

Participant Information Sheet/Consent Form

Interventional Study - Adult providing own consent

Flinders Medical Centre

Title	Phase I open label trial of intraperitoneal paclitaxel in combination with intravenous cisplatin and oral capecitabine in patients with advanced gastric cancer and peritoneal metastases
Short Title	Chemo into the peritoneum for gastric cancer
Protocol Number	007
Project Sponsor	Flinders Centre for Innovation in Cancer, Flinders Medical Centre
Location	Flinders Medical Centre

Part 1 What does my participation involve?

1 Introduction

You are invited to take part in this research project. This is because you have *Stomach Cancer*. The research project is testing a new treatment for *Stomach Cancer*. The new treatment is called *intraperitoneal paclitaxel*.

This Participant Information Sheet/Consent Form tells you about the research project. It explains the tests and treatments involved. Knowing what is involved will help you decide if you want to take part in the research.

Please read this information carefully. Ask questions about anything that you don't understand or want to know more about. Before deciding whether or not to take part, you might want to talk about it with a relative, friend or your local doctor.

Participation in this research is voluntary. If you don't wish to take part, you don't have to. You will receive the best possible care whether or not you take part.

If you decide you want to take part in the research project, you will be asked to sign the consent section. By signing it you are telling us that you:

- Understand what you have read
- Consent to take part in the research project
- Consent to have the tests and treatments that are described
- Consent to the use of your personal and health information as described.

You will be given a copy of this Participant Information and Consent Form to keep.

2 What is the purpose of this research?

The aim of the study is to determine the safe dose of chemotherapy to treat patients with stomach cancer with chemotherapy, some of which is given directly into the abdomen as well as into the vein. This study will also determine how safe this chemotherapy approach is, what side-effects it causes and how it affects quality of life.

There is a gap in our knowledge as to how to best treat patients with stomach cancer who have extension of the disease in the peritoneum (peritoneum is the membrane that forms the lining of the abdominal cavity). Researchers in Japan have used *intraperitoneal paclitaxel* treatment in patients with stomach cancer who had disease extension in the peritoneum and have reported promising results. Nevertheless, the other drugs used by those researchers are different from the standard of care in Australia and also there might be differences in the way stomach cancer behaves in different populations from different backgrounds.

Intraperitoneal paclitaxel has been given safely to people with other types of cancer and is part of a standard treatment for patients with cancer of the ovary or peritoneum.

With the results of this study we will be able to design a larger study to define the effectiveness of this treatment option.

The drugs used in this study consist of two drugs (*capecitabine* and *cisplatin*) that are part of the standard treatment for patients with advanced stomach cancer, and a the third drug called *paclitaxel* which is registered in Australia to be used in other cancers (both through intravenous catheter or directly into abdomen)

Medications, drugs and devices have to be approved for use by the Australian Federal Government. Paclitaxel is approved in Australia to treat cancer of ovary and peritoneum, breast cancer and cancer of the lung. *However it is not approved to treat Stomach cancer. Therefore, it is an experimental treatment for Stomach Cancer. This means that it must be tested to see if it is an effective treatment for Stomach Cancer.*

This research has been initiated by the study doctor, Associate Professor Chris Karapetis and Dr Tim Bright

This research has been funded by the Medical Oncology Clinical Research Unit of the Flinders Medical Centre.

3 What does participation in this research involve?

The consent form will be signed prior to any study assessments being performed.

First we need to make sure about the diagnosis and the extent of the disease: this will include: physical examination, some routine blood tests to check your blood count and your kidney and liver function, a CT scan (of chest abdomen and pelvis) and an endoscopy. (all of these tests are usually done as part of standard work up prior to starting treatment for stomach cancer.)

This study does not involve the use of placebo

Before you participate in this study, you will need to have a catheter placed in your abdomen. This small tube – called intraperitoneal port - will allow the doctors to give you the chemotherapy directly into the abdomen. This tube can be put in when you are having your endoscopy. However, your doctor may decide to put it in at a later date. The port is inserted in the operating theatre. You will be given a general anaesthetic. Your doctor or nurse will give you more

information on what you need to do to prepare for the procedure. You may be allowed to go home on the same day of the procedure if there are no complications.

You will need to see your treating doctor before each cycle of chemotherapy. At this visit, a physical examination will be performed. Before each visit with the treating doctor you will have a blood test.

A cycle of treatment is given every 21 days (3 weeks). You will get a maximum of 6 cycles of treatment.

During your chemotherapy you will be treated with 3 different drugs, they are *capecitabine* tablets (The tablets are taken TWICE a day with a glass of water within 30 minutes after the end of a meal), these tablets are taken for the first two weeks (day 1 to 14) of each chemotherapy cycle.

The second drug is *cisplatin* (given by a drip into a vein, this takes around 4 hours) and is given once every 21 days on day 2. You will need to have fluids given into the vein for several hours, before and after cisplatin and this will mean you may have to stay in hospital for one night. You will also be given medication to prevent nausea and vomiting.

The third drug is *paclitaxel*, this drug will be given into your abdomen through an intraperitoneal port on days 1 and 8 of each cycle, this will take 4 hours. Intraperitoneal chemotherapy will be given to you by a nurse who has been trained to give this treatment. Before this treatment begins you will have fluids and anti-sickness medication by a drip. You will also get medications into the vein beforehand to prevent any allergic reactions. You will also need to empty your bladder. Once the treatment begins you will be on bed rest and you will need to ask for a bedpan if required. The skin over the port site is cleaned with an antiseptic lotion. A needle is inserted through the skin into the port and fluids and chemotherapy will be given. The amount of time required for this treatment will vary depending on the volume of fluids and the chemotherapy that is being given. When the chemotherapy is finished, the needle will be removed. You will then be required to change your position in bed every 15 minutes for 1 hour. When the hour has passed it is important that you get up out of bed and move around. The intraperitoneal port will be removed by your doctor after completing the study.

You will have repeat CT scans of chest abdomen and pelvis after 9 weeks into the treatment and after completing the treatment course. The frequency of the scans is not different than what is routinely used in patients receiving standard chemotherapy treatment for stomach cancer.

During the follow-up period, you will be required to see your treating doctor for a check-up every 3 months up to a maximum of two years. During each visit you will be asked questions about your symptoms and will be examined by your doctor. A routine blood test and repeat CT scan will be done prior to the visit. After the mentioned follow-up period, further follow up plan will be decided by your doctor. .

You will be asked to complete a questionnaire on your quality of life at certain time points during the study; at the start of treatment, after the 3rd cycle and at the end of treatment at the end of the treatment (after 6 cycles) and then every 3 months during your follow up visits. These questionnaires will take about 15 - 20 minutes to complete.

There are no additional costs associated with participating in this research project, nor will you be paid. All medication, tests and medical care required as part of the research project will be provided to you free of charge.

You may be reimbursed for any reasonable travel, parking, meals and other expenses associated with the research project visit.

It is desirable that your local doctor be advised of your decision to participate in this research project. If you have a local doctor, we strongly recommend that you inform them of your participation in this research project.

4 What do I have to do?

- No specific Lifestyle restrictions are required e.g. physical restrictions, participation in sport
- No specific Dietary restrictions are required
- Some of your regular medication may interact with chemotherapy drugs; your doctor will ask you about your regular medications and will advise you accordingly
- You cannot donate blood

5 Other relevant information about the research project

This study will be running in Flinders Medical Centre. Patients will be joining the study in groups of 3, and given a specific dose of intraperitoneal paclitaxel; depending on the side effects and how well they tolerate the dose, the next group of patients will receive a similar or different dose. The study has been designed this way to define the appropriate dose of this drug for patients with stomach cancer.

Depending on the results a further study based on the doses suggested by this study will be designed to investigate the effectiveness of this treatment approach in similar patients.

Researchers from different departments (surgical department and medical oncology department) will be working together in this project

6 Do I have to take part in this research project?

Participation in any research project is voluntary. If you do not wish to take part, you do not have to. If you decide to take part and later change your mind, you are free to withdraw from the project at any stage.

If you do decide to take part, you will be given this Participant Information and Consent Form to sign and you will be given a copy to keep.

Your decision whether to take part or not to take part, or to take part and then withdraw, will not affect your routine treatment, your relationship with those treating you or your relationship with Flinders Medical Centre

7 What are the alternatives to participation?

You do not have to take part in this research project to receive treatment at this hospital. Other options are available; these include using the combination of *capecitabine* and *cisplatin* (same as this study without the intraperitoneal paclitaxel) or palliative and supportive care. Your study doctor will discuss these options with you before you decide whether or not to take part in this research project. You can also discuss the options with your local doctor.

8 What are the possible benefits of taking part?

We cannot guarantee or promise that you will receive any benefits from this research; however, possible additional benefits include potential improvement control of the disease especially in the peritoneum, potential improvement in ascites symptoms, potential improvement in delaying disease recurrence, potential improvement in survival or possible development of a more effective treatment approach for future patients.

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

Medical treatments often cause side effects. You may have none, some or all of the effects listed below, and they may be mild, moderate or severe. If you have any of these side effects, or are worried about them, talk with your study doctor. Your study doctor will also be looking out for side effects.

There may be side effects that the researchers do not expect or do not know about and that may be serious. Tell your study doctor immediately about any new or unusual symptoms that you get.

Many side effects go away shortly after treatment ends. However, sometimes side effects can be serious, long lasting or permanent. If a severe side effect or reaction occurs, your study doctor may need to stop your treatment. Your study doctor will discuss the best way of managing any side effects with you.

Intraperitoneal catheter: Most ports are inserted and used throughout treatment without any complications. Complications may include:

- Infection, including infection of the abdominal wall or infection inside the abdominal cavity (this is called 'peritonitis'). Such infections may require hospital admission for antibiotic therapy,
- Abdominal pain,
- Development of intra-abdominal adhesions: Abdominal Adhesions are fibrous bands that form between tissues and organs, often as a result of injury during surgery. The most important implication of abdominal adhesions is Adhesion-related twisting and pulling of internal organs which can result in complications such as abdominal pain or intestinal obstruction. Intestinal obstruction can be a medical emergency and can be potentially life threatening.
- Risk of organ perforation

Possible Adverse Effects of Chemotherapy:

- **Nausea and Vomiting**
- **Changes in Sense of Smell and Taste**
- **Chest Pain:** Chest pain is uncommon, but may occur at any time during treatment. If you feel short of breath or develop chest pain call an ambulance, do not delay.
- **Increased Risk of Infection :** If you develop a fever 38°C or higher, have shivers, shakes or feel unwell call an ambulance to take you to the nearest hospital emergency department. Do not delay as this is life-threatening.
- **Low Red Blood Cell Count**
- **Low platelets and Increased Risk of Bleeding**
- **Sore Mouth**
- **Diarrhoea**
- **Stomach Pain**
- **Heartburn, difficult and painful swallowing**
- **Feeling Tired**
- **Numbness and Tingling in Fingers and Toes**

- **ringing in the ears and loss of hearing:** Changes in hearing, such as ringing in the ears and hearing loss, may happen. If you develop hearing changes, tell your doctor.
- **Impaired Kidney Function**
- **Hand Foot Syndrome :** Your skin may become red, hot and tender. Small blisters can form and your skin may peel.
- **Hair Loss:** Hair loss may start within a few weeks of beginning treatment.
- **Nail Damage**
- **Poor concentration :** Memory changes and being unable to concentrate are common but generally improve once treatment is completed.
- **Yellowing of the skin and eyes:** Yellowing of your skin and eyes are uncommon. It is caused by the drugs affecting your liver. You will have regular blood tests to check your liver function. If you notice your urine is a dark colour or the whites of your eyes look yellow tell your doctor or nurse.

Possible Adverse Effects of intraperitoneal Chemotherapy:

- **Risks:**

During treatment with chemotherapy directly into the abdomen the following concerning side effects may occur,

- Increased abdominal pressure,
 - Increased abdominal pain
 - Increased abdominal bloating
- **You may also experience the following side effects**
 - Diarrhoea
 - Nausea
 - Vomiting

With medication and appropriate counselling, most side effects can be prevented or reduced.

The effects of *intraperitoneal paclitaxel* on the unborn child and on the newborn baby are not known. Because of this, it is important that research project participants are not pregnant or breast-feeding and do not become pregnant during the course of the research project. You must not participate in the research if you are pregnant or trying to become pregnant, or breast-feeding. If you are female and child-bearing is a possibility, you will be required to undergo a pregnancy test prior to commencing the research project. If you are male, you should not father a child or donate sperm for at least 3 months after the last dose of study medication. Both male and female participants are strongly advised to use effective contraception during the course of the research and for a period of 3 months after completion of the research project. You should discuss methods of effective contraception with your study doctor.

[For female participants] If you do become pregnant whilst participating in the research project, you should advise your study doctor immediately. Your study doctor will withdraw you from the research project and advise on further medical attention should this be necessary. You must not continue in the research if you become pregnant.

[For male participants] You should advise your study doctor if you father a child while participating in the research project. Your study doctor will advise on medical attention for your partner should this be necessary.

If you become upset or distressed as a result of your participation in the research, the study doctor will be able to arrange for counselling or other appropriate support. Any counselling or support will be provided by qualified staff who are not members of the research project team. This counselling will be provided free of charge.

Chemotherapy may cause temporary or permanent sterility. Please discuss this with your study doctor if you have any concerns about future fertility.

Having a drug injected or blood (or tissue sample) taken may cause some discomfort, bruising, minor infection or bleeding. If this happens, it can be easily treated.

These days, whilst anaesthesia is generally very safe there are some risks associated with anaesthesia. The most common problems associated with anaesthesia are feeling unwell or vomiting, bruising at the site of injections, sore throat or hoarse voice. Most patients do not have these problems. If these problems do happen, they usually get better very quickly. Damage to teeth may occur, but this is rare. The risk of brain damage or death due to anaesthesia is very rare.

The risk of problems from anaesthesia increases for patients who are having more major surgery, those with medical problems and those that require difficult anaesthetic procedures. If you have any concerns about these issues, you should discuss them with the study team.

10 What will happen to my test samples?

During the assessment procedures before enrolling into the study and after you have signed the consent form; an endoscopy will be performed by your doctor. During the endoscopy 4 small tissue samples will be taken from the cancer in the stomach and also small tissue samples will be taken from the cancer in the peritoneum. These samples will be stored for future analyses to see if there are any markers that can predict different response to treatment. All the tissue samples will be held in Flinders Medical Centre

11 What if new information arises during this research project?

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

Also, on receiving new information, your study doctor might consider it to be in your best interests to withdraw you from the research project. If this happens, he/ she will explain the reasons and arrange for your regular health care to continue.

12 Can I have other treatments during this research project?

Whilst you are participating in this research project, you may not be able to take some or all of the medications or treatments you have been taking for your condition or for other reasons. It is important to tell your study doctor and the study staff about any treatments or medications you may be taking, including over-the-counter medications, vitamins or herbal remedies, acupuncture or other alternative treatments. You should also tell your study doctor about any changes to these during your participation in the research project. Your study doctor should also explain to you which treatments or medications need to be stopped for the time you are involved in the research project.

13 What if I withdraw from this research project?

If you decide to withdraw from the project, please notify a member of the research team before you withdraw. This notice will allow that person or the research supervisor to discuss any health risks or special requirements linked to withdrawing.

If you do withdraw your consent during the research project, the study doctor and relevant study staff will not collect additional personal information from you, although personal information already collected will be retained to ensure that the results of the research project can be measured properly and to comply with law. You should be aware that data collected by the sponsor up to the time you withdraw will form part of the research project results. If you do not want them to do this, you must tell them before you join the research project.

14 Could this research project be stopped unexpectedly?

This research project may be stopped unexpectedly for a variety of reasons. These may include reasons such as:

- Unacceptable side effects
- The drug/treatment/device being shown not to be effective
- The drug/treatment/device being shown to work and not need further testing

15 What happens when the research project ends?

You will be followed up for a maximum of 2 years after completing the study, after that your doctor will discuss further follow up plans with you.

After completing this study, treatment with intraperitoneal paclitaxel will not be available. When further treatment is indicated your medical oncologist will advise you on the treatment options.

It is usual for a number of years to elapse before definitive results of this type of study are available. These are published in medical journals that are available to the public. You should feel free to ask your doctor about this.

Part 2 How is the research project being conducted?

16 What will happen to information about me?

By signing the consent form you consent to the study doctor and relevant research staff collecting and using personal information about you for the research project. Any information obtained in connection with this research project that can identify you will remain confidential. All the information will be kept in medical oncology clinical trials unit in flinders medical centre Your information will only be used for the purpose of this research project and it will only be disclosed with your permission, except as required by law.

Information about you may be obtained from your health records held at this and other health services for the purpose of this research. By signing the consent form you agree to the study team accessing health records if they are relevant to your participation in this research project.

It is anticipated that the results of this research project will be published and/or presented in a variety of forums. In any publication and/or presentation, information will be provided in such a way that you cannot be identified.

Information about your participation in this research project may be recorded in your health records.

In accordance with relevant Australian privacy and other relevant laws, you have the right to request access to your information collected and stored by the research team. You also have the right to request that any information with which you disagree be corrected. Please contact the study team member named at the end of this document if you would like to access your information.

Any information obtained for the purpose of this research project that can identify you will be treated as confidential and securely stored. It will be disclosed only with your permission, or as required by law.

17 Complaints and compensation

If you suffer any injuries or complications as a result of this research project, you should contact the study team as soon as possible and you will be assisted with arranging appropriate medical treatment. If you are eligible for Medicare, you can receive any medical treatment required to treat the injury or complication, free of charge, as a public patient in any Australian public hospital.

18 Who is organising and funding the research?

This research project is being conducted by *A/Prof Chris Karapetis and Dr Tim Bright*

You will not benefit financially from your involvement in this research project even if, for example, your samples (or knowledge acquired from analysis of your samples) prove to be of commercial value to *Flinders Medical Centre*

No member of the research team will receive a personal financial benefit from your involvement in this research project (other than their ordinary wages).

19 Who has reviewed the research project?

All research in Australia involving humans is reviewed by an independent group of people called a Human Research Ethics Committee (HREC). The ethical aspects of this research project have been approved by the HREC of *Flinders Medical Centre*

This project will be carried out according to the *National Statement on Ethical Conduct in Human Research (2007)*. This statement has been developed to protect the interests of people who agree to participate in human research studies.

20 Further information and who to contact

The person you may need to contact will depend on the nature of your query.

If you want any further information concerning this project or if you have any medical problems which may be related to your involvement in the project (for example, any side effects), you can contact the principal study doctor on *08 8204 8997* or any of the following people:

Clinical contact person

Name	
Position	
Telephone	
Email	

For matters relating to research at the site at which you are participating, the details of the local site complaints person are:

Complaints contact person

Name	
Position	
Telephone	
Email	

If you have any complaints about any aspect of the project, the way it is being conducted or any questions about being a research participant in general, then you may contact:

Local HREC Office contact (Single Site -Research Governance Officer)

Name	
Position	
Telephone	
Email	

Consent Form - *Adult providing own consent*

Title Phase I open label trial of intraperitoneal paclitaxel in combination with intravenous cisplatin and oral capecitabine in patients with advanced Gastric cancer and peritoneal metastases

Short Title Chemo into the peritoneum for gastric cancer

Protocol Number 007

Project Sponsor Flinders Centre for Innovation in Cancer,
Flinders Medical Centre

Coordinating Principal Investigator Medical Oncology Clinical Trials Unit

Location Flinders Medical Centre

Declaration by Participant

I have read the Participant Information Sheet or someone has read it to me in a language that I understand.

I understand the purposes, procedures and risks of the research described in the project.

I give permission for my doctors, other health professionals, hospitals or laboratories outside this hospital to release information to *Flinders Medical Centre* concerning my disease and treatment for the purposes of this project. I understand that such information will remain confidential.

I have had an opportunity to ask questions and I am satisfied with the answers I have received.

I freely agree to participate in this research project as described and understand that I am free to withdraw at any time during the study without affecting my future health care.

I understand that I will be given a signed copy of this document to keep.

Name of Participant (please print) _____

Signature _____ Date _____

Name of Witness* to
Participant's Signature (please print) _____

Signature _____ Date _____

* Witness is not to be the investigator, a member of the study team or their delegate. In the event that an interpreter is used, the interpreter may not act as a witness to the consent process. Witness must be 18 years or older.

Declaration by Study Doctor/Senior Researcher†

I have given a verbal explanation of the research project, its procedures and risks and I believe that the participant has understood that explanation.

Name of Study Doctor/ Senior Researcher [†] (please print) _____	
Signature _____	Date _____

[†] A senior member of the research team must provide the explanation of, and information concerning, the research project.

Note: All parties signing the consent section must date their own signature.

I understand that, if I decide to discontinue the study treatment, I may be asked to attend follow-up visits to allow collection of information regarding my health status. Alternatively, a member of the research team may request my permission to obtain access to my medical records for collection of follow-up information for the purposes of research and analysis.

I consent to the storage and use of blood and tissue samples taken from me for use, as described in the relevant section of the Participant Information Sheet, for:

- This specific research project
- Other research that is closely related to this research project
- Any future research.

By signing this consent section, I agree to the use of tissue samples obtained previously from my *routine biopsy or surgery* for the purposes of additional testing for *Molecular testing*

Name of Participant (please print) _____	
Signature _____	Date _____

Name of Witness* to Participant's Signature (please print) _____	
Signature _____	Date _____

* Witness is not to be the investigator, a member of the study team or their delegate. In the event that an interpreter is used, the interpreter may not act as a witness to the consent process. Witness must be 18 years or older.

Name of Study Doctor/ Senior Researcher [†] (please print) _____	
Signature _____	Date _____

[†] A senior member of the research team must provide the explanation of and information concerning the research project.

Note: All parties signing the consent section must date their own signature.

Form for Withdrawal of Participation - *Adult providing own consent*

Title Phase I open label trial of intraperitoneal paclitaxel in combination with intravenous cisplatin and oral capecitabine in patients with advanced Gastric cancer and peritoneal metastases

Short Title Chemo into the peritoneum for gastric cancer

Protocol Number 007

Project Sponsor Flinders Centre for Innovation in Cancer,
Flinders Medical Centre

Coordinating Principal Investigator Medical Oncology Clinical Trials Unit

Location Flinders Medical Centre

Declaration by Participant

I wish to withdraw from participation in the above research project and understand that such withdrawal will not affect my routine treatment, my relationship with those treating me or my relationship with *Flinders Medical Centre*

Name of Participant (please print) _____
Signature _____ Date _____

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Declaration by Study Doctor/Senior Researcher†

I have given a verbal explanation of the implications of withdrawal from the research project and I believe that the participant has understood that explanation.

Name of Study Doctor/ Senior Researcher† (please print) _____
Signature _____ Date _____

† A senior member of the research team must provide the explanation of and information concerning withdrawal from the research project.

Note: All parties signing the consent section must date their own signature.