NCI Community Oncology Research Program – Kansas City

(NCORP-KC)

Testing the Addition of the Drug Nivolumab after Surgery for Non-Small Cell Lung Cancer

Official Study Title for Internet Search on http://www.ClinicalTrials.gov/:

EA5142: Adjuvant Nivolumab in Resected Lung Cancers (ANVIL)

A Randomized Phase III Study of Nivolumab After Surgical Resection and Adjuvant Chemotherapy in Non-Small Cell Lung Cancers

Version Date: April 20, 2018

What is the usual approach to my lung cancer?

You are being asked to take part in this research study because you have non-small cell lung cancer, which has been removed by a surgeon. People who are not in a research study are usually offered standard treatment which may include chemotherapy and/or radiation therapy. They are then monitored after treatment in case their cancer returns.

What are my other choices if I do not take part in this study?

If you decide not to take part in this study, you have other choices for your care. For example:

- you may choose to have the usual approach described above or as otherwise recommended by your treating physician
- you may choose to take part in a different research study, if one is available
- or you may choose not to be treated and monitored for your cancer

Why is this study being done?

The purpose of this study is to find if adding the study drug, nivolumab (also known as OPDIVO®), will limit lung cancer from growing back in patients with early stage non-small

cell lung cancer. Nivolumab is a drug that may turn on the body's immune system to attack any cancer cells that may remain after surgery. The addition of nivolumab may help prevent your cancer from returning, but it could also cause side effects. This research study will allow researchers to find out whether this different treatment is better, the same, or worse than the usual treatment for lung cancer. The study drug, nivolumab, is already FDA-approved for use in non-small cell lung cancer that has previously been treated with chemotherapy. The use of nivolumab in this study is investigational (not approved by the FDA) in your type of cancer.

It is anticipated that there will be about 714 people taking part in this research study.

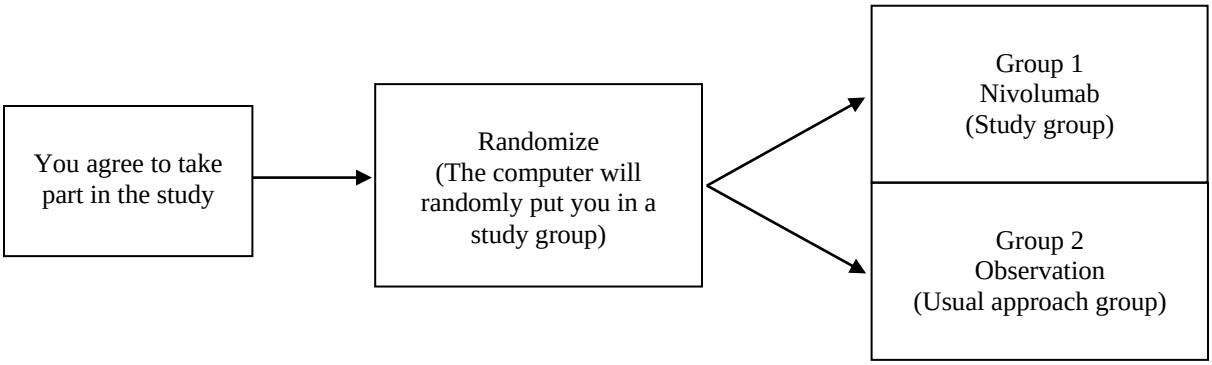
What are the study groups?

This research study has two study groups.

- Group 1 will get the study drug, nivolumab. Nivolumab is administered by an intravenous (IV) infusion over 30 minutes once every 4 weeks. If you are already receiving nivolumab on this study once every 2 weeks, your treatment will change to once every 4 weeks within the next month. Treatment will continue for a maximum of 1 year of nivolumab or until you have side effects, your cancer returns, or you decide to stop.
- Group 2 will be monitored with standard post-operative follow-up treatment.

A computer will by chance assign you to the groups in the research study. This is called randomization. This is done by chance because no one knows if one study group [treatment] is better or worse than the others. You will have an equal (50%) chance of being placed in either group. You and your doctor will be informed of your group.

Another way to find out what will happen to you during this research study is to read the chart below. Start reading at the left side and read across to the right, following the lines and arrows.



How long will I be in this study?

You will receive nivolumab one time every 4 weeks for up to 1 year. After you finish taking nivolumab, or if you are assigned to the observation group, your doctor will continue to watch you and follow your condition for up to 10 years. This follow-up in both groups will include CT scans of your chest to monitor your status.

What extra tests and procedures will I have if I take part in this study?

Most of the exams, tests, and procedures you will have are part of the usual care for your cancer. However, there are some exams, tests and procedures that you will need to have if you take part in this research study. You will be asked to take part in the "ALCHEMIST Screening Trial" (as referred to in the next section), if you do not consent to take part, you will not be able to participate in this study.

Before you begin the study:

You will need to have the following extra exams and tests to find out if you can be in the research study:

- CT scan of your chest
- Blood or urine pregnancy test, if you are a woman of child-bearing potential
- In addition, to participate in this study you need to agree to take part in the A151216 study. A151216 is also called the "Alchemist Screening" trial. This is a screening trial that tests small pieces of cancer tissue removed during your previous surgery and/or biopsies. It will be sent to a central laboratory and tested to look for a protein called PD-L1. This test is investigational and is not used to select you for the study.

- Depending on your cancer type, the tissue may also be tested for markers call EGFR and ALK. Only patients without a mutation in the EGFR and ALK markers may participate in this treatment trial.
- If you have a history of heart problems, you will need to have an EKG/echocardiogram to test how your heart is functioning.

If the exams and tests show that you can take part in the research study and you choose to take part, then you will need the following extra exams, tests, and procedures. Some of these tests are not part of the usual care for your type of cancer.

During the study:

- For patients receiving nivolumab, blood tests will be done prior to every dose (every 4 weeks for 1 year), 6 weeks after the last dose of nivolumab and then every 3 months for the following year.
- For patients receiving nivolumab, a symptom evaluation and physical examination will be done to establish a baseline condition for future comparison of condition on nivolumab treatment to evaluate the efficacy and potential bad effects related to nivolumab.
- For patients assigned to observation, symptom evaluation, physical examination and basic blood test will be done every 3 months for the first two years, every 6 months for the next two years, and then every 12 months while you are 5-10 years from study entry.
- For all patients, a CT scan of chest will be done every 6 months until you are 4 years from study entry, then every 12 months while you are 5-10 years from study entry.
- If you have a history of heart problems, you will need to have an EKG/echocardiogram to test how your heart is functioning.

If your cancer returns:

- CT scan of chest or other imaging that your doctor feels is necessary.
- Your doctor may take a biopsy to confirm that your cancer has returned

What possible risks can I expect from taking part in this study?

If you choose to take part in this research study, there is a risk that:

- You may lose time at work or home and spend more time in the hospital or doctor's office than usual.
- You may be asked sensitive or private questions which you normally do not discuss.

- The study drug may not be better, and could possibly be worse, than the usual approach for your cancer.

1. The drug used in this research study, nivolumab, may affect how different parts of your body work such as your liver, kidneys, lungs and blood. The study doctor will be examining you and testing your blood and will let you know if changes occur that may affect your health. The most common risks related to drawing blood from your arm are brief pain and possibly a bruise.

These risks are described in more detail below.

There is also a risk that you could have other side effects from the study drug.

Here are important points about side effects:

- The study doctors do not know who will or will not have side effects.
- Some side effects may go away soon, some may last a long time, or some may never go away.
- Some side effects may interfere with your ability to have children.
- Some side effects may be serious and may even result in death.

Here are important points about how you and the study doctor can make side effects less of a problem:

- Tell the study doctor if you notice or feel anything different so they can see if you are having a side effect.
- The study doctor may be able to treat some side effects.
- The study doctor may stop or adjust the schedule of the study drug to try to reduce side effects.

The tables below show the most common and the most serious side effects that researchers know about. There might be other side effects that researchers do not yet know about. If important new side effects are found, the study doctor will discuss these with you.

Possible Side Effects of Nivolumab

COMMON, SOME MAY BE SERIOUS **In 100 people receiving nivolumab, more than 20 and up to 100 may have:**
• Tiredness

OCCASIONAL, SOME MAY BE SERIOUS

In 100 people receiving nivolumab, from 4 to 20 may have:

- Anemia which may require blood transfusion
- Swelling and redness of the eye
- Pain in belly
- Diarrhea, nausea, loss of appetite
- Dry mouth
- Fever
- Swelling and redness at the site of the medication injection
- Bruising, bleeding
- Pain or swelling at the joints
- Reaction during or following a drug infusion which may cause fever, chills, rash

Nivolumab may cause your immune system to attack normal organs and cause side effects in many parts of the body. These problems may include but are not limited to:

- Lung problems (pneumonitis and pleural effusion). Symptoms may include: new or worsening cough, chest pain, shortness of breath.
- Intestinal problems (colitis) that can rarely lead to tears or holes in your intestine. Signs and symptoms of colitis may include: diarrhea or increase in bowel movements, blood in your stools or dark, tarry, sticky stools, severe belly pain or tenderness.
- Skin: itching, rash, blisters including inside the mouth; loss of skin pigment
- Liver problems (hepatitis) which can cause liver failure. Signs and symptoms of hepatitis may include: yellowing of your skin or the whites of your eyes, severe nausea or vomiting; drowsiness; pain in the right upper belly.
- Hormone gland problems (especially the thyroid, pituitary and adrenal glands, and pancreas). Signs and symptoms may include: headaches that will not go away or unusual headaches, extreme tiredness or changes in mood or behavior decreased sex drive; weight loss or weight gain; excessive thirst or urine; dizziness or fainting.

RARE, AND SERIOUS In 100 people receiving nivolumab, 3 or fewer may have:
• Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat
BMS-936558 (nivolumab) may cause your immune system to attack normal organs and cause side effects in many parts of the body. These problems may include but are not limited to:
• Visual disturbances which may cause double vision, blurred vision, or loss of vision with a chance of blindness
• A condition with high blood sugar which leads to tiredness, frequent urination, excessive thirst, headache, nausea and vomiting, and can result in coma
• Kidney problems, including nephritis and kidney failure requiring dialysis. Signs of kidney problems may include; decrease in the amount of urine, blood in your urine, ankle swelling.
• Heart problems including inflammation and heart failure. Symptoms and signs of heart problem may include: Shortness of breath, swelling of the ankle and body.
• Problem of the muscle, including inflammation, which can cause muscle pain and severe muscle weakness sometimes with dark urine
• Inflammation of the brain (meningitis/encephalitis), which may cause: headache, confusion, sleepiness, seizures, and stiff neck
• Problem of the nerves that can cause paralysis. Signs and symptoms may include: numbness, tingling of hands and feet; weakness of the arms, legs and facial muscle movement.
• Complications associated with stem cell transplant using donor stem cells (allogeneic stem cell transplant). These complication are caused by attack of donor cells on the host organs (inducing liver, skin and gut), and can lead to death. If you are considering an allogeneic stem transplant after participating in this study, please tell your doctor that you have received BMS-936558 (nivolumab) therapy, since the risk and severity of transplant-associated complications may be increased.

Let your study doctor know of any questions you have about possible side effects. You can ask the study doctor questions about side effects at any time.

Reproductive risks:

You should not get pregnant, breastfeed, or father a baby while in this study and for at least 31 weeks after the last dose of nivolumab. The potential harm of nivolumab to an unborn baby is not known. Avoiding sexual activity is the only certain method to prevent pregnancy. However, if you choose to be sexually active, you must agree to use an appropriate method of birth control during the study and continuing for 31 weeks after the last dose of the study drug. Check with the study doctor about what types of birth control, or pregnancy prevention, to use while in this study. If you choose to be sexually active during the study, you must accept that pregnancy could still result, exposing you or your sexual partner to potential loss

of pregnancy as well as other unknown effects on the developing unborn baby. If a woman becomes pregnant while on this study or within 100 days after the last dose of study drug, she will be asked for information concerning the outcome of her pregnancy. If a female partner of a male patient becomes pregnant while the male patient is on the study or within 100 days after the last dose of study drug, the male patient must notify the investigator.

What possible benefits can I expect from taking part in this study?

It is not possible to know at this time if the study drug is better than the usual care for this cancer so this research study may or may not help you. But, this research study will help researchers learn things that will help people in the future.

Can I stop taking part in this study?

Yes. You can decide to stop at any time. If you decide to stop for any reason, it is important to let the study doctor know as soon as possible so you can stop safely. If you stop, you can decide whether or not to let the study doctor continue to provide your medical information to the organization running the study.

The study doctor will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

The study doctor may take you out of the study:

- If your health changes and the study is no longer in your best interest
- If new information becomes available
- If you do not follow the study rules
- If the study is stopped by the sponsor, IRB or FDA.

What are my rights in this study?

Taking part in this research study is your choice. No matter what decision you make, and even if your decision changes, there will be no penalty to you. You will not lose medical care or any legal rights.

For questions about your rights while in this study, call the NCI Community Oncology Research Program – Kansas City Institutional Review Board at 913-948-5588.

What are the costs of taking part in this study?

The nivolumab will be supplied at no charge while you take part in this research study. It is possible that the nivolumab may not continue to be supplied while you are on the study. Although not likely, if this occurs, your study doctor will talk to you about your options.

You and/or your health plan/insurance company will need to pay for all of the other costs of preventing or treating your cancer while in this research study, including the cost of study drug preparation and administration, tests, procedures, or medicines to manage any side effects, unless you are told that certain tests are being done at no charge. Before you decide to be in the research study, you should check with your health plan or insurance company to find out exactly what they will pay for.

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

What happens if I am injured or hurt because I took part in this study?

If you are injured or hurt as a result of taking part in this research study and need medical treatment, please tell your study doctor. The study sponsors will not offer to pay for medical treatment for injury. Your insurance company may not be willing to pay for research study-related injury. If you have no insurance, you would be responsible for any costs.

If you feel this injury was a result of medical error, you keep all your legal rights to receive payment for this even though you are in a research study.

Who will see my medical information?

Your privacy is very important to us and the researchers will make every effort to protect it. Your information may be given out if required by law. For example, certain states require doctors to report to health boards if they find a disease like tuberculosis. However, the researchers will do their best to make sure that any information that is released will not identify you. Some of your health information, and/or information about your specimen, from this study will be kept in a central database for research. Your name or contact information will not be put in the database.

The ECOG-ACRIN Cancer Research Group is conducting this study. ECOG-ACRIN is a cancer research group that conducts studies for the National Cancer Institute. Your doctor is a member of ECOG-ACRIN or another group that is participating in this study. To help protect your privacy, ECOG-ACRIN has obtained a Confidentiality Certificate from the Department of Health and Human Services (DHHS). With this Certificate, ECOG-ACRIN cannot be forced (for example, by court subpoena) to disclose information that may identify you in any federal, state or local civil, criminal, administrative, legislative or other

proceeding. Disclosure will be necessary, however, upon request of DHHS for audit or program evaluation purposes.

There are organizations that may inspect your records. These organizations are required to make sure your information is kept private, unless required by law to provide information. Some of these organizations are:

- The study sponsor, ECOG-ACRIN, Southwestern Oncology Group (SWOG), Alliance for Clinical Trials in Oncology (ALLIANCE), NRG Oncology Foundation, or any drug company supporting the study.
- The Institutional Review Board, IRB, is a group of people who review the research with the goal of protecting the people who take part in the study.
- The Food and Drug Administration and the National Cancer Institute in the U.S., and similar ones if other countries are involved in the study.

Where can I get more information?

You may visit the NCI Web site at http://cancer.gov/ for more information about studies or general information about cancer. You may also call the NCI Cancer Information Service to get the same information at: 1-800-4-CANCER (1-800-422-6237).

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.

Who can answer my questions about this study?

You can talk to the study doctor about any questions or concerns you have about this study or to report side effects or injuries. Contact your study doctor _____ (*insert name of study doctor[s*]) at _____ *(insert telephone number).*

ADDITIONAL STUDIES SECTION:

This section is about optional studies you can choose to take part in.

This part of the consent form is about optional studies that you can choose to take part in. You will not get health benefits from any of these studies. The researchers leading this optional study hope the results will help other people with cancer in the future.

The results will not be added to your medical records and you or your study doctor will not know the results.

You will not be billed for these optional studies. You can still take part in the main study even if you say 'no' to any or all of these studies. If you sign up for but cannot complete any of the studies for any reason, you can still take part in the main study.

Optional Sample Collections for Biobanking for Possible Future Studies

Researchers are trying to learn more about cancer and other health problems. Much of this research is done using samples of tissue, blood, urine, or other fluids. Through these studies, researchers hope to find new ways to prevent, detect, treat, or cure health problems.

Some of these studies may be about genes. Genes carry information about features that are found in you and in people who are related to you. Researchers are interested in the way that genes affect how your body responds to treatment.

At this time, we are requesting that you allow the storage of samples of your cancer and blood for research projects that may be done later date. These specimens will be stored in a "biobank". The Biobanks are run by ECOG-ACRIN staff and researchers and they are financially supported by the National Cancer Institute.

What is involved if you provide your samples for research?

If you agree to take part, here is what will happen next:

2. About 2-3 tablespoons of blood will be collected using a needle before you begin treatment and if your disease returns or becomes worse. The blood should be collected at the same time as the blood to monitor your health is collected. However, sometimes an additional stick may be done to collect the blood samples.
3. If your disease returns or becomes worse, a small piece of tumor tissue from your biopsy, if performed, will be sent to the Biobank for storage. Only samples from procedures performed as part of your standard care will be sent. No additional procedures will be done to collect these research tissues samples.

4. Your samples and some related information will be stored in the Biobanks, along with samples and information from people who took part in this or other research studies. The samples will be kept until they are used up.
5. Only qualified researchers can submit a request to use the materials stored in the Biobanks. A committee of experts at ECOG-ACRIN, and/or the National Cancer Institute, will review each request to use the samples for research. All research projects using these samples will also be reviewed by an ethics or institutional review board to ensure that the request is necessary and proper. Researchers will not be given your name or any other information that could directly identify you.
6. Neither you nor your study doctor will be notified when research will be conducted or given reports or other information about any research that is done using your samples.
7. Results from the research may be placed in centralized storage systems called databases. It is possible that some of your genetic information and your health information may be placed in these databases. It is also possible that some of these databases may be public.

What are the possible risks in providing your samples for research?

8. The most common risks related to drawing blood from your arm are brief pain and possibly a bruise.
9. There is a risk that someone could get access to the personal information in your medical records or other information researchers have stored about you.
10. There is a risk that someone could trace the information in a central database back to you. Even without your name or other identifiers, your genetic information is unique to you. The researchers believe the chance that someone will identify you is very small, but the risk may change in the future as people come up with new ways of tracing information.
11. In some cases, this information could be used to make it harder for you to get or keep a job or insurance. There are laws against the misuse of genetic information, but they may not give full protection. There can also be a risk in knowing genetic information. New health information about inherited traits that might affect you or your blood relatives could be found during a study. The researchers believe the chance these things will happen is very small, but cannot promise that they will not occur.

When my samples are used for research, how will information about me be kept private?

Your privacy is very important to the researchers and they will make every effort to protect it. Here are just a few of the steps they will take:

12. When your sample(s) is sent to the researchers, no information identifying you (such as your name) will be sent. Samples will be identified by a unique code only.

13. The list that links the unique code to your name will be kept separate from your sample and health information. Any Biobank and ECOG-ACRIN staff with access to the list must sign an agreement to keep your identity confidential.
14. Researchers to whom ECOG-ACRIN sends your sample and information will not know who you are. They must also sign an agreement that they will not try to find out who you are.
15. Information that identifies you will not be given to anyone, unless required by law.
16. When research results are published, your name and other personal information will not be used.

What are the Possible Benefits of allowing my samples to be used for research?

You will not benefit from taking part. The researchers, using the samples from you and others, might make discoveries that could help people in the future.

Are there any costs or payments associated with providing my samples for research?

There are no costs to you or your insurance. You will not be paid for taking part. If any of the research leads to new tests, drugs, or other commercial products, you will not share in any profits.

What if I change my mind about allowing my samples to be used for research?

If you decide you no longer want your samples to be used, you can call the study doctor, _____, *(insert name of study doctor for main trial)* at _____ *(insert telephone number of study doctor for main trial)* who will let the researchers know. Then, any sample that remains in the bank will no longer be used and related health information will no longer be collected. Samples or related information that have already been given to or used by researchers will not be returned.

What if I have more questions?

If you have questions about the use of your samples for research, contact the study doctor, _____, *(insert name of study doctor for main trial)*, at _____ *(insert telephone number of study doctor for main trial)*.

Please circle your choice of "yes" or "no" for the following study:

SAMPLES FOR FUTURE RESEARCH STUDIES:

- **My samples and related information may be kept in a Biobank for use in future health research.**

YES **NO**

This is the end of the section about optional studies.

Release

By signing this form you authorize NCORP-KC to access and obtain information that is required for the study. this may include your medical records, labs, radiologic films and reports and pathology specimens. This authorization to disclose your medical records shall not expire, even upon death, unless specifically revoked in writing by you.

You will get a copy of this form. If you want more information about this study, ask your study doctor.

My signature agreeing to take part in the main study

I have read this consent form or had it read to me. I have discussed it with the study doctor and my questions have been answered. I will be given a signed copy of this form. I agree to take part in the main study and any additional studies where I circled 'yes.'

Participant _____

Participant's signature _____

Date of signature _____

Person obtaining consent _____

Person obtaining consent signature _____

Date of signature _____