ALBERT EINSTEIN COLLEGE OF MEDICINE
MONTEFIORE MEDICAL CENTER

DOCUMENTATION OF INFORMED CONSENT AND HIPAA AUTHORIZATION

Introduction

You are being asked to participate in a clinical trial called **The Selective Personalized Radio-Immunotherapy for Locally Advanced NSCLC Trial (SPRINT).** Your participation is voluntary - it is up to you whether you would like to participate. It is fine to say "no" now or at any time after you have started the study. If you say "no," your decision will not affect any of your rights or benefits or your access to care.

The researcher in charge of this project is called the "Principal Investigator." His name is **Nitin Ohri, MD.** You can reach Dr. Ohri at:
Office Address: 111 E 210th Street
Bronx, NY 10467
Telephone #: (718)920-7750
For questions about the research study, or if you believe you have an injury, contact the Principal Investigator or the IRB.

The Institutional Review Board (IRB) of the Albert Einstein College of Medicine and Montefiore Medical Center has approved this research study. The IRB # is in the stamp in the upper right-hand corner of this page. If you have questions regarding your rights as a research subject you may contact the IRB office at 718-430-2253, by e-mail at irb@einstein.yu.edu, or by mail:

Einstein IRB
Albert Einstein College of Medicine
1300 Morris Park Ave., Belfer Bldg #1002
Bronx, New York 10461

Support for this research study is provided by MERCK Pharmaceuticals

Why is this study being done?

The goal of this study is to determine if, for locally advanced non-small cell lung cancer patients whose tumors have high levels of PD-L1 (a marker associated with benefits from immunotherapy), a combination of immunotherapy and a personalized 4-week radiotherapy course is safe and effective. Standard treatment for these patients is a combination of chemotherapy and radiotherapy. Immunotherapy is a form of medication intended to stimulate a person's immune system to fight cancer. The immunotherapy that will be used in this study is called Keytruda, or pembrolizumab. Pembrolizumab is already approved as an initial treatment for patients with metastatic non-small cell lung cancer with high PD-L1 expression, but it has not been tested in combination with radiotherapy for patients without metastatic disease. Patients in this study who are found to have low tumor levels of PD-L1 will be treated with standard chemotherapy and radiotherapy.

Why am I being asked to participate?

You are being asked to participate in this study because you have recently been diagnosed with locally advanced non-small cell lung cancer. Your cancer has not spread outside the chest, but your physicians do not believe that you will benefit from surgery.

How many people will take part in the research study?

You will be one of about 63 people who will be participating in this study.

How long will I take part in this research?
This study will take place over a period of up to one year. As standard clinical care for a patient with lung cancer, your physicians will continue to follow you indefinitely after that. Outcomes beyond one year, such as how long you live, may be included in study results.

What will happen if I participate in the study?
There are two treatment groups in this study. If you decide to participate, you will be placed in one of these groups based on tests performed on the same biopsy sample that was used to diagnose your lung cancer. Enrollment on this trial will not require an extra biopsy.

Patients whose tumors are found to have high PD-L1 levels will receive three intravenous treatments with pembrolizumab, followed by four weeks of daily radiotherapy, followed by up to 12 more treatments with pembrolizumab. Pembrolizumab is given as an intravenous infusion once every three weeks. This treatment course will last up to one year.

Patients whose tumors are found to have low PD-L1 levels will receive radiotherapy over a course of four to seven weeks. During radiotherapy, patients will also receive two standard chemotherapy agents (carboplatin and paclitaxel) once each week. Following completion of chemotherapy and radiotherapy, patients may receive additional treatments with chemotherapy or immunotherapy as part of routine care. These treatments are optional.

All Subjects:
Before you take part in this study, you will have some tests and procedures to be sure you qualify for the study. This may take place in a screening visit, which can take about an hour and includes many procedures that are performed as part of standard care for patients with your disease. The study doctor will review the results of these tests and procedures. If you are not eligible for this study, the study doctor will explain why. At this visit we will:

- Ask you about your medical history
- Perform a physical exam, including height, weight, and “vital signs” (blood pressure, temperature, heart rate, breathing rate, and pain score)
- Draw a blood sample. We will be looking for circulating tumor DNA or other tumor markers of immune system activation found in the blood.
- Test your blood for pregnancy, if you are a female able to become pregnant. Pregnant women cannot take part in this research study.
- Order whole body PET/CT and brain MRI if these have not already been done.

Once we have the results of these tests, if we have determined that you are eligible to participate in the study, you will also have a number of visits with your doctor while on treatment, which is standard practice for all patients. The schedule for treatments will depend on your treatment group:

Pembrolizumab plus radiotherapy:

Immunotherapy (before radiation)	Three infusions, every 3 weeks
Radiation Therapy	Daily (Monday-Friday) for 4 weeks

Immunotherapy (after radiation)	12 infusions, every 3 weeks

Chemotherapy plus radiotherapy:

Radiotherapy	Daily (Monday-Friday) for 4-7 weeks
Chemotherapy	Weekly during radiotherapy
OPTIONAL Chemotherapy or Immunotherapy after Radiotherapy	Variable

At these treatment visits, we will:

- Check your vital signs
- Ask you about side effects or health problems since your last visit
- Draw a blood sample. In addition to routine blood tests, we will draw a small quantity of extra blood at several time points to test for markers of immune activation and the presence of cancer cells' DNA in your blood.
- Give you some questionnaires to fill out
- Review your medication diaries

When you are done, or taken off treatment, we will continue to see you for follow-up as standard care. You will undergo CT scans approximately every three months after completing radiotherapy, which is standard.

A description of this clinical trial will be available on 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.

Optional Activity Monitoring

You may be asked to participate in an optional activity monitoring component of this trial. If you choose to participate in this portion of the study, we will give you a wearable activity monitor, which will be placed on your wrist. When you are given the device, it will be activated, synced with a computer or mobile device, and set to show the time. We will show you how to remove the device (similar to removing a watch) if needed, but we will ask you to keep the device on continuously throughout the course of treatment. With this device, we will be able to track your daily step counts, which may provide information about side effects from treatment and your general health. The device will be yours to keep. There is no additional cost to participate in this portion of the study.

INITIAL ONE (1) OF THE FOLLOWING OPTIONS

_____ I consent to participate in the optional activity monitoring portion of the study and agree to wear the fitness tracker throughout the course of my treatment.

_____ I do NOT consent to the optional activity monitoring portion of the study.

Genetic Testing

This study will not involve genetic research or genetic testing.

Specimen Banking (Future Use and Storage)

We will store your specimens and information about you in a "biobank", which is a library of information and specimens (tissue and blood) from many studies. These specimens and information cannot be linked to you. In the future, researchers can apply for permission to use the specimens and information for new studies to prevent, diagnose, or treat disease, including genetic research. Your specimens and information may be kept for a long time, perhaps longer than 50 years. If you agree to the future use, some of your de-identified genetic and health information (not linked to you) may be placed into one or more scientific databases. These may include databases maintained by the federal government.

INITIAL ONE (1) OF THE FOLLOWING OPTIONS

_____ I consent to have my specimens and information about me used for future research studies.

_____ I do NOT consent to have my specimens and information about me used for future research studies. Information about me will be kept as long as required by regulations and institutional policy, but will not be used for future studies.

Will I be paid for being in this research study?

You will not receive any payment or other compensation for taking part in this study.

Some researchers may develop tests, treatments or products that are worth money. You will not receive payment of any kind for your specimens and information or for any tests, treatments, products or other things of value that may result from the research.

Will it cost me anything to participate in this study?

Taking part in this study will not involve added costs to you. If you are in the group receiving pembrolizumab plus radiotherapy, the pembrolizumab will be provided free of charge by the study sponsor (Merck Pharmaceuticals). Other treatments in this study are considered standard care and will be billed to your insurance company.

What will happen if I am injured because I took part in this study?

If you are injured as a result of this research, only immediate, essential, short-term medical treatment, as determined by the participating hospital or sponsoring company, will be available for the injury without charge to you personally.

- No monetary compensation will be offered.
- You are not waiving any of your legal rights by signing this informed consent document.
- In addition, the sponsor will provide reimbursement for the reasonable costs of medical treatment.

Immediately report any discomforts, problems or injuries you experience during the course of your participation in the study to Dr. Nitin Ohri at 718-920-7750.

What else do I have to do?

- You must tell the research study doctor about any past and present diseases or allergies you are aware of and about all medications you are taking including "over-the-counter" remedies and nutritional supplements or herbs.
- ***Drugs may cause a reaction that, if not treated promptly, could be life-threatening. It is important that you report all symptoms, reactions and other complaints to the research study doctor.***
- If you think you have become pregnant, contact your research study doctor immediately.
- If any other doctor recommends that you take any medicine, please inform him/her that you are taking part in a research study. You should give the other doctor the research study doctor's name and phone number.
- You may carry out all your normal daily activities.

Confidentiality

We will keep your information confidential. Your research records will be kept confidential and your name will not be used in any written or verbal reports. Your information will be given a code number and separated from your name or any other information that could identify you. The form that links your name to the code number will be kept in a secure manner and only the investigator and study staff will have access to the file. All information will be kept in a secure manner and computer records will be password protected. Your study information and specimens will be kept as long as they are useful for this research.

Medical information collected during the research, such as test results, may be entered into your Montefiore electronic medical record and will be available to clinicians and other staff at Montefiore who provide care to you.

The only people who can see your research records are:

- the research team and staff who work with them
- the organization that funded the research, Merck Pharmaceuticals
- groups that review research (the Einstein IRB, and the Office for Human Research Protections**,** and the US Food and Drug Administration)

These people, who receive your health information, may not be required by privacy laws to protect it and may share your information with others without your permission, if permitted by laws governing them. All of these groups have been asked to keep your information confidential.

Are there any risks to me?

Radiation Risks

You will be receiving radiation as part of study treatment. You may have side effects while on study that are **common with all radiation therapy treatment for lung cancer**. If you are in the PembroRT cohort, you will receive a relatively short course of radiotherapy (4 weeks). If you are in the ChemoRT cohort, you will receive a standard radiotherapy course that may span 4-7 weeks, at the discretion of your treating physicians. We are using a 4-week radiotherapy course in the PembroRT cohort because we believe that for patients receiving immunotherapy it will be

at least as safe and effective as the standard course (approximately 6 weeks). However, it is possible that the 4-week treatment may be less effective than a standard longer course.

Some of the side effects of radiation include:

Common side effects:
- Difficulty, pain, or burning sensation when swallowing, which often is temporary
- Tiredness, which is temporary
- Tanning, redness of skin, and hair loss within the treatment area, which is temporary
- Skin in treatment area may remain permanently dry, and chest hair may not grow back
- Scarring in the lung, which sometimes causes collapse of the lung
- Fluid collection in the lung sac

Less common side effects:
- Cough and some difficulty in breathing (or shortness of breath) due to lung inflammation or scarring, which may be severe at times
- Irritation of the heart sac
- Irritation of the heart muscle
- Injury to the tube that carries food to your stomach
- Injury to the tube that carries oxygen to your lungs
- Bleeding from injury to the large blood vessels

Uncommon and Rare side effects:
- Inflammation of the spinal cord
- A second cancer caused by the radiation you receive

Risks to Women Who Are or May Become Pregnant
The effects of radiation and chemotherapy on an embryo or fetus (developing baby still in the womb), or on a breastfeeding infant, may be harmful. Because of these unknown risks, women cannot take part in this study if they are:
- Pregnant
- Trying to become pregnant
- Breastfeeding or sharing breast milk

If you are a menopausal woman and have not had a menstrual period for the past 12 months or more, you will not need to have a pregnancy test. Also, you will not need to have a pregnancy test if you have had a hysterectomy (surgical removal of your uterus and/or ovaries). All other female subjects must have a negative pregnancy test before starting the study drug.
If you are sexually active and able to become pregnant, you must agree to use one of the birth control methods listed below. You must use birth control for the duration of the study.

Acceptable birth control methods for use in this study are:
- Hormonal methods, such as birth control pills, patches, injections, vaginal ring, or implants
- Barrier methods (such as a condom or diaphragm) used with a spermicide (a foam, cream, or gel that kills sperm)
- Intrauterine device (IUD)
- Abstinence (no sex)

Pembrolizumab Side Effects
The immunotherapy you will receive, pembrolizumab, is a standard treatment for metastatic lung cancer whose side effects have been studied carefully. The strategy of giving pembrolizumab before and after radiotherapy is considered experimental, so the side effects of this combination cannot fully be predicted. Pembrolizumab treats cancer by working with your immune system. It can sometimes cause your immune system to attack normal organs and tissues in any area of your body and can affect the way they work. These problems can sometimes become serious or life-threatening.

Very common side effects seen in at least 20% of patients include:

- Itching of the skin
-
- Loose or watery stools

Common side effects seen in at least 10% and less than 20 % of patients include:

- Joint pain
- Fever
- Back pain
- Rash

Side effects seen in at least 1% and less than 10 % of patients include:

- Low level of salt in the blood that may cause you to feel tired, confused, headache, muscle cramps or sick to your stomach
- Pain in your belly
- Inflammation of the lungs so you may feel short of breath and cough. Rarely this might lead to death
- Inflammation of the bowels/gut that may cause pain in your belly with loose or watery stools
- Not enough thyroid hormone so you may feel tired, gain weight, feel cold, have infrequent or hard stools
- Too much thyroid hormone so you may feel anxious, angry, can't sleep, weak, tremble, sweat, tired, have loose and watery stools
- Inflammation of the skin so you may have peeling of the skin, itching, skin redness
- Loss of skin color
- Dizziness or fainting (low blood pressure), flushing, rash, fever, shortness of breath or sick to your stomach at the time of receiving your infusion or just after or pain at the site of infusion

Serious side effects seen in between 1% and 4% of patients include:

- Inflammation of the lungs so you may feel short of breath and cough. Rarely this might lead to death
- Inflammation of the bowels/gut that can cause pain in your belly with loose or watery stools
- Fever

Serious side effects seen in 1% or less of patients include:

- Inflammation of the skin so you may have widespread peeling of the skin, itching, skin redness. More sever skin reactions may involve the inside of your mouth, the surface of your eyes, and genital areas, and/or may cause the top layer of your skin to peel from

all over your body which can cause severe infection. Rarely these reactions lead to death.
- Inflammation of the liver that may cause a poor appetite, feeling tired, mild fever, muscle or joint aches, sick to your stomach and vomiting, pain in your belly, yellow eyes and skin, and dark urine
- Inflammation of the pituitary gland (a gland in the head) which may cause headaches, sick to your stomach, changes in behavior, double vision, few to no menstrual cycles, weakness, vomiting and dizziness or fainting.
- Too much thyroid hormone so you may feel anxious, angry, can't sleep, weak, tremble, increased sweating, weight loss, hair loss, tired, have loose and watery stools
- Not enough thyroid hormone so you may feel tired, gain weight, feel cold, have infrequent or hard bowel movements
- Inflammation of the kidney so you may pass less urine or have cloudy or bloody urine, swelling and low back pain
- Inflammation of the muscles so you may feel weak or pain in the muscles
- Inflammation of the pancreas (a gland in your abdomen that controls sugar levels) so you may have severe pain in the top part of your belly that may move to the back, sick to your stomach, and vomiting that gets worse when you eat
- Inflammation of the eye so you may have redness of the eye, blurred vision, sensitive to light, have eye pain, see floaters or have headaches
- Adrenal glands (glands on top of the kidneys) not making enough hormone causing tiredness, weight loss, muscle weakness, feeling faint, joint, muscle and abdominal aches, nausea, vomiting, loose or watery stools, fever, salt craving, and sometimes darkening of the skin like a suntan
- Inflammation of the nerves that may cause pain, weakness, or tingling in the hands and feet, and may spread to the legs, arms and upper body leading to severe muscle weakness and possible temporary paralysis
- Too much sugar in your blood (diabetes), so you may feel thirsty, and are likely to need regular insulin shots
- Inflammation of the middle layer of your heart wall (myocarditis) that may cause your heart to have difficulty pumping blood throughout your body, which can cause chest pain, shortness of breath and swelling of the legs. You may experience a fast or irregular heartbeat that may cause you dizziness or fainting. Sometimes this condition can lead to death.
- Dizziness or fainting (low blood pressure), flushing, rash, fever, shortness of breath or sick to your stomach at the time of receiving your infusion (IV) or just after, or pain at the site of infusion

Chemotherapy Side Effects

Common side effects could include:
- Low white blood cell counts, which may result in serious or even fatal infections
- Low red blood cell counts, which may result in tiredness or weakness
- Low platelet counts, which may result in bruising or bleeding
- Nausea
- Vomiting
- Loss of appetite
- Diarrhea

- Fatigue
- Hair loss
- Muscle weakness
- Joint and muscle aches
- Lightheadedness
- Headaches
- Numbness in the hands and feet
- Changes in blood pressure
- Skin irritation at site of drug injection

Less likely side effects could include:

- Sores in mouth and/or throat
- Alterations in taste
- Allergic reaction (including flushing, skin rash, changes in blood pressure and/or difficulty breathing)
- Stomach cramps
- Loss of blood supply to the intestines, which may require surgery
- Inflammation of the pancreas (an organ in the abdomen), which may result in abdominal pain and/or weight loss
- Dizziness and shooting back pain when bending your neck forward
- Confusion
- Blurred vision or a sensation of flashing light
- Mood change
- Kidney damage
- Liver damage and/or failure
- Seizures
- Fainting
- Irregular heartbeat
- Heart attack

Questionnaire
You may feel uncomfortable answering questions about your current health or overall quality of life. You can choose not to answer questions that make you feel uncomfortable.

Blood Draw
Rarely, the vein where we insert the needle will become sore or red. Sometimes, a bruise may develop. Very rarely, fainting may occur.

New Findings
If we learn any significant new findings during the study that might influence your decision to participate, we will contact you and explain them.

Unknown Risks
We have described all the risks we know. However, because this is research, there a possibility that you will have a reaction that we do not know about yet and is not expected.

Are there possible benefits to me?

There is no guarantee that you will benefit from being a subject in this study. While doctors hope that the schedule of immunotherapy and radiotherapy will be more useful against cancer compared to the usual treatment, there is no proof of this yet. The information from this study may help doctors learn more about the effectiveness of this approach as a treatment for cancer. This information could help future cancer patients.

What choices do I have other than participating in this study?

You can refuse to participate in the study. If you decide not to participate, the medical care providers at this facility will still give you all of the standard care and treatment that is appropriate for you.

Are there any consequences to me if I decide to stop participating in this study?

No. If you decide to take part, you are free to stop participating at any time without giving a reason. This will not affect your care and you will continue to be treated at this facility. However, some of the information may have already been entered into the study and that will not be removed. The researchers and the sponsor may continue to use and share the information they have already collected.

To revoke (take back) your consent and authorization, you must contact the Principal Investigator in writing at the address on page 1 of this form. However, you may first call or speak to the Principal Investigator and he will stop collecting new information about you. If you take back your consent and authorization, you will not be allowed to continue to participate in this research study.

Can the study end my participation early?

Your participation could end if the investigator, the study sponsor, the U.S. Food and Drug Administration, or the committee that oversees this study to safeguard subjects' rights stops the study earlier than expected.

CONSENT TO PARTICIPATE

I have read the consent form and I understand that it is up to me whether or not I participate. I know enough about the purpose, methods, risks and benefits of the research study to decide that I want to take part in it. I understand that I am not waiving any of my legal rights by signing this informed consent document. I will be given a signed copy of this consent form.

Printed name of participant	Signature of participant	Date	Time
Printed name of the person conducting the consent process	Signature	Date	Time