Patient Information Sheet C (Randomisation)

LORIS

A Phase III Study of Surgery versus Active Monitoring for Low Risk Ductal Carcinoma *In Situ* (DCIS)

ISRCTN27544579

We would like to invite you to take part in a UK clinical trial (research study) run by the University of Birmingham. Before you decide if you want 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 if you wish, discuss it with friends, relatives or your General Practitioner (GP). A member of your hospital research team will go through the information sheet with you and answer any questions you have. This leaflet is divided into two parts.

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

Additionally, you can also watch a DVD which explains the study. You can also view the contents of the DVD online, to do so please see the LORIS website details at the bottom of this Information Sheet.

Please tell a member of your hospital research team if anything is not clear or if you would like more information. Take your time to decide whether or not you want to take part. If you decide not to take part, this will not affect your standard of care.

Part 1

What is DCIS?

DCIS stands for Ductal Carcinoma *In Situ* and DCIS looks like specks of white (calcium) when viewed on mammograms. DCIS means that there are abnormal cells in the breast milk ducts but not in any other breast tissue. Before breast screening took place, a diagnosis of DCIS was extremely rare but now it is common.

When doctors look at your biopsy tissue under the microscope they can divide it into different groups – high, intermediate and low grade DCIS and then even lower still e.g. ADH (atypical ductal hyperplasia). The dividing lines between these grades are not black and white. Because high grade DCIS is more likely to become breast cancer, it is treated as if it is an invasive cancer. Invasive cancer means that the cancer can spread to other parts of the body. But the LORIS study is only for patients like you, who have "low risk disease" which most doctors think is at a low risk of becoming an invasive cancer.

What is the purpose of the study?

The LORIS study will help us learn which women with low grade or low-intermediate grade DCIS can safely avoid surgery. A report in 2012 showed that breast screening can save lives but that many women are having unnecessary breast surgery. We are trying to improve things by only operating on women who really need it.

To begin to address the issue of potentially unnecessary surgery for DCIS, the LORIS study compares Surgery with Active Monitoring. Active Monitoring is explained later. The study is taking place in many hospitals all across the UK.

Why have I been invited to take part in this research?

You have been invited because you have "low risk disease" which was confirmed by a team of pathology experts.

Do I have to take part?

You do not have to take part, it is entirely voluntary. If you do agree to join and then change your mind, you can withdraw at any time without giving a reason.

If you don't take part or decide to withdraw, it will not affect the standard of care you receive. You will have surgery and possibly some radiotherapy or hormone treatment, as usual if you do not join the study.

What will happen to me if I take part in the study?

If you agree to take part you will be asked to sign a Consent Form (Consent Form C) and fill in some short questionnaires. These ask how you are feeling and about your Quality of Life. They should take about 15 minutes to complete.

Then you will be put into (allocated to) one of two groups:

A) Surgery (standard treatment)

B) Active Monitoring

Randomisation

Neither you or your doctor or nurse will be able to choose which group you go in. The allocation to groups is done by a process called randomisation. This may sound strange but is done so that we can make a fair comparison with equal numbers of patients of different ages and state of health in each group. At the end of the study, we can be sure that any differences found are due to the group you are in, rather than anything else.

Group 1: Surgery

In this group, patients will receive the standard treatment for DCIS which is breast surgery (either mastectomy or wide local excision removing the area of the breast where the DCIS has been seen) and possibly radiotherapy or hormone therapy. Patients will have follow-up mammograms annually for 10 years and will then return to regular breast screening every 3

years if they are still in the screening age group. Patients will be told the result of each mammogram either by letter, by the research team in person or by telephone.

Group 2: Active Monitoring

In this group, patients will not have breast surgery but will be actively monitored by annual mammograms for at least 10 years. Patients will be told the result of each mammogram, either by letter, by the research team in person or by telephone.

In both groups, if you are concerned at all and want to see a doctor you can contact your hospital research team.

Expenses and payments

Funding is not available for the payment of any patient expenses.

What will I have to do?

Below is a summary of what will happen if you decide to take part in the study.

- You will be asked to complete Consent Form C
- Then you will fill in some short questionnaires before being randomised to a study group, these should take about 15 minutes.
- Randomisation will allocate you to either the Surgery group or the Active Monitoring group.
- You will be invited to attend your local Breast Unit or Screening Unit for mammograms every year for 10 years and will be informed of the results as soon as possible, usually within 2 weeks.
- You will be sent questionnaires about your Quality of Life that take about 10 minutes to fill in:-
    - 3 times in year 1 (at 3, 6 and 12 months)
    - Once in years 2, 3, 4 & 5
    - You will also be sent a short questionnaire that helps us compare any costs to the patients in each group
- If you are happy to do so, a researcher may contact you following randomisation to carry out a telephone interview to find out more about your thoughts on the study.
- If you are in the Surgery group, you may need to go for clinic visits at your hospital each year for up to 5 years if this is the standard care at your hospital. Once you are discharged from the hospital, a member of your hospital research team will telephone you each year to see how you are doing, until you have completed 10 years of follow up within the trial. The telephone call will take about 10 minutes.
- If you are in the Active Monitoring group, you will be telephoned once a year for 10 years by a member of your hospital research team in order to see how you are doing. The telephone call will take about 10 minutes.
- The Trial Office will collect information about you from the hospital research team for 10 years.
- After 10 years, we will follow you up lifelong through the national health registries. We will keep any samples or images provided until the end of the research, when all patients have been followed for as long as possible.

- With your permission, if there is enough tissue available, we will collect tissue samples from your biopsy and from any future breast investigations or surgery you may have for research.

The questionnaires are sent out by Sussex Health Outcomes Research and Education in Cancer (SHORE-C) based at Sussex University (contact details are at the end of this leaflet). A member of the SHORE-C team may contact you if they have sent questionnaires that have not been returned.

What are the alternatives for diagnosis or treatment?

If you decide not to take part in the study you will get the standard treatment for DCIS which is surgery and possibly radiotherapy or hormone therapy. Your doctor will explain what this would involve.

What are the possible disadvantages and risks of taking part?

There is a small chance that patients from both groups will develop higher grade DCIS or invasive breast cancer which will require treatment. Therefore patients in the Active Monitoring group may require surgery and possibly radiotherapy at a later date and patients in the Surgery group may require further surgery and possibly radiotherapy and hormone therapy at a later date.

What are the side effects of any treatment received when taking part?

All patients entering the study will have mammography every year for 10 years. This is longer than is recommended for standard care, which is currently 5 years but studies are also being undertaken to see if 10 years should be standard for all patients. Patients who have not had a mastectomy will need to have a mammogram taken of each breast. Mammograms use x-rays to give an image of the breast. The radiation dose from having mammograms of both breasts is usually less than 3 months of natural background radiation in the UK. All patients will have also had a biopsy of the breast which also involves the use of x-rays. The procedure may have been additional for some patients. The dose from this is similar to a mammogram. The risk from these procedures causing additional breast cancer is very small compared to the natural risk of breast cancer.

Patients in the Surgery group: There are risks associated with having a general anaesthetic and surgery (mastectomy or a wide local excision removing the area of the breast where the DCIS has been seen) such as, bleeding and wound infections. There are also risks and side effects of radiotherapy and hormone therapy. Your doctors and or specialist nurse can give you more information about these risks.

What are the possible benefits of taking part?

Patients in the Active Monitoring group may avoid unnecessary surgery and other unnecessary treatments with their associated side effects.

You will be taking an active role in your care and the information we get from this study will help us to improve the future treatment of all women with DCIS and their quality of life by reducing unnecessary treatments.

In the LORIS study, you will have more mammograms and monitoring by the research team at your hospital than you would receive outside of a clinical trial.

What happens when the research study stops?

At the end of trial, after 10 years, all patients in the LORIS study will return to regular breast screening (if they are still of screening age).

Will my taking part in the study be kept confidential?

Yes. We will follow ethical and legal practice and all information about you will be handled in confidence. The details are included in Part 2.

This completes Part 1 of the Information Sheet.

If the information in Part 1 has interested you and you are considering participation, please read the additional information in Part 2 before making any decision.

Part 2

What if relevant new information becomes available?

Sometimes during the course of a study, new information becomes available. If this happens, your specialist will tell you and discuss whether you should continue in the study. If you decide not to carry on, your specialist will make arrangements for your care to continue.

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

If you change your mind about taking part, you are free to withdraw at any time. You do not have to give a reason. We would however like to ask your permission for your hospital to continue to send information about your progress to the LORIS Trial Office (based at the Cancer Research UK Clinical Trials Unit, University of Birmingham) until 10 years after study entry. This is information that is routinely taken and you will not need to do anything extra. After 10 years, the LORIS Trial Office will obtain information about your progress from the national health registries, with your permission.

If you withdraw from the study your doctor will advise you about your treatment.

What if there is a problem?

If you have a concern about any aspect of this study, you should contact the researchers 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.

Harm

In the unlikely event that something does go wrong and you are harmed during the study there are no special compensation arrangements. The University of Birmingham (the Sponsor of the study) does not hold insurance against claims for compensation for injury caused by participation in this study and they cannot offer any indemnity. If you are harmed and this is due to someone's negligence then you may have grounds for legal action for compensation against the Sponsors or your NHS Trust but you may have to pay your legal costs. NHS Trust and Non-Trust Hospitals have a duty of care to patients treated, whether or not the patient is taking part in a clinical study and the normal NHS complaints mechanisms will still be available to you, if appropriate.

Complaints

If you have any complaints about the treatment you receive you should speak to your study doctor or one of the research nurses. If your complaint is not resolved you can complain to your local Primary Care Trust (PCT).

Will my taking part in this study be kept confidential?

All information collected about you for this study will be subject to the Data Protection Act 1998 and will be kept strictly confidential. All clinical information will be securely stored at the LORIS Trial Office on paper and electronically and will only be accessible by authorised personnel.

Your hospital research team will be able to request a second opinion on your follow-up mammograms from the LORIS expert radiologists. If this occurs, your name, date of birth and hospital number may be viewed on a secure NHS computer. In addition, your mammogram images will be stored anonymously at The National Co-ordinating Centre for the Physics of Mammography (NCCPM - based at Royal Surrey County Hospital) and the University of Surrey image library as part of the CR UK Cancer Imaging Programme (C30682/A10350) known as OPTIMAM. Most hospitals taking part in the LORIS trial can send the mammogram images electronically to an NHS computer. However, some hospitals may need to send the mammogram images securely on a CD by post. If this occurs, the CD will only contain your unique study number, date of birth and the date that the mammogram was taken. The images will be kept until the end of the research.

The Quality of Life data you provide will be securely stored at Sussex Health Outcomes Research and Education in Cancer (SHORE-C) at the University of Sussex on paper and electronically and will only be accessible by authorised personnel. SHORE-C will also hold your personal details including, forename, surname, full address and telephone number. This is so that Quality of Life questionnaires can be sent direct to your home address and any queries dealt with efficiently.

Your hospital research team will also notify your GP that you intend to participate in the study. They will also send a copy of your signed consent form in the post to the LORIS Trial Office and your GP.

In the LORIS Trial Office, you will be identified by a unique study number. In routine communication between your hospital and the LORIS Trial Office you will only be identified by your study number, initials and date of birth.

We will also need to record your personal details, your forename, surname, NHS number or in Scotland the Community Health Index (CHI) number, hospital number, GP details, which are required to keep track of your long-term progress and to send Quality of Life questionnaires to your home address. Data may be provided to the LORIS Trial Office verbally (over the telephone), on paper or electronically.

By taking part in the study you will be agreeing to allow research staff from the LORIS Trial Office to look at your study records, and this includes your medical records. It may be necessary to allow authorised personnel from other, agencies for example the Sponsor (University of Birmingham) or NHS bodies to have access to your personal data. This is to ensure that the study is being conducted to the highest possible standards.

If you choose to donate tissue from your diagnostic biopsies, initial surgery and from any other surgeries you may have, your pathology number will be collected to identify the tissue samples.

In addition, anonymised data from the study may be provided to other third parties (e.g. other academic institutions) for research. This may include institutions outside the UK.

We will obtain information about your progress from your hospital research team over the next 10 years and would ideally like to follow your progress for life. To do this, we will obtain information about your progress through the national health registries (such as the Cancer

Registries or the Data Linkage and Extract Service). In order to do this, we will need to provide your full name and NHS (CHI) number.

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

If you choose to withdraw from the study, we would still like to collect relevant information about your health, as this will be invaluable to our research. If you have any objection to this please let your doctor know.

You can withdraw your consent to our processing of your data at any time. Under the provisions of the Data Protection Act 1998 you have the right to know what information the LORIS Trial Office have recorded about you. If you wish to view this information please contact Legal Services at the address below. Please note that a small fee may be payable to retrieve this information.

Legal Services
University of Birmingham
Edgbaston
BIRMINGHAM
B15 2TT

Will my GP be informed of my involvement?

Your GP will be informed that you are taking part in the study. If you are in the Active Monitoring group, a copy of the letter detailing the outcome of your annual mammogram will be sent to your GP. Your study doctor or research nurse may contact your GP for an update on your progress if you are no longer attending clinic or for mammograms.

What will happen to any samples I give?

We want to learn more about why low or low-intermediate grade DCIS can become invasive breast cancer in some women. When you had the biopsy to confirm your diagnosis, your tissue was analysed by a specialist team to decide if you were eligible for the study. With your permission, if there is enough tissue available, we would like to collect tissue from your biopsies and from your initial surgery (if you are allocated to the Surgery group) and any future surgery or biopsies that you may have, whichever group you are in. Your tissue samples will be identified by your pathology number and study number only and these samples will be sent to the Edinburgh Cancer Research Centre at the University of Edinburgh where they will be analysed by our experts which will allow us to learn more about the natural history of low and low-intermediate grade DCIS. The tissue samples will be kept until the end of the research. Any tissue left over at the end of the research will be stored for use in future ethically approved research projects. This may be research on your tissue samples that is conducted outside the UK.

If you have any further biopsies taken from your breast, your study doctor may want these to be reviewed by the trial's expert pathologists, as they did for your recent biopsy. The tissue from the biopsy would be sent to the Human Biomaterials Resource Centre at the University of Birmingham and a digital image will be taken of each microscope slide before they are returned to your hospital. These images will be labelled with your unique study number and pathology number only. We will store any images taken until the end of the research.

What will happen to any mammogram images collected?

We want to learn more about how low or low-intermediate grade DCIS can change in some women. To do this, we would like to collect the digital images of the mammogram you had before study entry and of each mammogram you have until the end of the research. Your hospital research team will send the digital images of your mammograms to Royal Surrey County Hospital where they will be stored by the National Co-ordinating Centre for the

Physics of Mammography. Your images will only be identified by your unique study number, date of birth and the date that the mammogram was taken. This also allows the trial's expert radiologists to look at your mammogram images and provide a second opinion service to your hospital if they feel they need it. The images will be kept on a secure facility until the end of the research, when all patients have been followed up for as long as possible.

Will any genetic tests be done?

We will be looking at the expression of genes within the tissue sample that you give to see how these change over time and to see whether we can predict which patients DCIS is most likely to progress to an invasive cancer. We will therefore be analysing DNA and RNA (gene messages) in your tissue samples. Some of the genes studies may be inherited. However, currently none of the genes we intend to study are known to be of medical significance. It is unlikely that any information will arise from the analysis of your samples that will be of medical importance to you or your family.

What will happen to the results of the research?

The results will be published in medical journals and presented at conferences as soon as there is enough information to be sure the results are reliable. It is possible that a small number of quotes from the telephone interviews will be published anonymously. You will not be identified in any report or publication. The results will help to decide how to treat low risk DCIS in the future. Patients taking part in this study can find out about the results from their study doctor once the results have been published. The results will also be available on the CancerHelp website.

Who is organising and funding the research?

This study is being organised by a team of doctors and other experts. It is being managed by the Cancer Research UK Clinical Trials Unit (CRCTU) at the University of Birmingham. It has been funded by National Institute for Health Research Health Technology Assessment Programme.

The lead surgeon (Chief Investigator) is Miss Adele Francis at University Hospitals Birmingham NHS Foundation.

Who has reviewed the study?

All research in the NHS is looked at by independent group of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed and given favourable opinion by West Midlands – Solihull Research Ethics Committee and also by the Research and Development Office at your hospital.

What happens now?

You will have some time to think about the study and make your decision. You will also be given a Patient Information DVD to watch either at home or at the hospital which explains the study. You may wish to discuss the study with your family and friends. If you choose to take part, you will receive a copy of this information sheet and a copy of your signed consent to keep.

Further Information and Contact Details

If at any time, you have any questions about the study you should contact your study doctor or research nurse using the details below.

Your study doctor is: _____

☎ _____

Your research nurse is: _____

☎ _____

If you need to contact the Quality of Life Team:

LORIS Quality of Life Coordinator
Sussex Health Outcomes Research & Education in Cancer (SHORE-C)
University of Sussex
Science Park Road
Falmer, Brighton, East Sussex
BN1 9RX
Tel: 01273 877 919 Fax: 01273 873 022

You may also find it helpful to contact CancerHelp, an information service about cancer and cancer research studies by Cancer Research UK.

Information about the LORIS study can also be found on the CancerHelp website.

Freephone: 0808 800 4040 website: http://www.cancerhelp.org.uk/.

Thank you for taking the time to read this leaflet

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NHS National Institute for Health Research

Further details on the LORIS study and the patient DVD that provides further information about the trial can be viewed at web address below:

www.birmingham.ac.uk/loris