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SAMPLE Informed Consent Form

A PHASE III PROSPECTIVE DOUBLE BLIND PLACEBO CONTROLLED RANDOMIZED STUDY OF ADJUVANT MEDI4736 IN COMPLETELY RESECTED NON-SMALL CELL LUNG CANCER

Trial Code: BR.31

Researcher: Dr. _____

Sponsor: Canadian Cancer Trials Group

Le formulaire de consentement est disponible en français sur demande.

Note to centre: If an REB approved French consent is not used at your institution you should remove the above statement.

Emergency Contact Number (24 hours / 7 days a week): _____

Non-Emergency contact numbers are noted at the end of this document under the section heading “Contacts”.

INTRODUCTION

You are being invited to participate in a clinical trial (a type of study that involves research). Clinical trials only include participants who choose to take part. You are invited to participate in this trial because you have had non-small cell lung cancer (NSCLC) that was completely removed with surgery. You may or may not have received chemotherapy after this surgery. You currently do not have lung cancer and there is no standard anti-cancer treatment that you would receive at this stage. This consent form provides you with information to help you make an informed choice. Please read this document carefully and take your time in making your decision. You may find it helpful to discuss it with your friends and family.

Taking part in this study is voluntary. You may choose not to take part or may leave the study at any time without giving a reason. Deciding not to take part or deciding to leave the study later will not result in any penalty or any loss of benefits to which you are entitled. If you decide to stop participating in the study, your doctor will discuss other options with you and continue to treat you with the best means available.

Immune responses directed against tumours are one of the body's natural defenses against the growth and spread of cancer cells. However, over time cancers develop strategies to evade these responses allowing them to grow and spread.

MEDI4736 is a new type of drug for lung cancer. Laboratory tests show that MEDI4736 works by preventing one of the ways that cancer may be using to avoid detection from the immune system (PD-1 and PD-L1 interaction). By preventing this interaction and reactivating the immune response this may help to slow down the growth of lung cancer or may cause cancer cells to die.

Health Canada, the regulatory body that oversees the use of drugs in Canada, has not approved the sale or use of MEDI4736 to treat this kind and/or stage of cancer, although they have allowed its use in this study. The research ethics board, who oversees the ethical conduct of research involving humans in your hospital/clinic, has reviewed and accepted this study.

PURPOSE

The purpose of this study is to find out whether it is better to receive a new drug, MEDI4736, or better to receive no further treatment after surgery (and possibly chemotherapy) for lung cancer. To do this, two-thirds of the participants in this study will get MEDI4736 and the other third will receive a placebo (a substance that looks like the study drug but does not contain an active drug).

This research is being done because there is currently no standard treatment for patients with this type of lung cancer who have already had their cancer removed with surgery (and possibly followed by chemotherapy).

MEDI4736 has been shown to shrink tumours in animals and has been studied in a few people and seems promising but it is not clear if it can offer better results than no further treatment.

The standard or usual treatment at this Centre for your disease is treatment with *[describe the standard treatment]*.

Note to centre, please adjust this section to reflect standard or usual treatment in accordance with your local policy.

ALTERNATIVE TREATMENTS

You do not have to take part in this study in order to receive treatment/care; other options may include, but are not limited to:

- no therapy at this time
- other experimental studies may be available if you do not take part in this study

Please talk to your study doctor or usual cancer doctor (if different from the study doctor) about the known benefits and risks of these other options before you decide to take part in this study. Your cancer doctor can also discuss with you what will happen if you decide not to undertake any treatment at this time.

EXPECTED NUMBER OF PARTICIPANTS

About 1,360 people from Canada, France, Australia and other countries will take part in this study.

This study should take 3 years to complete accruing participants. Early results may be known in about 6 years and final results will be known in about 10-11 years.

Your study doctor will be informed of the results of this study once they are known.

ASSIGNMENT TO A GROUP

If you decide to participate in this study you will first be registered to the study and then randomized to a treatment group.

Registration (entering the study):

If you decide to participate then you will be registered to the study. At that time, blocks of tissue from the cancer (and the area around it) that was removed at the time of your surgery will be sent to a central laboratory to test your “PD-L1 status” (amount of this PD-L1 protein in your cancer tissue). The PD-L1 test is investigational and its performance in identifying patients who respond to the investigational therapies has not yet been established. Regardless of your PD-L1 status, you will be able to be enrolled in the study providing the results are available to CCTG prior to the randomization (neither you nor your doctor will be told what the results are).

Randomization (assignment to a group):

You will be "randomized" into one of the groups described below. Randomization means that you are put into a group by chance (like flipping a coin). There is no way to predict which group you will be assigned to. You will have a two in three chance (67%) of being assigned to the MEDI4736 treatment group and a one in three chance (33%) of being placed in the placebo group. Neither you nor your doctor can choose what group you will be in.

This is a double-blind study, which means that neither you nor your doctor will know if you are receiving MEDI4736 or placebo. Your experimental treatment will be identified (a process called unblinding) if medically necessary. Requests to unblind your experimental treatment for your information or participation in other clinical trials will not be considered until this study has been completed and the results from the final analysis are known and the trial is unblinded. However, in the event that it is necessary in the future to know what treatment you received in order to determine whether you qualify for an approved, standard-of-care therapy, then on request by your physician you may be provided with this information.

Group 1 (EXPERIMENTAL TREATMENT): *MEDI4736*

If you are randomized to Group 1 you will receive the experimental drug MEDI4736. This drug will be given into one of your veins by needle once every 28 days for up to 13 treatments over a one year period. The procedure will take about 1 hour. If you have side effects, a scheduled dose may be skipped before continuing with your treatment.

Group 2 (NON-EXPERIMENTAL TREATMENT): *Placebo*

If you are randomized to Group 2 you will receive a placebo (a substance that looks like the study drug but does not contain an active drug). This placebo will be given by needle into one of your veins once every 28 days for up to 13 treatments over a one year period. The procedure will take about 1 hour. If you have side effects, a scheduled dose may be skipped before continuing with your treatment.

Treatment(s)	Route	Length of Time	Dose and Schedule*
MEDI4736 or placebo	IV (intravenous)	60 minutes	**20mg/kg**** on weeks 0, 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, and 48

* From randomization to one calendar year taken from the date of the first dose. No further doses after one calendar year from the date of the first dose even if all doses described in protocol have not been received.

** Four week minimum interval between doses must be maintained; if dose cannot be administered it should be omitted until the next planned dose

NON-EXPERIMENTAL PROCEDURES (Screening Procedures)

The following tests will be done at the hospital or clinic to make sure that you are eligible for this study:

Some of these tests may have been done as part of your standard care, in which case the results of those tests may be used.

- blood tests
- physical examination
- pregnancy test (for women who may become pregnant)
- magnetic resonance imaging (MRI) – a scan that uses a strong magnet to produce pictures of areas inside the body such as organs and other tissue, and inside of bones.
- computed tomography (CT) scan- a series of x-rays of the body from many angles that are turned into 3-dimensional pictures on a screen. CT scans often involve injecting a dye into your vein.
- ECG – electrocardiogram of your heart

- positron emission tomography (PET) – a scan to help show how organs and tissues are working by tracing where a small amount of glucose (a sugar) that includes a tiny, harmless amount of radioactivity, goes in your body after it has been injected into one of your veins.
- lung function tests
- possible insertion of a central venous catheter (also called central venous line, central line or central catheter). This is a small tube attached to a needle which is inserted into a large vein (in the neck, chest or groin) that leads to the heart. It allows easy access to veins for taking blood and giving medications and transfusions through the small tube so that you do not need a needle poke each time.
- a special x-ray to study the heart (MUGA or ECHO)

You may have received a summary of how frequently you would have clinic visits. The timing of these planned procedures or visits may have changed or may change in the future. Some visits may happen over the phone or video conference or with your family doctor.

Some of the tests that you undergo as part of this protocol may be missed, rescheduled or done at other hospitals or laboratories, or may not be done. There may also be changes to your treatment schedule as well as where and how you receive your study drug. We will also collect information about screening you may have for COVID-19.

The study team will let you know if changes are required and will make changes if it is safe to do so.

Many of these tests will also be repeated during the study. Some of these tests may be done more frequently than if you were not taking part in this study. The pregnancy test, lung function tests, ECG and urine test are done to participate in this trial and might otherwise not be done.

Experimental Procedures and Medical Tests:

The following test is considered experimental and will only be done for participants on this study:

- lung function tests

QUESTIONNAIRES

You will be provided with each questionnaire before starting this study, and while on study. If you speak or read one of the languages the questionnaires are available in and you are physically able to complete the questionnaire, you must do so to be enrolled in the study.

The information you provide is for research purposes only and will remain strictly confidential.

Some of the questions are personal; you can choose not to answer these if you wish. The individuals (e.g. doctors, nurses, etc.) who are not involved in the study will not review your responses to these questions—if you wish them to know this information please bring it to their attention.

Quality of Life (QoL):
You will be asked to complete a questionnaire before starting the study.

You will also be asked to fill out this questionnaire while you are receiving treatment (4, 12, 24, 36 and 48 weeks from randomization) and then every 12 weeks when you are finished your treatment until 2 years from randomization, unless your cancer comes back or you develop a new cancer. The purpose of the questionnaire is to understand how your treatment and illness affects your quality of life. Each questionnaire will take about 10 minutes to complete.

Patient Preferences Questionnaire:
You will be asked to complete a questionnaire before starting the study.

You will also be asked to fill out this questionnaire at your second follow up visit after you stop treatment (12 weeks after your last treatment). The purpose of the questionnaire is to understand what benefits you judge are necessary to make this treatment worthwhile and to understand what influences your preferences. The questionnaire will take about 10 minutes to complete.

Health Utilities Index:
You will be asked to complete a questionnaire about your overall health before starting the study.

You will also be asked to fill out this questionnaire while you are receiving treatment (4, 12, 24, 36 and 48 weeks from randomization) and then every 12 weeks when you are finished your treatment until 2 years from randomization. If your cancer comes back or you develop a new cancer, you will be asked to fill out the questionnaire at your next visit and then additional questionnaires will no longer be required. The questionnaire will take about 10 minutes to complete.

ECONOMIC ANALYSIS INFORMATION COLLECTION

You will be asked information on health care resources used in your care. The aim of this is to assess the costs of this new treatment (MEDI4736) compared to no active treatment (placebo) compared to any benefits (such as QoL).

You will be asked for this information while you are receiving treatment (at each visit) and then at each follow up visit. However, if your cancer comes back or you develop a new cancer, you will be asked these questions at the time of your next visit and then they will no longer be required.

MANDATORY SAMPLE COLLECTION

The researchers doing this study need to do tests on samples (described below) to find out whether levels of PD-L1 protein in your cancer sample are related to your response to treatment on this protocol. The tests also will help to understand more about non-small cell lung cancer, and to look for markers that will help predict which patients are most likely to be helped by the study drug, MEDI4736. We do not plan hereditary genetic testing (to find out if cancer runs in your family) on these samples.

The collection of theses samples is a necessary part of this study and will be used only for these purposes. The samples will not be sold. Once these tests have been completed, any leftover samples will be returned to the facility from which they were obtained if needed or destroyed, unless you wish to give permission for other future research purposes, in which case you will be given a separate optional consent form to sign.

Reports about any research tests done with your samples will not be given to you or your oncologist, or family doctor. These reports will not be put in your medical records.

Tissue Collection (Required)

A small sample of your tumour and other tissue that has already been removed by a previous surgery or biopsy will be obtained by the researchers doing this study. No further surgeries or biopsies are required of you for this purpose.

NOTE to participating centres outside of North America: please revise this information as per the Protocol and Patient Enrollment and Tissue Submission Manual and your country requirements.

These tissue samples will be sent to two different places:

- The tissue samples will first be sent to a laboratory at Clarient Diagnostic Services Inc., A NeoGenomics Company, Aliso Viejo, California, USA to find out how much of the PD-L1 protein is in your cancer specimen. Other labs may also be set up for other countries/regions to send their samples to.
- Once you have been successfully randomized to the trial, the samples will be sent to a laboratory at the Canadian Cancer Trials Group in Kingston, Ontario, Canada (with the exception of samples from France which will be sent to the IFCT Repository) and then sent to a research laboratory for further tests, including the search for markers that will help predict how patients respond to treatment. If you are not randomized to the trial, your tissue samples will be returned.

Blood Collection (Required)

Blood samples will be taken by inserting a needle into a vein in your arm. These will be taken at the same time as your study related tests whenever possible e.g. at entry to the study, at the time you stop study treatment and if your cancer comes back or you develop a new cancer (after you have stopped study treatment). For all patients, approximately three tubes of blood (approximately 25 ml or 5 teaspoons total) will be collected at each of these times. Patients in selected countries will also have additional samples taken prior to the first, second and seventh cycle of treatment and approximately 90 days post last dose of treatment. One to two tubes will be taken at each time point (approximately 5 ml or 1 teaspoon).

NOTE to participating centres outside of North America: please revise this information as per the Protocol and Correlative Studies Manual and your country requirements.

These blood samples will be sent to a laboratory at the Canadian Cancer Trials Group in Kingston, Ontario, Canada (with the exception of samples from France which will be sent to the IFCT Repository), then sent to a research laboratory where they will be examined for several reasons, including finding out how the immune system responds to the study drug, MEDI4736.

Confidentiality of Samples

To protect your identity, the information that will be on your samples will be limited to study code, patient identification number, pathology specimen number and may include your initials.

Withdrawal of Required Samples

If you no longer want your samples to be used in this research, you should tell your study doctor. Your study doctor will notify the sponsor who will ensure the samples are returned to the hospital from which they were obtained if needed, or destroyed. If tests have already been done on your sample(s) it will not be possible to withdraw those results. The tissue samples that will be tested to see how much PD-L1 protein is in your cancer specimen cannot be returned or destroyed after the PD-L1 testing is done (done between registration and randomization). Once you request that your samples be withdrawn, no further testing will be done on any of them.

The submission of samples is a requirement to join the study, however if you withdraw these samples at a later date you may still continue to participate in the study.

Optional Sample Collection and Banking

The researchers doing this study are interested in doing additional research now or in the future on the samples collected from you. You will be given an additional optional study consent form to read and sign if you wish to give permission for the samples to be banked (stored) for future research purposes. You may decide not to participate in the "optional" study and still participate in this main study.

RESPONSIBILITIES

If you choose to participate in this study, you will be expected to:

- Tell your study doctor about your current medical conditions;
- Tell your study doctor about all prescription and non-prescription medications and supplements, including vitamins and herbals, and check with your study doctor before starting, stopping or changing any of these. This is for your safety as these may interact with the treatment you receive on this study. Tell your study doctor if you are thinking about participating on another research study
- Return any questionnaires to the study doctor that you take home to complete
- Tell your study doctor if you become pregnant or father a child while participating on this study

LENGTH OF PARTICIPATION

Your treatment with MEDI4736 will last for about 12 months if you are randomized to Group 1 (Experimental Treatment). If you are randomized to Group 2 (Non-Experimental Treatment) your treatment will last for about 12 months as well.

***Note to centres**: Centres should indicate the overall length of time required beyond that of the standard or usual care at the Centre - specifying the difference in the number of visits and the length of time for each visit plus the time needed to complete questionnaires or diaries.*

No matter which group you are randomized to, and even if you stop treatment early, we would like to keep track of your health for the rest of your life to look at the long-term effects of your participation on this study.

EARLY END TO PARTICIPATION

The researchers can take you off the study treatment early for reasons such as:

- The treatment does not work for you and your cancer comes back or you develop a new cancer.
- You are unable to tolerate the study treatment.
- New information shows that the study treatment is no longer in your best interest.
- Your doctor no longer feels this is the best treatment for you.
- The CCTG decides to stop the study
- If you become pregnant

RISKS OF PARTICIPATION

Participating in this study will put you at risk for the side effects listed below. You should discuss these with your doctor. As with any experimental drug additional unexpected and sometimes serious side effects are a possibility.

Your doctor will watch you closely to see if you have side effects. When possible, other drugs will be given to you to make side effects less serious and more tolerable. You may need treatment with high doses of drugs called steroids to help with the side effects. You may need replacement treatment with hormones (such as thyroid replacement, cortisol replacement or insulin) if MEDI4736 has effects on your hormone glands as listed below. Many side effects go away shortly after treatment is stopped but in some cases side effects can be serious, long-lasting, permanent, or may even cause death.

In addition to the risks identified for patients treated with MEDI4736 other immune-related side effects are possible. These side effects can result in inflammation in any organ or tissue and are related to how the drug works. While stimulating your body's immune response to help fight cancer, this drug may also cause the immune system to attack normal organs and tissues in many areas of your body (such as heart and kidney, eyes, skin, joints), affecting the way they work. These "immune-related" side effects can sometimes be serious or life threatening.

If you experience serious side effects that require treatment between regular clinic/hospital visits, it is very important that you contact or return to the clinic/hospital where MEDI4736/placebo was given. Because MEDI4736/placebo is an experimental drug and is only used in clinics/hospitals involved in research studies, any serious side effects of the drug may be best treated by these clinics/hospitals. If you need immediate treatment and are unable to return to the clinic/hospital where MEDI4736/placebo was given, you should go to the nearest medical clinic/hospital and tell them that your study doctor should be contacted as soon as possible.

Your safety is our first priority, and the risks and benefits of continuing on this study during COVID-19 will be discussed with you. If you experience any side effects, including fever or other signs of infection, please contact your study team as soon as possible.

Your study doctor will discuss any additional risks or changes to your treatment with you.

Risks and side effects related to the experimental drug MEDI4736 we are studying include:

Very likely (21% or more, or more than 20 people in 100):
- fatigue/tiredness
- decreased or loss of appetite, which may result in weight loss
- cough
- inflammation of the small intestine and /or large bowel causing abdominal pain and diarrhea which may be severe and life threatening

Less likely (5 – 20% or between 5 and 20 people in 100):
- pain and/or inflammation in various areas including muscles, joint, belly, back, chest; headache
- flu-like symptoms such as body aches, fever, chills, tiredness, loss of appetite, cough
- constipation
- dizziness
- shortness of breath
- infection, which may rarely be serious and become life threatening
- nausea and vomiting
- dehydration
- skin inflammation, redness or rash which may include hives or blistering, and may rarely be severe and/or life threatening
- anemia which may cause tiredness, or may require blood transfusion
- itching
- abnormal liver function seen by blood tests. This can be caused by inflammation of the liver or the bile ducts and may rarely lead to abdominal pain, jaundice (yellowing of the skin and whites of eyes) and be severe or life threatening.
- abnormal function of your thyroid gland which cause changes in hormonal levels. A decrease in thyroid function as seen on blood tests may cause you to feel tired, cold or gain weight while an increase in thyroid function may cause you to feel shaky, have a fast pulse or lose weight.
- swelling of arms and/or legs (fluid retention)

- changes in the level of body salts as seen on blood tests which may or may not cause you to feel symptoms
- inflammation of the pancreas that results in increased level of digestive enzymes (lipase, amylase) seen in blood tests and may cause abdominal pain
- inflammation of the lungs (including fluid in the lungs) which could cause shortness of breath, chest pain, new or worse cough. It could be serious and/or life threatening. May occur more frequently if you are receiving radiation treatment to your chest or if you are Japanese.
- decrease of a protein in your blood called albumin that may cause fluid retention and results in swelling of your legs or arms
- elevated level of sugar (glucose) in the blood which may cause increased thirst, increased urination, weight loss and fatigue and may be caused by new or worsening type 1 diabetes and require insulin treatment. In rare cases, type 1 diabetes may present as a serious condition with high levels of acids (ketones) in your blood and with the additional following symptoms that may include nausea, vomiting, belly pain, tiredness, shortness of breath, fruity-scented breath, and confusion.

Rarely (1 – 4% or less than 5 in 100 people):

- change in hormonal levels which may be due to inflammation in your hormone glands. This may lead to abnormal (usually low) function of your pituitary gland, adrenal and other glands (such as ovaries or testes) which cause changes in hormonal levels. A decrease in hormonal levels may cause you to feel tired, cold, dizzy, have low blood pressure, hot flashes or have weight changes. You may also have headache and vision changes. Very rarely, you may have increased thirst and need to urinate more often.
- changes to the heart, including inflammation to the heart muscle (myocarditis). Symptoms can include chest pain, rapid or abnormal heart beat, shortness of breath and swelling of your legs. **Tell your study doctor right away if you experience any of these symptoms.**
- blood clots in veins which could cause new swelling in the arms or legs or could cause sudden breathing problems and be life threatening if the clot moves to the lungs. Blood clots may also form in the arteries, for example in your brain, heart or limbs which may reduce blood flow and lead to stroke, heart attack or pain in your limbs.
- decreased blood platelets (thrombocytopenia) makes it harder for blood to clot, and can cause you to bruise or bleed easily and may require you to have a blood transfusion. Rarely, bleeding can occur in your lungs (causing you to cough up blood) or in your intestine (which may cause vomiting of blood and black bowel movements).
- increased blood platelets which may cause increased clotting or blockage of your arteries or veins
- low blood pressure (hypotension) which may cause feeling faint
- high blood pressure (hypertension) which may cause headaches, dizziness, blurred vision
- changes in the levels of white blood cells (cells that fight infection) as seen on blood tests. This may or may not cause you to have symptoms. When your number of white blood cells are low, you are at risk of infections that might be serious and life threatening. Your doctor will explain to you what to do if this happens.
- changes in kidney function which may lead to changes in blood tests and protein in your urine and if severe (rarely), decreased urine output and fatigue. This may be life threatening.
- reaction during or following infusion of the drug which may cause fever, chills, rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat. The reaction could be serious or life threatening.

- confusion
- depression
- dry skin
- night sweats
- inflammation of the stomach lining which may cause stomach pain, heartburn
- passing gas
- difficulty sleeping
- runny nose
- redness and pain around lips and/or sores (may be creamy white) in mouth and/or throat which may cause difficulty swallowing; infections in mouth and teeth
- muscle weakness and soreness/tenderness which may rarely be secondary to inflammatory disease/condition and unexplained injury. Symptoms may include muscle cramps, pain, tenderness, stiffness, weakness, spasm or dark urine. This may be early signs of a rare muscle problem (rhabdomyolysis) that could lead to serious kidney problems.
- numbness or tingling in the hands or feet which may be associated with muscle weakness in the arms or legs. Rarely this may spread to the chest and body and lead to problems with breathing which can become life-threatening.
- fluid around the heart or the lungs which may cause chest pain, cough, fever, tiredness, shortness of breath, hiccups
- skin irritation (including itchiness, redness, pain, swelling and possibly infection) if the drug leaks from the vein into the surrounding skin near the injection site
- change in the sound of your voice (hoarseness)
- inflammation of the urinary bladder. Symptoms may include frequent, painful urination
- discoloured (usually lighter) skin patches
- skin changes such as thickening of the skin
- decrease in blood sugar that can make you feel hungry, sweaty, weak or shaky

Very Rare (less than 1% or less than 1 person in 100):

- angiopathy- disease of the blood vessels (arteries, veins and capillaries) causing changes such as thickening of the walls of blood vessels
- choroidal effusion – increased fluid in the part of the eye between the retina and the white covering which may cause sudden eye pain and vision loss
- blockage, tear or hole in the bowel/intestines which may cause abdominal pain, vomiting and may require surgery and could be life threatening
- inflammation of the brain which may cause headache, fever, confusion

It is possible that other drugs (prescription and non-prescription drugs), vitamins, or herbals can interact with the drugs used in this study. This can result in either the drugs not working as expected or result in severe side effects.

Long term effects of the treatment or tests (for example X-rays) used in this study include an increased risk of developing other cancers.

Some cancer treatments such as chemotherapy or other drugs may slightly increase the risk of blood clots in your veins. Please tell your doctor if you have any new swelling in a leg or arm or have a sudden problem with your breathing. These may be signs of a clot forming or a clot moving to your lungs. Clots can be treated with blood thinners. If you experience any of these symptoms you should go to the nearest medical clinic or hospital and contact your study doctor as soon as possible.

A Data Safety Monitoring Board, an independent group of experts, will be reviewing the data from this research throughout the study.

REPRODUCTIVE RISKS

The effects that MEDI4736 may have on an unborn baby (fetus), nursing a baby, your ability to have children in the future and other reproductive issues are unknown. You should discuss these issues with your study doctor.

The effects that MEDI4736 may have on an unborn baby (fetus) are unknown. You must not become pregnant or father a baby while taking MEDI4736 and for 90 days after the last dose. Your study doctor will discuss methods with you to ensure that you do not become pregnant or father a baby during the study.

Women should not nurse (breastfeed) a baby while taking study treatment and for 90 days after the last dose because the drugs used in this study might be present in breast milk and could be harmful to a baby.

If you become pregnant or father a child during this study or for 90 days after you stop taking the study drug, then you should immediately notify your study doctor. Your study doctor will let the sponsor know about the pregnancy.

If you become pregnant, the researchers or sponsors for this study will access information on the outcome of the pregnancy (the child's health etc.). This information will be gathered from your medical/study record. This may also involve contacting you to ask about the health of your child. We may also ask to contact the child's father to get information related to the pregnancy. If you become pregnant and do not want the researchers/sponsors to collect this information, you must let your study doctor know.

If you father a child, the researchers or sponsor for this study will ask to contact the child's mother to collect information on the outcome of the pregnancy (the child's health, etc.). Your partner will be given a separate consent document to sign to give permission for the collection of this information, if a pregnancy should happen.

If you nurse (breastfeed) a child while you are on this study or for 90 days after you stop taking the study drug, you should immediately notify your study doctor. Your study doctor will let the sponsor know. The researchers for this study will then access information on the health of the child. This information may be gathered from your or your child's medical/study record. This may also involve contacting you for the next 90 days to ask about the health of your child. If you breastfeed a child and do not want the researchers to collect this information, you must let your study doctor know.

BENEFITS

If you agree to take part in this study, there may or may not be direct benefit to you. We hope the information learned from this study will help other patients in the future. However, you are not expected to benefit if you are randomized to receive a placebo only.

CONFIDENTIALITY

Records identifying you at this centre will be kept confidential and, to the extent permitted by the applicable laws, will not be disclosed or made publicly available, except as described in this consent document.

Qualified representatives of the following organizations may look at your original (identifiable) medical/clinical study records at the site where these records are held, for quality assurance (to check that the information collected for the study is correct and follows proper laws and guidelines).

- Canadian Cancer Trials Group (CCTG), the research group coordinating this study
- The research ethics board who oversees the ethical conduct of this study in your hospital/clinic
- The company or organization (AstraZeneca) which makes the drug MEDI4736
- U.S. Food and Drug Administration (because they oversee the use of drugs in the U.S.)
- Health Canada (because they oversee the use of drugs in Canada)
- Other regulatory authorities (because they oversee the use of drugs in other countries)

Qualified representatives of the following organizations, in addition to those listed above, may receive information related to the study from your medical/clinical study records, containing your participant code, initials, sex, and date of birth, for quality assurance and data analysis. Copies of medical reports and tests you undergo may be collected for the purposes of the study as the information could help the researchers understand how you tolerate the study treatment, any side effects you may have or your response to the treatment. These medical reports could include notes from your doctor/nurse or the study team, images, blood or urine tests, tissue samples or reports about a surgery or other procedures you may have. Your name or other information that may identify you will not be used.

NOTE to participating centres outside of North America: please revise this information as per the Protocol and Patient Enrollment and Tissue Submission Manual and your country requirements.

- Central laboratories located in Aliso Viejo, California, USA and elsewhere

Note to centres: *If there is planned disclosure of personal identifiers, or if they are used on any research-related information/documents, or if they are part of the unique identifier, this must be justified in the REB application and approved. Please ensure that you are aware of your local REB's and your centre's policies with respect to the disclosure of personal identifiers; specifically date of birth and initials. If the REB or the centre mandates the disclosure only of partial date of birth (year/month), and/or of scrambled/coded initials, this will be accepted by CCTG.*

Studies involving humans now routinely collect information on race and ethnicity as well as other characteristics of individuals because these characteristics may influence how people respond to different medications. Providing information on your race or ethnic origin is voluntary.

Your name or other information that may identify you will not be used.

To ensure your safety, clinical trials are usually monitored at your centre by the group overseeing the trial to make sure the protocol is followed and side effects are reported. Because of COVID-19, the group overseeing this trial cannot visit the centre where you are being treated. Copies of some documents such as scan reports are already being collected, but more, such as copies of laboratory reports and clinic reports, may now be collected as part of this study and reviewed by researchers in Canada. The copies will be kept until the end of the study monitoring period when they will be destroyed. To protect your identity, the information that will be on these documents will be limited to your participant study code and initials.

If the results of this study are published, your identity will remain confidential. It is expected that the information collected during this study will be used in analyses and will be published/ presented to the scientific community at meetings and in journals. This information may also be used as part of a submission to regulatory authorities around the world to support the approval of drugs used in this research.

All of the organizations listed in the above confidentiality sections are required to have strict policies and procedures to keep the information they see or receive about you confidential, except where disclosure may be required by law. The study doctor will ensure that any personal health information collected for this study is kept in a secure and confidential location as required by law. There are federal and provincial laws that these organizations must comply with to protect your privacy.

Your study records also will be stored for future use. However, your name and other personal information will not be used. Some types of future research may include looking at your records and those of other patients to see who had side effects across many studies or comparing new study data with other study data. However, we don’t know what research may be done in the future using your information. This means that:

- You will not be asked if you agree to take part in the specific future research studies using your health information.
- You and your study doctor will not be told when or what type of research will be done.
- You will not get reports or other information about any research that is done using your information.

Even though the likelihood that someone may identify you from the study data is very small, it can never be completely eliminated.

A copy of the consent form that you sign to enter the study may be included in your health record/hospital chart.

Your family doctor /health care provider will be informed that you are taking part in a study so that you can be provided with appropriate medical care. If you do not want your family doctor/health care provider to be informed, please discuss with your study doctor.

Any information and/or samples, sent outside of Canadian borders may increase the risk of disclosure of information because the laws in those countries dealing with protection of information may not be as strict as in Canada. However, all study data and/or samples, that is transferred outside of Canada will be coded (this means it will not contain your personal identifying information such as your name, address, medical health number or contact information). Any information will be transferred in compliance with all relevant Canadian privacy laws. By signing this consent form, you are consenting to the disclosure of your coded information to organizations located outside of Canada.

Because this is a study that also falls under U.S. regulation, in some circumstances the U.S. Food and Drug Administration (US FDA) may seek to copy records that contain your personal identifying information. If this occurs, you will be informed before the records are copied, but a separate consent may not be sought from you. You should be aware that privacy protections on personal information may differ in other countries.

Registration of Clinical Trials

A description of this clinical trial will be available on http://www.clinicaltrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

COSTS

The study drug, MEDI4736/placebo, will be given to you free of charge unless the following occurs:

- You stop participating on this study.
- The study closes

Your study doctor will discuss these options with you, as well what will happen if there is no more drug available.

The costs of your medical treatment will be paid for by your provincial medical plan to the extent that such coverage is available. There may be extra costs that are not covered by your medical plan that you will have to pay yourself, some examples may be physiotherapy or certain pain medications.

Taking part in this study may result in added costs to you (i.e. transportation, parking, meals, or unpaid leave from work). You may have to pay for medication prescribed to treat or prevent side effects, and you may have to visit the hospital more often than if you were not participating in this study. Please talk to your study doctor or research staff about the possibility of reimbursement for certain expenses related to research visits.

COMPENSATION

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

It is possible that the research conducted using your samples and/or study data may eventually lead to the development of new diagnostic tests, new drugs or other commercial products. There are no plans to provide payment to you if this happens.

In the case of research-related side effects or injury, medical care will be provided by your doctor or you will be referred for appropriate medical care.

Although no funds have been set aside to compensate you in the event of injury or illness related to the study treatment or procedures, you do not give up any of your legal rights for compensation by signing this form. This consent form does not relieve the investigator, the hospital, the sponsor, and their agents from their legal and professional responsibilities.

RIGHTS

If you decide to stop participating in the study, your doctor will discuss other options with you and continue to treat you with the best means available.

You will be told, in a timely manner, about new information that may be relevant to your willingness to stay in this study.

You may withdraw your permission to use your personal health information for this study at any time by letting the study doctor know. However, this would also mean that you withdraw from the study. Your study data that was recorded before you withdrew will be used but no information will be collected or sent to the sponsor after you withdraw your permission. You may withdraw your permission to use any samples collected for the study at any time by letting the study doctor know. The results from any tests that have already been done on the samples will still be used but no further tests will be done and the samples will be returned to the facility from which they were obtained if needed, or destroyed.

Your rights to privacy are legally protected by federal and provincial laws that require safeguards to ensure that your privacy is respected.

By signing this form you do not give up any of your legal rights against the investigators, sponsor or involved institutions for compensation, nor does this form relieve the investigators, sponsor or involved institutions of their legal and professional responsibilities.

You will be given a copy of this signed and dated consent form prior to participating in this study.

CONFLICT OF INTEREST

Note to centres: Please include details of any actual or potential conflict of interest concerning this study.

This centre is receiving funds from the Canadian Cancer Trials Group to help offset the costs of conducting this research. CCTG is a non-profit research group based on donated support. The researchers, this centre, and the CCTG will not receive any direct benefit for conducting this study.

CONTACTS

If you have questions about taking part in this study, or if you suffer a research-related injury, you should talk to your study doctor. Or, you can meet with the doctor who is in charge of the study at this institution. That person is:

Name	Telephone

If you have questions about your rights as a participant or about ethical issues related to this study, you can talk to someone who is not involved in the study at all. That person is:

Name	Telephone

SIGNATURES

- All of my questions related to the consent form and appendix have been answered,
- I understand the information within this informed consent form and appendix,
- I allow access to my medical records and specimens and transfer of my personal information as explained in this consent form and appendix,
- I do not give up any of my legal rights by signing this consent form and appendix,
- I agree to take part in this study.

Signature of Participant	Printed Name	Date
Signature of Person Conducting the Consent Discussion	Printed Name	Date

Participant Assistance

Complete the following declaration only if the participant is unable to read:

- The informed consent form and appendix were accurately explained to, and apparently understood by, the participant, and,
- Informed consent was freely given by the participant.

Signature of Impartial Witness	Printed Name	Date

Complete the following declaration only if the participant has limited proficiency in the language in which the consent form and appendix are written and interpretation was provided as follows:

- The informed consent discussion was interpreted by an interpreter, and,
- A sight translation of this document including the appendix was provided by the interpreter as directed by the research staff conducting the consent.

Interpreter declaration and signature:

By signing the consent form I attest that I provided a faithful interpretation for the discussion that took place in my presence, and provided a sight translation of this document and appendix as directed by the research staff conducting the consent.

Signature of Interpreter	Printed Name	Date

Version date and/or REB approval date of this form: _____

Appendix 1: General Data Protection Regulation (GDPR) Privacy & Confidentiality

Who is responsible?

The Canadian Cancer Trials Group (CCTG) is the global sponsor of this study and is based in Kingston, Ontario, Canada at Queen's University. The study database, which contains the study records is located in Kingston, Ontario, Canada. CCTG and delegates will comply with the European Union General Data Protection Regulation (GDPR).

What personal information will be collected and used?

Participating in this study requires your personal information to be collected, retained and analyzed. This is essential to the study. The purpose of collecting your personal information is for scientific research. The study team may collect information about your health, race/ethnicity, biometric (such as fingerprints or an image to identify you) and genetic information. It is possible some information may be related to your political opinion, religious or philosophical belief, union membership, sex life or sexual orientation. You do not have to participate in this study to receive medical care. To protect your identity, the personal information collected about you is limited to your initials (or a two/three letter code), a participant study code, a code to track biological samples, your date of birth and sex. The information stored about you will be coded, which means that it will not contain identifying information such as your name, address, health card number, or phone number. Anyone looking at the data will not be able to identify you. If the results of this study are published, your identity will remain confidential. Even though the likelihood that someone may identify you from the study data is very small, it can never be completely eliminated.

Copies of medical reports and tests you undergo may be collected for the purposes of the study as the information could help the researchers understand how you tolerate the study treatment and any side effects you may have. These medical reports could include notes from your doctor/nurse or the study team, images, blood or urine tests, tissue samples or reports about a surgery or other procedures you may have.

Who will see my personal information?

Authorized representatives of CCTG may receive coded information or medical reports and tests from your medical or study records for quality assurance or data analysis purposes. Some of these organizations will be outside of Canada. These organizations may include:

- Canadian Cancer Trials Group (CCTG), the research group coordinating this study;
- The research ethics board who oversees the ethical conduct of this study in your hospital/clinic;
- The company or organization (AstraZeneca) which makes the drug MEDI4736;
- U.S. Food and Drug Administration (because they oversee the use of drugs in the U.S.);

- Health Canada (because they oversee the use of drugs in Canada);
- Other regulatory authorities (because they oversee the use of drugs in other countries);

NOTE to participating centres outside of North America: please revise this information as per the Protocol and Patient Enrollment and Tissue Submission Manual and your country requirements.

- Central laboratories located in Aliso Viejo, California, USA and elsewhere

Some of the above listed organizations are located outside of the European Union, the European Economic Area, and Canada (which the European Commission found to have adequate data protection laws). These may include the United States. Any of your personal information and/or samples sent outside of European Union or Canadian borders may increase the risk of disclosure of information. This may be the case if laws in other countries are not as strict, if they don't give you the same rights or if your ability to pursue legal action is limited. For example, laws in the United States permit authorities to access your personal data. However, all study data and/or samples that are transferred outside of Canada or the European Union will be coded. Any information will be transferred in compliance with all relevant privacy laws, and in some cases in accordance with agreements between the organizations. An updated list of those responsible for your personal information, including laboratories, is available, along with their locations. This list may be provided by your study doctor at your request. Your study records may be stored and shared for future use.

Some types of future research may include looking at your information and information from other participants to see who had side effects across many studies or comparing new study data with other study data. However, right now we don't know what research may be done in the future using your information. This means that:

1. You will not be asked if you agree to take part in the specific future research studies using your health information.
2. You and your study doctor will not be told when or what type of research will be done.
3. You will not get reports or other information about any research that is done using your information.

CCTG and delegates will keep copies of medical reports, tests and coded information about you for at least 25 years after the study has ended. Thereafter, CCTG and delegates will assess whether it will or can keep your data. This assessment will take into account applicable legislation, the relevance of your data for scientific research, the scope of your consent and the choices you made.

What are my rights?

- You can ask at any time about your personal information being stored, who has access and the purpose;
- You can request a copy of your personal information for your own use or to send to others in a commonly used format;
- You can correct the personal information you provided;

- You can request the deletion of your personal information;
- You can object to or limit the use of your personal information;
- You can object to a decision made about you based on automatic processing of your personal information.

At any time during the study you can decide to stop participating. This means that any personal information collected while you are participating will be retained but no further personal information will be collected about you after your decision to stop participating. Please speak to your study team if you want to stop participating in the study.

Your rights above may be limited if it:

- Limits CCTG and delegates to comply with obligations to ensure study participant safety and wellbeing;
- Impacts reliability and integrity of the study research;
- Significantly oversteps the rights of other study participants.

If you wish to ask about how CCTG and delegates handled your personal data, you should contact your study hospital (insert local contact details). This person will investigate further and may contact CCTG. You can contact the Office of Compliance and Oversight of CCTG. However, CCTG may not be able to reply in your language. If you are not satisfied or believe CCTG is using your personal data in a way that is not appropriate, you can contact the Data Protection authority in your country.

Who can I contact at CCTG?

The Office of Compliance and Oversight of CCTG at privacy@ctg.queensu.ca. You can write to "Office of Compliance and Oversight" care of CCTG at Queen's University, Kingston, Ontario, Canada, K7L 3N6.

You can also contact the main office of CCTG by writing to CCTG at Queen's University, Kingston, Ontario, Canada K7L 3N6.

SAMPLE -OPTIONAL - Informed Consent Form

A PHASE III PROSPECTIVE DOUBLE BLIND PLACEBO CONTROLLED RANDOMIZED STUDY OF ADJUVANT MEDI4736 IN COMPLETELY RESECTED NON-SMALL CELL LUNG CANCER

Trial Code: BR.31

Researcher: Dr. _____

Sponsor: Canadian Cancer Trials Group

Le formulaire de consentement est disponible en français sur demande.

Note to centre: If an REB approved French consent is not used at your institution you should remove the above statement.

Tissue and Blood Collection and Banking

Required tissue and blood collection: The researchers doing this study are interested in doing studies on tissue samples from your cancer to look for any markers in your cancer cells that might help predict which patients are most likely to be helped by the study drug MEDI4736. They are also interested in doing studies on your blood samples that have been collected during the study. These blood samples may help us understand who will benefit the most from this type of treatment. The collection of tissue samples from your lung cancer, that has already been removed by biopsy or surgery, as well as blood samples, is a necessary part of this study. Since you have agreed to take part in this study and have signed the main consent form, you have already consented to having your tissue and blood collected to find out how much of the PD-L1 protein is in your cancer sample, to understand more about non-small cell lung cancer, and to look for markers that will help predict which patients are most likely to be helped by the study drug, MEDI4736

Optional tissue and blood banking: The researchers doing this study are also interested in doing further research studies on tissue samples from your cancer specimen as well as your blood samples to better understand the nature of cancer and how patients respond to treatment. The research that may be done with your tissue or blood may not directly benefit you. It may help people in the future who have the same kind of cancer as you have. If you wish to support such research, you may choose to have your tissue and blood stored at a central tissue bank for use now or in the future. This storage of tissue and blood for future use is called “banking”. The “banking” of this tissue and blood is an optional part of this study. You may refuse to have your tissue and blood banked and still may take part in the main study. If you agree to have the tissue and blood (*left over from the required studies*) stored for future research, please read and sign this consent form, which deals specifically with tissue and blood banking for future research.

WHAT IS INVOLVED IN OPTIONAL TISSUE AND BLOOD BANKING?

If you agree to donate your tissue, the samples collected will be from your cancer and adjacent normal tissue that has already been removed by biopsy or surgery. No further surgeries or biopsies are needed for this purpose. If you agree to donate your blood samples for banking, they will be comprised of any blood samples that are remaining after the tests done as required by the main study have been completed. No further blood draws are required.

Any tissue collected will be stored at a central tissue bank (a facility where tissues are stored for future research) located at the Canadian Cancer Trials Group in Kingston (with the exception of samples from France which will be sent to the IFCT Repository), Ontario. The samples will be kept indefinitely, or until they are returned to the hospital where you had your surgery or biopsy. Tissue will be used for research purposes only and will not be sold. The research done with your tissue may or may not help develop commercial products or tests. There are no plans to provide payment to you if this happens.

Any blood samples collected will be stored at a central tissue bank (a facility where tissues, including tumours and blood, are stored for future research) located at the Canadian Cancer Trials Group in Kingston (with the exception of samples from France which will be sent to the IFCT Repository), Ontario. The samples will be kept until they are used up. The samples will be used for research purposes only and will not be sold. The research done with your samples may or may not help develop commercial products or tests. There are no plans to provide payment to you if this happens.

WHAT ARE YOUR RIGHTS AS A PARTICIPANT?

Taking part in the optional tissue and blood banking part of this study is voluntary. You may choose not to take part, or may at any time withdraw your consent for this portion of the study and ask that the collected tissue / blood samples not be used. Deciding not to take part, or deciding to withdraw your consent for this portion of the study later, will not result in any penalty or loss of benefits to which you are entitled. If you decide to stop participating, and no longer want your tissue / blood samples to be used in this research, you should tell your doctor. Your doctor will notify the Canadian Cancer Trials Group (CCTG) who will ensure the samples are destroyed *(if blood)* ***or*** returned to the hospital where you had your original biopsy or surgery *(if tumour block)*. If tests have already been done on your sample and included in an analysis or publication, it will not be possible to withdraw these.

All the information provided in the main study consent form about confidentiality, costs, your rights as a participant, and who to contact with questions, applies to this tissue/tumour collection and banking consent form as well.

HOW WILL THE IDENTITY OF MY SAMPLES BE PROTECTED?

The identification that will be on your tissue and blood samples kept in the bank may include your pathology identification number, initials and tumour bank code. Samples will be given only to researchers whose proposals have been approved by the Canadian Cancer Trials Group and who are bound by a confidentiality agreement. Any research done on your tissue will have been approved by a research ethics board. A research ethics board oversees the ethical conduct of a study, including protection of patient rights, confidentiality and safety. Tissue and blood used for research is identified only by a special code to protect your identity and privacy.

Reports about any research done with your samples will not be given to you or your doctor. These reports will not be put in your medical records. The research using your samples will not affect your care.

In the future, people who do research with your sample may need to know more about your health. While the researchers coordinating this study may give them reports about your health, they will not give them your name, address, phone number or any other information that will let them know who you are.

WILL GENETIC TESTING BE DONE ON MY TISSUE SAMPLES?

All cancers are caused by changes in our genes or by changes in when or how these genes are expressed. CCTG does not consider the study of changes in the genetic material of cancer cells to be “genetic research”, as these changes are acquired after you are born and not passed on in families. This type of testing may be done on your samples if you agree to allow your samples to be banked for future research.

Some changes in genes that are inherited may determine the way a person will respond to treatment. These changes may also determine what kind of side effects a person will have when they receive different kinds of treatment. These genetic changes do not cause cancer or other diseases and the study of these changes is not considered by the CCTG to be “genetic testing”. This type of testing may be done on your samples if you agree to allow your samples to be banked for future research.

Some cancers are a result of genetic changes that are inherited (passed on in families). Some genes that are inherited may determine a person’s chance of developing a particular disease, including cancer. Studies to look for these inherited genes that may cause cancer or other diseases are considered “genetic testing”. As part of future studies, researchers may want to study the genetic material that is inherited through families and that may cause cancer or other diseases. This type of testing may be done on your samples if you agree to allow your samples to be used for future “genetic testing”.

Participating in “genetic testing” (testing for inherited genes that may cause cancer or other diseases) can involve risks for participants and their families. If you are identified as belonging to a high-risk group for developing a specific disease it could affect employment, health or life insurance, or might alter decisions about having children. This is why “genetic testing” results are not given to you, they are not put into your medical records and every effort is made to protect the privacy and confidentiality of these results. The chance of genetic test results being released in a way that can be linked to you is very small, however you should be aware of the risks. If you do not wish to have your samples used for “genetic testing”, you may indicate your wish at the end of this consent form.

SIGNATURES

☐ I agree to allow tissue samples from my tumour with adjacent normal tissue which were already collected based on my consent to participate in the trial, to be banked for the purposes described here.

☐ I do not agree to allow tissue samples from my tumour with adjacent normal tissue to be banked for the purposes described here.

☐ I agree to allow blood samples to be banked for the purposes described here.

☐ I do not agree to allow blood samples to be banked for the purposes described here.

☐ I agree to allow my samples to be used for genetic testing to see if my cancer may be hereditary.

☐ I do not agree to allow my samples to be used for genetic testing to see if my cancer may be hereditary.

PLEASE CHECK THE APPROPRIATE BOXES ABOVE BEFORE SIGNING

Signature of Participant	Printed Name	Date
Signature of Person Conducting the Consent Discussion	Printed Name	Date

Participant Assistance

Complete the following declaration only if the participant is unable to read:

- The informed consent form was accurately explained to, and apparently understood by, the participant, and,
- Informed consent was freely given by the participant.

Signature of Impartial Witness	Printed Name	Date

Complete the following declaration only if the participant has limited proficiency in the language in which the consent form is written and interpretation was provided as follows:

- The informed consent discussion was interpreted by an interpreter, and,
- A sight translation of this document was provided by the interpreter as directed by the research staff conducting the consent.

Interpreter declaration and signature:

By signing the consent form I attest that I provided a faithful interpretation for the discussion that took place in my presence, and provided a sight translation of this document as directed by the research staff conducting the consent.

_____	_____	_____
Signature of Interpreter	Printed Name	Date