**Phase II Randomised, Double Blind, Placebo Controlled Trial**

**of Neoadjuvant Artesunate in Stage II/III Colorectal Cancer (NeoART Trial)**

**Participant Information Sheet Version 2.0 3 May 2016**

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**Invitation to take part in a study:**

Your doctors have told you that you have cancer of the bowel (colon/rectum) and have invited you to participate in a research study called **“NeoART”**.Before you decide whether 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.  ***We will go through the information sheet with you and answer any questions you have.*** *We suggest this should take about 25 minutes.*

*Part 1 of the PIS tells you the purpose of this study and what will happen to you if you take part.*

*Part 2 gives you more detailed information about the conduct of the study.*

*Please ask us if there is anything that is not clear. Take time to decide whether or not you wish to take part.*

**Part 1 - What is the purpose of the study?**

The most important treatment for localised bowel cancer is surgery to remove the cancer, along with part of the bowel. For many patients this operation can result in a complete cure. However in some patients, tiny cancer deposits, too small to see or detect, called ‘metastases’ can spread before or during the operation; these can then further develop into a cancer months or years later. In some patients, a course of drug treatment after the operation may be recommended to reduce the risk of the cancer recurring. This treatment is known as ‘adjuvant chemotherapy’.

There is research evidence that artesunate, which is a safe and effective treatment for malaria, can cause the death of cancer cells. We would like to know whether a short course of artesunate 2 weeks before surgery can cause colon cancer cells to die and reduce the risk of metastases and the cancer returning after surgery.

We recently published a small similar study of oral artesunate treatment given to patients at St George’s Hospital who were diagnosed with bowel cancer. Patients received 14 days treatment whilst waiting for surgery to remove the tumour. Although this was a small study (20 patients in all), only one patient in the group receiving artesunate treatment had a recurrence of cancer after 42 months, compared to 6 in the placebo group. We now need to do a larger study: to see if these results are confirmed.

**Why have I been invited?**

You are waiting to have curative surgery for bowel cancer. We are recruiting about 200 patients in your position. Your specialist will have invited you to consider taking part in NeoART because you have a form of bowel cancer that may be cured with surgery, for which pre-operative treatment with artesunate may be helpful.

**Do I have to take part?**

No. It is up to you to decide whether to take part. We will describe the study and go through this Patient Information Sheet with you. If you decide to participate in this study, you will be given this Patient Information Sheet to keep and you will be asked to sign a consent form. You are free to withdraw from the study at any time and without giving a reason. A decision to withdraw at any time or not to take part will not affect the standard of care you receive now or at any point in the future.

If you choose to withdraw from the study at any stage, you can ask to have any information we have already collected about you that remains identifiable to be confidentially destroyed.

**What will happen to me if I take part?**

If you decide to take part we will ask you to sign a consent form. Once the date of your surgery is known you will be prescribed your NeoART study medication which you will need to collect from the hospital pharmacy. Once you have signed a consent form we will continue with the routine clinical review on Day 1 of the study which would include asking questions about any symptoms you may be experiencing and any medication you may be taking. You will be asked at this visit to complete 3 questionnaires about your quality of life. You will be asked to complete these questionnaires again at each visit and hand them back to the research team looking after you. We will take a blood sample from you (about 2 teaspoonfuls of blood) to check your blood results at baseline and store a sample of your blood for future molecular analysis as part of the study.

**What treatment will I get?**

Sometimes we don’t know which way of treating patients is best. To find out, we need to compare different treatments. We put people into groups and give each group a different treatment. The results are compared to see if one treatment is better compared to another treatment. To try to make sure the groups are the same to start with, each patient is allocated to a treatment group randomly by chance (like flipping a coin). You will get one of two treatments.

**Group 1** Artesunate; **Group 2** Placebo.

Two tablets must be taken once every day for 14 days to finish as planned the day before your surgery. You will be instructed which date to start taking your tablets.

You will have an equal chance of receiving artesunate or placebo. Neither you, the Research team nor your doctor will know which treatment you are receiving. However, if your doctor needs to find out they can do so. You will be provided with a NeoART Trial card that will contain details including a NeoART team 24 hour emergency number. You should carry this card (the size of a credit card) on you at all times and present it to any physician that may be treating you or contact the research team if you are worried or do not feel well.

You will be seen in clinic by the research team after taking the tablets for 7 days and again on day 14 of taking the tablets. Please remember to bring your tablets with you to each visit. You will be reviewed by the research team to make sure you are well and you will be asked if you have experienced any potential side effects. We will also check if there are any changes to the other medications that you are taking. We will take a blood sample from you (about a teaspoonful of blood) to check that there have been no changes from your baseline bloods and that your white blood cell count is normal. White blood cells help fight infections and if the level becomes low we may need to stop the study tablets or prescribe you a medicine to help boost your white blood cell count.

At both of these visits you will again be asked to complete 3 quality of life questionnaires and hand them back to the research team.

Whilst you are in hospital following your surgery the research team may visit you to check on your progress and to make sure you are well.

You will be asked to attend for a blood test 2 weeks after your surgery (Day 28). This is important. We will need about 5mls (a teaspoonful) of blood to monitor your red blood cell count (haemoglobin) levels. This is because there have been rare cases reported of haemolytic anaemia in patients taking artesunate for malaria.

On Day 42 of the study (4 weeks after surgery) you will be reviewed again in clinic and we will ask you about your recent health, perform a physical examination and take another blood sample to check that your blood counts are normal. We will again ask you to complete the 3 quality of life questionnaires and hand them back to the research team.

Following surgery you will be followed up every 6 months for 5 years as part of routine follow up. At each visit we will take a medical history, perform a clinical examination and perform a blood test to monitor your blood Carcinoma Embryonic Antigen (CEA) tumour marker level.

At the end of year 1, you will undergo a routine colonoscopy. At the end of year 1, 2 and 5 you will undergo a routine restaging CT scan of the chest, abdomen and pelvis to check that there is no evidence of cancer recurrence.

At each visit we will ask you to complete the quality of life questionnaires and return these to the research team.

**What are the alternatives for diagnosis or treatment?**

At present, surgery is the standard care for patients with Stage II/III colorectal cancer. Some patients require postoperative chemotherapy depending on certain tumour characteristics found at surgery.

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

Participation in this study will require you to attend 3 - 4 extra hospital visits and may increase the length of time you have to spend at each clinic visit whilst you are completing the quality of life questionnaires. We will also need to perform extra blood tests on 3 of these visits in addition to your routine care. The information that we will collect for this study will be important so we will need your kind co-operation.

You are due to receive the main treatment for bowel cancer (surgery) and participation in this study will not affect this or delay its timing.

A very small number of people (about 5%) prescribed artesunate experience stomach upsets (including nausea, diarrhoea or abdominal cramps). Rashes can occur rarely, as well as skin tingling, chest palpitations and allergic reactions. Slight changes in blood counts and liver function tests may occur but these are all reversible on stopping the drug.

Whilst you are taking the tablets we will carry out a clinical review on Day 1, Day 7 and Day 14 of the study. We will ask about any symptoms and side effects and take some blood to monitor your blood count.

There have been very rare reports of people developing anaemia 3-4 weeks after treatment with artesunate for malaria (anaemia is a condition where the red blood cells or haemoglobin in the blood are low). You will be asked to provide a blood sample 28 days after you start the tablets to monitor for this rare side effect.

We may also visit you whilst you are recovering from your surgery to check on your progress. You may find these extra visits intrusive or inconvenient. However we hope you find some reassurance in the fact that should you have any questions or concerns we will address them quickly and adjust your care accordingly.

**Possible Harm to the unborn child**

Artesunate may harm the unborn child if taken during the first three months of pregnancy. For this reason, you will not be included in the study if you are pregnant. Female patients must have a negative pregnancy test within 72 hours of starting the study. If you are a woman of childbearing capacity or a man with a partner of childbearing capacity, you must agree to use a reliable form of contraception from the time you sign the study consent form till 6 weeks after you finish taking the study drug [eg. oral contraceptive and condom, intra-uterine device (“coil”) and condom, diaphragm with spermicide and condom or agreement of true abstinence (i.e. withdrawal, calendar, ovulation, symptothermal and post ovulation are not acceptable methods)]. If you discover that you or your partner do become pregnant during the first phase of the study, we ask that you tell the NeoART study team immediately.

The NeoART team will work closely together with an Obstetric Specialist and Foetal Medicine Specialist to monitor the pregnancy closely on a fortnightly basis. Following the successful delivery of your baby the paediatric team will need to monitor your baby for 12 months to ensure that your baby is developing normally.

**What are the possible benefits of taking part in this study?**

If you do take part, you will be participating in important research investigating whether or not artesunate could prevent cancer from recurring after bowel cancer surgery. We cannot promise the study will definitely help you as an individual. Participation in this study may however enhance the post-operative care that you receive as the NeoART team will be following your health and clinical progress closely.

**Will my GP be told of my participation in this study?**

Yes, once you agree to participate in this study and with your permission, we will notify your GP. We will provide a copy of this information sheet for entry into your GP medical records. You may also wish to discuss your participation in this study with your GP at your next visit.

We will also seek your permission to contact your GP during the NeoART 5 year study duration in relation to your ongoing health or if we lose contact with you.

**What happens when the research study stops?**

Following your surgery you will continue to be managed according to the normal clinical care pathways. After the final study visit which will occur 5 years after your surgery, participation in the NeoART trial will end. You will continue to be cared for in accordance with your clinical needs and may be discharged back to your GP.

**Will taking part in this study cost me anything and will I be paid?**

There is no financial cost incurred by participating in the study and we are not allowed to give you any financial incentive for taking part in the NeoART study. However we will reimburse any travel expenses you may incur as a result of participating in the study. Please speak to your clinical trial nurse about this.

**Will my taking part in the study be kept confidential?**

If you decide to take part in the NeoART study, the information collected about you during the course of the trial will be kept strictly confidential in the same way as all of your other medical records. Any information about you or samples taken will have your name removed so that you cannot be recognised. Any data or samples on paper and electronically will be stored in password protected files in locked rooms that only the researchers (and relevant regulatory bodies) have access to, under the provisions of the 1998 Data Protection Act and/or applicable laws and regulations. Your GP and the other doctors involved in your clinical care, will be kept informed of your progress, but otherwise all information about you and your treatment will remain confidential.

**Will my taking part in the study be kept confidential?**

Yes. We are bound by legislation and the NHS confidentiality code of practice to safeguard your confidentiality during and after the study.

* It is possible that authorised persons from either the Sponsor organisation and/or the regulatory authorities that monitor the quality of research such as this may require access to view your medical records for the purposes of audit or monitoring.
* Data collected for this study may be retained on a secure database kept on NHS computers for up to a year following study closure whilst results are being analysed. Once the study is closed following analysis, study hard copy data records may be kept for a further 15 years in a secure location. However, no information will be kept, which allows your identity to be revealed.

**What if there is a problem?**

Any complaint about the way you have been treated or any possible harm you might suffer will be addressed thoroughly. Detailed information on this process is given in part 2.

**This completes Part 1.**

We hope that you have found the information in Part 1 interesting. If you are considering participation, please read the additional information in Part 2 before making your decision.

**Part 2- More detailed information about the conduct of the study**

**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 routine care to continue. If you decide to continue in the study you may be asked to sign an updated consent form. If the study is stopped for any other reason, we will tell you and arrange your continuing care according to normal clinical care pathways.

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

You can decide not to continue with the study treatment at any time. If you do decide to stop the study treatment however, we would still like to follow your progress. An important aim of the study is to find out how many patients complete their treatment and to see how patients do clinically if they withdraw from treatment. For this reason, your samples and data would remain on file and be included in the final study analysis. However if you withdraw consent for your data to be used, it will be confidentially destroyed.

**What if you wish to complain about the trial?**

If you wish to complain, or have any concerns about the way you have been treated during this study, you can talk to either your local NeoART research team or the NeoART co-ordinating team who will do their best to answer your questions or concerns (contact details for both teams are at the end of Part 2).

The National Health Service complaints mechanisms are also available to you. The Patient Advice and Liaison Service (PALS) are on Tel: 020 8725 2453.

If you are still not satisfied with the response you receive, you may contact:

The Sponsor Joint Research and Enterprise Office at St George’s, University of London on Tel: 0208 725 4986.

**What if there is a problem during or following your participation in the trial?**

St Georges, University of London has agreed that if you are harmed as a result of your participation in the study, you will be compensated, provided that, on the balance of probabilities, an injury was caused as a direct result of the intervention or procedures you received during the course of the study. These special compensation arrangements apply where an injury is caused to you that would not have occurred if you were not in the trial. We would not be bound to pay compensation where: -The injury resulted from a drug or procedure outside the trial protocol and/or the protocol was not followed. These arrangements do not affect your right to pursue a claim through legal action.

**What will happen to any samples I give and will any genetic tests be done?**

If you take part in NeoART, we would like to request your permission to take 2 extra blood samples and to store this along with some of the surplus material from your diagnostic biopsy and from the tumour removed at surgery for future genetic testing. As part of the NeoART study we would like to apply the latest molecular techniques and genetic tests to build on our understanding of how artesunate may work to kill cancer cells. The samples will be anonymised and only carry the participant study ID number assigned to you by the study team and the date the sample was taken. You are free to withhold this permission without affecting your participation in NeoART or the treatment you receive. Samples not sent for further genetic testing such as pregnancy tests, full blood count, kidney and liver function tests will be confidentially destroyed according to routine local laboratory procedures.

**What will happen to the results of the research study?**

You will not be identified in any report/publication. We intend to publish the results in scientific journals to make the results of the trial available to a wider audience. If you would personally like to know the outcome of the study, please inform us and we would be happy to provide this information.

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

The NeoART study was developed by a research team from the Colorectal Surgery Department and Institute of Infection and Immunity at St Georges University of London. The study is sponsored by St George’s University of London. The study is funded by the charity Bowel Disease UK and a public crowdfunding campaign via the FutSci crowdfunding platform. A pharmaceutical company called Dafra Pharma will

provide the study drug and placebo but is not involved in the organisation or running of the study. None of the doctors or researchers involved have received additional payment for their involvement in the study.

A member of our team is a junior doctor, currently taking time out of clinical training to facilitate this research study as part of an educational project. She may use data collected from this study towards obtaining a Research Degree from the University of London.

**Who has reviewed the study?**

All research in the NHS is reviewed by an independent group of people, called a Research Ethics Committee (REC), to protect patient interests. This study has been reviewed and approved by the London-Chelsea Research Ethics Committee. It has also been reviewed by your local hospital Trust Research and Development Department.

**Contact Details**

**Further information**

If you have any further questions about your diagnosis or clinical trials, please discuss them with your doctor. You may also find it helpful to contact an independent patient advisory group such as MacMillan Cancer Support (Freephone: 0808 808 00 00; [www.macmillan.org.uk)](http://www.macmillan.org.uk)).

If you are unhappy with any aspect of this study, or have any concerns please contact the: NeoART Research Team Emergency Number: **07553698174**

**Other useful contact numbers**

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