



## **SUBJECT INFORMATION AND CONSENT FORM**

### **PHASE I STUDY OF ABC-1 LIPOSOME INJECTION IN PATIENTS WITH ADVANCED SOLID TUMORS**

**BCCA Principal Investigator:** Dr. XXX, Medical Oncology  
BC Cancer Agency, Vancouver Centre  
Phone – 604 877 6000 local xxxx

**Sponsor:** XYZ Technologies, Inc.

#### **Emergency Contact Numbers (24 hours / 7 days a week)**

**For emergencies only:** Call the centre and ask for your usual oncologist,  
or if he or she is not available ask for the oncologist on call.

Vancouver Cancer Centre: 604 877 6000  
Vancouver Island Cancer Centre: 250 370 8000  
Fraser Valley Cancer Centre : 604 581 2211  
Centre for the Southern Interior : 250 862 4000

**Non Emergency contact numbers are noted at the end of this document  
under the section heading “Contact”**

## **1. Background**

You are being asked to take part in a research study. Before you decide, 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 relatives, friends, and your doctor if you wish.

Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

You are being asked to take part in this research study because you have an advanced cancer and your cancer has grown or spread after treatment with standard therapies. It is not yet known if the drug being evaluated in this study, ABC-1, will be able to kill cancer cells in people. 'Investigational' means that this drug, ABC-1, has not yet been approved by health authorities such as Health Canada or the US Food and Drug Administration as either a prescription or over the counter drug.

## **2. What is the purpose of this study?**

This is a phase I clinical trial. Phase I clinical trials are the first studies of a potential new treatment in humans. In these studies, researchers evaluate how a new drug should be given (for example by mouth, injected into the blood or otherwise), how often and what dose is safe. Because less is known about the possible risks and benefits in Phase I, these studies usually only include a limited number of subjects who have not been helped by other known treatments.

The purpose of this phase I study is to determine how much of a new drug can be safely given to subjects with cancer. This is done by starting at a dose lower than the one that was found safe in animals. Subjects are given the new drug and are watched very closely to see what side effects they have and to make sure the side effects are not severe. If the side effects are not severe, then more subjects are asked to join the study and are given a higher dose of the new drug. Subjects joining the study later on will get higher doses than subjects who join earlier. This will continue until a dose is found that causes severe but temporary side effects. Doses higher than that will not be given. Your study doctor will discuss with you what dose you will receive and what has been learned about the new drug from this study. Your safety is our primary concern and your study treatment will be discontinued if you experience severe side effects.

In addition to carefully noting any side effects you experience, you will have a number of blood tests to find out how the drug moves through and leaves your body. Scans and other tests will also be done to look at whether or not your cancer responds to treatment with ABC-1.

Studies have shown that the activity of cancer drugs can be increased when these drugs are used in combination. This has led, over the years, to the use of drug combinations in the clinic such that anticancer drug combinations are now standard in many forms of cancer chemotherapy. The doses of the drugs given in combination has usually been the highest dose that is tolerated. However, studies in the laboratory have shown that this may not be the best way to determine the doses. Studies have suggested that combining drugs in specific ratios of each other (specific levels) may be more effective in terms of killing cancer cells than simply using the highest tolerated dose for each. This may be due to how the body distributes the anticancer drug, and this may be different if the drug is given in a combination rather than as a single agent. Using this concept, tests have been done to determine what the best ratio or combination of two specific drugs is and a new drug that combines these drugs in that specific ratio has been developed in the laboratory.

Liposomes are fat particles. Chemotherapy drugs have been put into liposomes and these have been shown to circulate in the body longer than drugs that are free and not in a liposome. As well, many liposome drugs have fewer side effects than free drugs. ABC-1 is a new formulation that combines two known drugs, AB and C into one drug that is in the form of a liposome. C is a common drug used for the treatment of a number of cancers for over 30 years. AB is a newer drug that was approved in 1996 and since that time has become standard chemotherapy in a number of tumours, particularly colon cancer.

ABC-1 has shown to be more effective in cells and animal models in the laboratory than the free drugs given as a cocktail or as individual liposomal drugs

The purpose of this study is to determine the safety of ABC-1, to determine the future doses of ABC-1 to give to patients and to measure the levels of ABC-1 in the blood. As well the study will see if ABC-1 causes cancers to shrink but this is not the major goal of the study. The information learned in this study may be helpful in further development of ABC-1 for the treatment of cancer.

### **Who can participate in this study?**

You may participate in this study if:

- You have a cancer that cannot be effectively treated with standard anticancer therapy.
- You are 18 years of age or older
- You have adequate function of your heart, bone marrow, kidneys and liver.
- You have a tumour that can be measured so it can be followed for a response to therapy.
- You are able to be up and out of bed more than half the day.
- You are able to understand this study and sign a written informed consent.

## **Who should not participate in the study?**

You cannot participate in this study if:

- You have a lymphoma, primary brain tumour or hematological malignancies
- You have known brain metastases that have not been stable for at least 6 months.
- You have had any chemotherapy, radiation therapy or other anticancer therapy in the 4 weeks before getting the new investigational drug or have had Drug X or Drug Y in the last 6 weeks before entering the study.
- You have any infections or any other serious medical conditions, such as severe heart or lung disease, which would interfere with your participation in this study.
- You are pregnant or breast feeding or do not have a negative pregnancy test prior to entering the study.
- You have severe or active bowel disease or recent onset of diarrhea, defined as an excess of 2 to 3 stools above the normal daily rate within the prior four weeks.
- You have a history of Wilson's disease or other copper-related disorder.
- You are of childbearing potential and are not willing to use adequate birth control measures throughout the course of the study and for 60 days after the final treatment with ABC-1.

## **How many people will take part in this study?**

This is a Phase I clinical study and will include up to 30 patients and will take about 18 months to complete. The number of patients enrolled will be dependent upon tolerance to the escalation of the ABC-1 dose.

The study will start with a low dose of the drug, which will be given as an intravenous infusion (injected into a blood vessel through a line) over a 90 - 120 minute period. The starting dose will be ABC-1 30/10.9 mg/m<sup>2</sup> and will be given every 14 days. This dose is much lower than the doses used in the laboratory.

A cycle will be defined as four weeks. (28 days with two doses given at days 1 and 15). Subjects will be given ABC – 1 and will be watched closely to see what side effects may develop and to make sure that if side effects are seen, they can be taken care of rapidly. Groups of at least three subjects per dose level will be enrolled and evaluated for toxicity. If the side effects are not severe, than more subjects will be asked to join the study and will be given the same or a higher dose of ABC-1. Subject joining the study later on will get a higher dose of ABC-1 than subjects who join earlier will. This will continue until a dose is found that causes temporary but severe or unacceptable side effects. The dose for an individual subject will be the same for all their injections unless the subject has

severe or unacceptable side effects. Then the dose will be decreased or the treatment will be stopped.

ABC-1 will be given every 14 days as long as your disease does not become worse and you do not experience unacceptable side effects. If your disease becomes worse or you experience unacceptable side effects you will not be able to receive further doses of the study drug.

### **What will happen if you take part in this research study?**

If you agree to be in this study, you will have some tests done. These tests are of the same type that would be done if you were not taking part in the study. However there will be more tests done as described below and they may be done more often than if you were not in the study.

You will be asked to sign this informed consent document before any special study required procedures are performed.

### **3. Plan of Treatment**

If you agree to take part in this study a dose of ABC-1 will be given intravenously (through a vein) every 14 days. The 28 day period that **is** from the first dose on day 1, to a second dose at day 15 and then followed by another 14 days is called a treatment cycle. A total of 11 visits are required for the first treatment cycle (28 days). There are only 4 visits for all subsequent treatment cycles. Each visit that involves seeing the nurse and/or study doctor (every 2 weeks) will take one to two hours except on the first day of treatment when you will be asked to stay for the whole day (8 – 12 hours) after dosing to obtain blood samples to measure the levels of ABC-1 in your blood. Visits that are only for taking a blood sample will be shorter if you are feeling well and may take only 30 minutes or less. You will be asked to come back for blood tests on 4 days following the first cycle to take blood samples to measure the level of ABC-1 in your blood and see how long it takes to leave your system. Once a week you will have a urine test.

Every second cycle you will have repeat tests to measure the size of your cancer. This will involve a CT scan, ultrasound or MRI. Before each treatment you will see the study nurse and doctor and have a history and physical examination.

When you are taken off treatment, you will be asked to return for follow-up visits a month after your last dose of ABC-1 and every three months after that. These visits will take about ½ to one hour. As part of the study process, you may be required to undergo any or all of the tests and procedures listed below.

## **Screening Tests/Procedures: (within 28 days before the first dose of ABC-1)**

These tests/ procedures will be done to determine if you can take part in the study:

- Medical History including all medications (prescriptions, over the counter medications, vitamins, herbs) and a complete physical examination, including a performance assessment of your daily activities. .
- Body weight and vital signs (blood pressure, heart rate, respiratory rate, and temperature)
- Blood tests and urine tests, including a blood test for pregnancy if applicable, and for copper.
- Chest Xray and ECG (electrocardiogram)
- Assessment of your cancer; this may be done by scanning (CT or MRI), blood testing and /or physical examination.

### **On the first cycle of treatment with ABC-1 (Cycle 1)**

If after the initial screening tests your study doctor decides that you can participate in the study, you will return to the clinic for the first dose of ABC-1. The following procedures will be done at this visit;

On day 1 subjects will have an interim history, brief physical exam, and blood tests to measure that the blood clots normally and to assess the copper level. As well subjects will have a urine test. Blood samples for pharmacokinetics (to measure the level of ABC-1) in the blood will be done before, during and after the 90 minute infusion of ABC-1 and at specific times after the end of the infusion, including at 8 – 12 hours after the start of the infusion and on the 4 days following the infusion at 24, 48, 72 and 96 hours after the start of the ABC-1. Each of these tests will take 7 ml (a tablespoon) of blood. There will be 20 blood samples in the first 28 days which will include 13 after the first injection and 7 after the second injection.

If you develop any signs of diarrhea, loperamide 4 mg orally will be given, followed by 2 mg orally every 2 hours until there is complete resolution of the diarrhea for at least 12 hours. If you get diarrhea loperamide will also be given on subsequent cycles. Your doctor might give you other drugs before the treatment begins to help lessen some side effects like nausea and vomiting and allergic reactions. The dose of ABC-1 may be reduced or stopped if you have certain side effects.

The table below summarizes the tests you will have.

Investigations		Timing
History and Physical Exam including:	Weight Performance status Clinical tumor measurements	Day 1 of each cycle
Blood work	To test for bone marrow,	Twice Weekly
Blood work	To test liver and kidney function and levels of protein, calcium, magnesium, glucose and clotting factors	Weekly
Blood work	To measure the Copper level in your blood	Weekly for the first cycle, then day 1 only of following cycles.
Urinalysis	To check your urine	Day 1 of each cycle
Pharmacokinetics	To test the level of drug in your blood	During the first and second dosing of cycle one only
Radiology	Scans/X-rays to document disease	At end of every second cycle

#### **4. How long will you participate in this research study?**

Your treatment with ABC-1 will continue if your cancer does not grow and the side effects are not too severe and if you wish to continue. Before you start treatment, your cancer will be evaluated and it will be evaluated again after 2 cycles of treatment. If your disease remains stable or responds to treatment (gets smaller) and you are tolerating the treatment well, you will be able to receive more treatment cycles and your study doctor will continue to evaluate your cancer after every two cycles. Treatments with ABC-1 will stop if:

- The treatment dose not work for you and your cancer becomes worse.
- You are allergic to the study drug or are not able to tolerate it and have severe side effects.
- Your general health gets worse.
- New information becomes available that indicates the study treatment is no longer in your best interests.
- Your study doctor no longer feels that this is the best treatment for you.
- You choose to no longer participate
- You do not comply with the study procedures (for example you do not regularly attend visits)

If any new side effects or information about your disease or treatment are discovered during the study, you will be told.

**5. What are the possible side effects or risks of taking part in this research study?**

This is the first study in which ABC-1 will be given to humans. The component drugs of ABC-1, Drug A and Drug B have been used for a number of years and their side effects are well known. For this new treatment, they are contained within a liposome (fatty) carrier and although these carriers have been used for other drugs, ABC-1 is a new combination of liposome and drugs. ABC-1 also contains copper inside the liposome and copper can sometimes cause damage to organs such as the liver. The possible side effects you may be at risk for while on study are listed below. All care will be taken to lessen these side effects but as with any experimental treatment, additional, unexpected and/or severe or life-threatening side effects are possible. You should discuss these with your study doctor. Your study doctor will watch you closely to see if you have side effects. Other drugs will be given to make the side effects less serious and uncomfortable when possible. Many side effects may go away shortly after treatment is stopped, but in some cases, side effects may be serious or long-lasting or permanent.

**Possible side effects of ABC-1:**

Likely: (20 – 50 %)

- Diarrhea
- Decrease in blood counts which may lead to serious infection or bleeding
- High copper levels in the blood

Less likely: (< 20%)

- Allergic reactions (flushing, itching, rash, low blood pressure)
- Nausea
- Vomiting
- Loss of appetite
- Hair loss
- Dehydration
- Fever
- Mouth sores

Rarely: (< 5%)

- Damage to the liver or kidneys
- Damage to organs such as the liver due to copper

Side effects associated with blood tests and administration of the study drug may include infection, bruising, redness, discomfort or bleeding at the injection site.

You should tell your doctor or nurse if you experience any side effects. You should also talk to your study doctor before taking any new medications, both prescription and over the counter medications.

## **6. Reproductive Risk**

Because the effects that ABC-1 may have on an unborn baby are unknown, you should not become pregnant or father a baby while on this study. For this reason you will be asked to use an effective method of birth control while you are participating in this study. You should also not nurse your baby while on this study. If you or your partner becomes pregnant during the study you must tell the study doctor right away. Ask about counseling and more information about preventing pregnancy if you need this information.

## **7. What are the benefits of taking part?**

You are being offered this experimental drug because it has shown anticancer activity in preliminary experiments. However, since there is very little information about the drug's effect on cancer in humans, we do not expect that you will benefit from taking part in this study, although the knowledge gained may benefit others. The drug you receive may even be harmful.

## **8. Alternatives to being part of this research study.**

You do not have to participate in this research study to receive the best available care for the problems caused by your cancer. There may be other treatment choices available to you if you decide not to take part in this study. You should talk to your doctor about other possible treatments including:

- Surgery
- Radiation
- Other drugs
- Other experimental protocols
- Symptomatic care

## **9. Confidentiality of your Records**

Your confidentiality will be respected. No information that discloses your identity will be released or published without your specific consent unless required by applicable laws and/or regulations. Your identity will not be used in any reports about the study. In records that leave this centre you will be identified by a code number and your initials only. Your birth date will also be provided if requested by the sponsor or responsible regulatory agency. All information associated with this study will be kept behind locked doors or in secure computer files.

Research records and medical records identifying you may be inspected in the presence of the Investigator or his or her designate by representatives of XYZ Technologies Inc and its development partners, Health Canada, the US Food and Drug Administration, regulatory authorities of other countries, and the UBC BCCA Research Ethics Board for the purpose of monitoring the research. However no records that identify you will be allowed to leave the centre. These organizations have policies of strict confidentiality and the individuals inspecting your records must sign a BC Cancer Agency confidentiality form.

Reports containing your progress and photocopies of certain portions of your medical record, with personal identifiers obscured so that you are identified only by a code number and initials, may be sent to:

- XYZ Technologies Inc. (the sponsor of the study) and its development partners
- The UBC BCCA Research Ethics Board who oversees the ethical conduct of this study
- Health Canada (because it oversees the use of drugs in this country)
- The U.S. Food and Drug Administration
- Regulatory authorities of other countries
- PRA International, the Contract Research Organization (CRO) which is collecting the information about this study for XYZ Technologies

These organizations have policies of strict confidentiality and will not release any information concerning you except to other investigators involved in this study.

This information may include:

- Test results
- Reports about your treatment and side effects
- X-rays and other body scans

Even after your treatment is complete, information will still be sent on your progress to see how well the treatment worked. If you stop taking part in the study, information will also still be sent because it is important to follow the progress of all people who started out on the study, unless you choose to withdraw your consent for the release of information as well.

The information gathered from this study, with information identifying you removed will be shared with the sponsors of the trial, the governmental regulatory agencies that oversee such research, the investigators who have conducted this trial and other doctors and researchers throughout the world through publication of the results of this study.

You will not be identifiable in any publications resulting from this study. Your name will not be used in any reports about this study.

Your rights to privacy are protected and guaranteed by the Freedom of Information and Protection of Privacy Act of British Columbia. This act lays down safeguards respecting your privacy, and also gives you the right to access, and if needs be, correct any errors of your personal information. Further details about this act are available on request.

#### **10. What Are Your Rights As A Participant?**

You can discuss the information above with your doctor who will answer any questions about this treatment now or anytime in the future. Taking part in this study is voluntary. You may choose not to take part or may leave the study at any time and you will continue to be offered the best available medical care. If you decide to withdraw, you will be asked to return for final tests and to provide final blood and urine samples. If you decide to withdraw you should tell your study doctor of your decision so it can be documented in your chart.

We will tell you about the new information from this or other studies that may affect your health, welfare, or willingness to stay in this study. If you choose to enter this study and at a later date new and more effective treatment which is suitable for you becomes available, the new treatment will be offered to you.

#### **11. Remuneration/Compensation**

You will not be paid for participating in this study. Taking part in this study may result in added costs to you. You will not be reimbursed for extra costs such as parking, meals, or travel that you may have due to your participation in this trial.

If you are injured as a consequence of participation in the study due to the administration of the study drug or study procedures, your medical condition will be evaluated and medical care will be provided by one of the investigators or you will be referred for appropriate treatment. If you are injured as a result of participating in this study, the costs of your medical treatment will be paid for by your provincial medical plan.

No funds have been set aside to compensate you in the event of injury or illness related to study treatment or procedures.

You do not waive any of your legal rights for compensation by signing this form.

The sponsors of this study may reimburse the BC Cancer Agency for all or part of the costs of conducting this study or they may provide the BC Cancer Agency some or all of the standard or experimental medications being used in this study. However, the investigators conducting this study will not receive any personal payments for conducting this study. In addition, neither the BC Cancer Agency nor any of the investigators or staff conducting this study will receive any direct financial benefit from conducting this study.

## **12. After the Study is Finished**

You may not be able to receive the study treatment after your participation in the study is completed. There are several possible reasons for this, some of which include: the treatment may not turn out to be effective or safe; the treatment may not be approved for use in Canada; your oncologist may not feel it is the best option for you; coverage may not be available for this treatment in British Columbia and you may decide it is too expensive.

## **13. Contact**

You understand that if you have any questions or desire further information with respect to this study, or if you experience any adverse effects, you can ask your study doctor, who is:

Dr. \_\_\_\_\_ Telephone: \_\_\_\_\_

In the event of a research related injury, please speak to your study doctor (indicated above) or (after hours) call the centre nearest you and ask for your study doctor or, if he or she is not available, the oncologist on call.

Or, you can speak to the doctor who is the Principal Investigator, Dr. XXX at telephone (604) xxx-xxxx

Or, you can speak to the Head of Systemic Therapy Program of the BC Cancer Agency. That person can be reached at (604) xxx-xxxx

If you have any concerns about your treatment or rights as a research subject you may contact the Research Subject Information Line at the UBC Office of Research Services at the University of British Columbia at (604)-822-8598.

**14. Subject Consent:**

I understand that participation in this study is entirely voluntary and that I may refuse to participate or I may withdraw from the study at any time and I will continue to be offered the best available medical care. I understand that I may ask questions about this study in the future.

I have received a copy of this consent form, including all attachments, for my own records. I will receive a signed copy of this consent form.

I consent to participate in this study.

\_\_\_\_\_  
Subject's Signature

\_\_\_\_\_  
Printed name

\_\_\_\_\_  
Date

\_\_\_\_\_  
Witness' Signature

\_\_\_\_\_  
Printed name

\_\_\_\_\_  
Date

\_\_\_\_\_  
Signature of  
Person Obtaining Consent

\_\_\_\_\_  
Printed name

\_\_\_\_\_  
Study Role

\_\_\_\_\_  
Date

If this consent process has been done in a language other than that on this written form, with the assistance of a translator, indicate:

Language: \_\_\_\_\_

\_\_\_\_\_  
Translator's signature  
Date

\_\_\_\_\_  
Printed name