Cancer Research UK Clinical Trials Centre in Birmingham. Your doctor will not receive any financial payment for including you in this trial.

Who has reviewed the study?

This study was reviewed and approved by Cancer Research UK, and the West Midlands Multi-centre Research Ethics Committee. The local research ethics committee and research and development committee for your hospital have also given approval..

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What if I want more information?

If you have any concerns or questions about this study please contact one of the medical team caring for you. Please feel free to ask any further questions before deciding to take part in the trial, or at any time during the study. Before you make a decision, you may want to discuss the study with your family and friends and with your GP.

Your Specialist.....**Contact number**…….

Your Research Nurse.....**Contact number**……..

24 hour Contact number.....

If you prefer, you can contact one of the organisations below for more information or advice:

CancerBACUP (an independent patient advisory group)
Provides support and counselling to help people living with cancer
3 Bath place
Rivington Street
London EC2A 3RJ Tel: 0808 800 1234,
Or visit their website at: **www.cancerbacup.org.uk**

CancerHelp UK
Provides general information for patients about cancer and its treatment on their website:
www.cancerhelp.org.uk.

Cancer Research UK
Has cancer information nurses who provide a confidential service.
Tel: 020 7061 8355
or email: **cancer.info@cancer.org.uk**.

Please take as much time as you need to make a decision and then let your doctor know what you have decided so that your treatment can be arranged.

Thank you for taking the time to read this leaflet and considering taking part in this study.