NRG ONCOLOGY

NRG-GI007

(ClinicalTrials.gov Identifier NCT #04391049)

Phase I Trial with Expansion Cohort of OBP-301 (Telomelysin) and Definitive Chemoradiation for Patients with Locally Advanced Esophageal And Gastroesophageal Cancer Who are Not Candidates for Surgery

Research Study Informed Consent Document

Study Title for Participants: Testing the addition of the anti-cancer viral therapy Telomelysin to chemoradiation for patients with advanced esophageal cancer and are not candidates for surgery

Official Study Title for Internet Search on http://www.ClinicalTrials.gov: Protocol NRG-GI007, Phase I Trial with Expansion Cohort of OBP-301 (Telomelysin) and Definitive Chemoradiation for Patients with Locally Advanced Esophageal And Gastroesophageal Cancer Who are Not Candidates for Surgery, (NCT#04391049)

Overview and Key Information

What am I being asked to do?

We are asking you to take part in a research study. This study has public funding from the National Cancer Institute (NCI), part of the National Institutes of Health (NIH) in the United States Department of Health and Human Services. We do research studies to try to answer questions about how to prevent, diagnose, and treat diseases like cancer.

We are asking you to take part in this research study because you have advanced esophageal cancer and you are not a candidate for surgery.

Taking part in this study is your choice.

You can choose to take part or you can choose not to take part in this study. You also can change your mind at any time. Whatever choice you make, you will not lose access to your medical care or give up any legal rights or benefits.

This document has important information to help you make your choice. Take time to read it. Talk to your doctor, family, or friends about the risks and benefits of taking part in the study. It's important that you have as much information as you need and that all your questions are answered. See the "Where can I get more information?" section for resources for more clinical trials and general cancer information.

Why is this study being done?

This study is being done to answer the following question:

Is the combination of OBP-301 (which will now be referred to as telomelysin), a virus designed to only infect cancer cells, with chemotherapy and radiation therapy safe?

We are doing this study because we want to find out if this approach is better or worse than the usual approach for your esophageal cancer. The usual approach is defined as care most people get for esophageal cancer.

What is the usual approach to my esophageal cancer?

The usual approach for patients who are not in a study is treatment with the Food and Drug Administration (FDA) approved chemotherapy, along with radiation therapy. For patients who get the usual approach for this cancer, about 50 out of 100 have no evidence of remaining cancer in the esophagus after 3 years.

What are my choices if I decide not to take part in this study?

- You may choose to have the usual approach described above.
- You may choose to take part in a different research study, if one is available.
- You may choose not to be treated for cancer.
- You may choose to only get comfort care to help relieve your symptoms and not get treated for your cancer.

What will happen if I decide to take part in this study?

If you decide to take part in this study, you will get telomelysin injected into your tumor during a procedure called an endoscopy. An endoscopy is a procedure that uses a tiny camera at the end of a long flexible tube to view your esophagus. You had this procedure when you were first diagnosed with cancer. Telomelysin is a virus that has been designed to infect and destroy only cancer cells (although there is a small risk that it can also infect normal cells). You will receive the telomelysin injections for a total of 3 times every 14 days. You will receive the first injection before you start chemotherapy and radiation therapy and then you will receive the other 2 injections during the 5 ½ weeks of chemoradiation.

After you finish your treatment, your doctor and study team will watch you for side effects. They will check you 6 to 8 weeks after you complete radiation and then every 3 months for 2 years after treatment. This means you will keep seeing your doctor for 2 years after treatment.

What are the risks and benefits of taking part in this study?

There are both risks and benefits to taking part in this study. It is important for you to think carefully about these as you make your decision.

Risks

We want to make sure you know about a few key risks right now. We give you more information in the "What risks can I expect from taking part in this study?" section.

If you choose to take part in this study, there is a risk that the study agent may not be as good as the usual approach for your cancer at shrinking or stabilizing your cancer.

There is also a risk that you could have side effects from the study agent. These side effects may be worse and may be different than you would get with the usual approach for your cancer.

Some of the most common side effects that the study doctors know about are:

- Nausea
- Vomiting
- Infection
- Pain

- Hair loss
- Tiredness

There may be some risks that the study doctors do not yet know about.

Benefits

There is some evidence in people with esophageal cancer that adding telomelysin to the usual approach can stabilize cancer for longer than the usual approach alone. However, we do not know if this will happen in this study. This study may help the study doctors learn things that may help other people in the future. It is unlikely that this telomelysin injection will help you live longer than the usual approach alone.

If I decide to take part in this study, can I stop later?

Yes, you can decide to stop taking part in the study at any time.

If you decide to stop, let your study doctor know as soon as possible. It's important that you stop safely. If you stop, you can decide if you want to keep letting the study doctor know how you are doing.

Your 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.

Are there other reasons why I might stop being in the study?

Yes. The study doctor may take you off the study if:

- Your health changes and the study is no longer in your best interest.
- New information becomes available and the study is no longer in your best interest.
- You do not follow the study rules.
- For women: You become pregnant while on the study.
- The study is stopped by the National Cancer Institute (NCI) Institutional Review Board (IRB), Food and Drug Administration (FDA), or study sponsor NRG Oncology. The study sponsor is the organization who oversees the study.

It is important that you understand the information in the informed consent before making your decision. Please read, or have someone read to you, the rest of this document. If there is anything you don't understand, be sure to ask your study doctor or nurse.

What is the purpose of this study?

The purpose of this study is to find out if adding the anti-cancer viral therapy telomelsyin to the FDA-approved chemotherapy drugs, carboplatin and paclitaxel, and radiation is safe. Telomelysin is not approved by the FDA. There will be about 21 people taking part in this study.

What are the study groups?

In this study, you will get the usual radiation therapy and chemotherapy carboplatin/paclitaxel. You also will get the study agent telomelysin.

Treatment schedule: You will get telomelysin injections into your tumor, during an endoscopy, every 14 days for a total of 3 injections. You will receive the first injection approximately 3 days before you start chemotherapy and radiation. You will receive the other 2 injections during the 5 ½ weeks of chemotherapy and radiation.

You will not be able to get additional doses of the telomelysin. This therapy is not approved by the FDA for treatment of your disease.

What exams, tests, and procedures are involved in this study? (06-JAN-2021)

Before you begin the study, your doctor will review the results of your exams, tests, and procedures. This helps your doctor decide if it is safe for you to take part in the study. If you join the study, you will have more exams, tests, and procedures to closely monitor your safety and health. Most of these are included in the usual care you would get even if you were not in a study.

Listed below are exams, tests, and procedures that need to be done as part of this study to monitor your safety and health, but may not be included in the usual care. We will use them to carefully follow the effects of the study treatment, including preventing and managing side effects.

These exams, tests, and procedures to monitor your safety and health include:

- Blood tests prior to each telomelysin injection.

Some exams, tests, and procedures are a necessary part of the research study, but would not be included in usual care. Listed below are procedures that will be done for research purposes only.

- Endoscopy to administer the OBP-301 injection: you will undergo 3 endoscopy procedures to administer the OBP-301 injections.
- Optional biopsy of the tumor which will occur during each endoscopy to administer the OBP-301 injection and 6-8 weeks post radiation therapy if applicable. (This is an optional part of the study. There is more information about this part of the study at the end of the consent form. You will be asked if you would like to take part in this optional additional study.)
- Optional blood draws prior to each telomelysin injection and 6-8 weeks after the end of radiation therapy. (This is an optional part of the study. There is more information about this part of the study at the end of the consent form. You will be asked if you would like to take part in this optional additional study.)

What risks can I expect from taking part in this study? (19-MAY-2023)

General Risks
If you choose to take part in this study, there is a risk that the study agent may not be as good as the usual approach for your cancer at shrinking or stabilizing your cancer.

You also may have the following discomforts:

- Spend more time in the hospital or doctor's office.
- Be asked sensitive or private questions about things you normally do not discuss.
- May not be able to take part in future studies.

There is no evidence from prior studies that a patient injected with telomelysin can infect others but, as a precaution, you should wear a face mask for 48 hours after receiving endoscopic injection of telomelysin or if you develop a cough. Also, caregivers should wear a mask, gloves and an apron within 48 hours post telomelysin injection when interacting with you.

Individuals with a weak immune system or pregnant women should be limited from direct interaction with treated patients.

The telomelysin used in this study could be very harmful to an unborn or newborn baby. There may be some risks that doctors do not yet know about. It is very important that you check with your study doctor about what types of birth control or pregnancy prevention to use during the study and 6 months (for women) or 12 months (for men) after you have completed the study.

Endoscopy Risks
Common side effects of endoscopy and injection of the tumor by endoscopy are:

- Pain
- Bleeding, especially if a biopsy is done during the procedure
- Infection
- A tear or hole in the esophagus
- A reaction to the sedation used to keep your comfortable during the procedure.

Symptoms of these complications to watch out for are: fever, chest pain, shortness of breath, blood in your stool, difficulty swallowing, pain in your belly, vomiting especially if there is blood in your vomit.

Having 3 separate endoscopies and injections of the esophageal tumor can further increase the risk of any of the side effects above.

You may sign a separate consent form for the study endoscopy that describes the procedure and risks in more detail.

Follow the physician's instruction after the procedure. Usually, about 2 hours after the procedure, you can start to drink clear water, followed by soup or soft food. If you had difficulty swallowing before the procedure, continue to eat foods of the same consistency that you could previously

swallow. If you have severe chest / back pain, fever, cough, difficulty for swallowing, please contact your doctor immediately.

Biopsy Risks
Depending on the area from where tissue biopsy is taken, the risks may vary. Your doctor will discuss this with you in depth and a separate consent will be provided to you at the time to explain explicitly the risks based on the site to be biopsied. Common side effects of a biopsy are a small amount of bleeding at the time of the procedure, bruising, and pain at the biopsy site. Pain can be treated with regular pain medications. Rarely, an infection can occur. You may lose time at work or home and spend more time in the hospital or doctor's office than usual.

Side Effect Risks
The study agent used in this study may affect how different parts of your body work such as your liver, kidneys, heart, and blood. The study doctor will test your blood and let you know if changes occur that may affect your health.

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

Here are important things to know about side effects:

1. The study doctors do not know who will or will not have side effects.
2. Some side effects may go away soon, some may last a long time, and some may never go away.
3. Some side effects may make it hard for you to have children.
4. Some side effects may be mild. Other side effects may be very serious and even result in death.

You can ask your study doctor questions about side effects at any time. Here are important ways to make side effects less of a problem:

- If you notice or feel anything different, tell your study doctor. He or she can check to see if it is a side effect.
- Your study doctor will work with you to treat your side effects.
- Your study doctor may adjust the study agent to try to reduce side effects.

Drug Risks
The tables below show the most common and most serious side effects doctors know about. Keep in mind that there might be other side effects doctors do not yet know about. If important new side effects are found, the study doctor will discuss these with you.

Possible Side Effects of Paclitaxel (Table Version Date: October 14, 2020)

COMMON, SOME MAY BE SERIOUS In 100 people receiving Paclitaxel, more than 20 and up to 100 may have:
• Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat • Infection, especially when white blood cell count is low • Bruising, bleeding • Anemia which may cause tiredness, or may require blood transfusions • Sores in mouth which may cause difficulty swallowing • Diarrhea, nausea, vomiting • Pain • Muscle weakness • Numbness, tingling or pain of the arms and legs • Hair loss

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Paclitaxel, from 4 to 20 may have:
• Abnormal heartbeat • Blood clot which may cause swelling, pain, shortness of breath • Damage to the lungs which may cause shortness of breath

RARE, AND SERIOUS In 100 people receiving Paclitaxel, 3 or fewer may have:
• Heart attack or heart failure which may cause shortness of breath, swelling of ankles, and tiredness • A tear or a hole in the bowels which may cause pain or that may require surgery • Severe skin rash with blisters and peeling which can involve mouth and other parts of the body

Possible Side Effects of Carboplatin (Table Version Date: October 18, 2021)

COMMON, SOME MAY BE SERIOUS In 100 people receiving Carboplatin, more than 20 and up to 100 may have:
• Infection, especially when white blood cell count is low • Bruising, bleeding • Anemia which may cause tiredness, or may require blood transfusions • Vomiting, nausea • Hair loss

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Carboplatin, from 4 to 20 may have:
• Diarrhea, constipation, belly pain • Changes in taste • Numbness and tingling in fingers and toes • Weakness • Swelling, redness, and pain at the site of the medication injection

RARE, AND SERIOUS In 100 people receiving Carboplatin, 3 or fewer may have:
• Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat • Visual loss • Difficulty hearing

Possible Side Effects of OBP-301 (Telomelysin)

COMMON, SOME MAY BE SERIOUS In 100 people receiving OBP-301 (Telomelysin) more than 20 and up to 100 may have:
• Chills and fevers • Muscle or bone aches • Tiredness • Pain • Injection site pain and swelling

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving OBP-301 (Telomelysin)from 4 to 20 may have:
• Joint swelling • Increased heart rate (which can be felt as palpitations) • Nausea, vomiting • Skin changes including dryness, redness, change in color, swelling • Headache • Bleeding from the tumor, tumor tissue damage

RARE, AND SERIOUS In 100 people receiving OBP-301 (Telomelysin), 3 or fewer may have:
• None

Additional Drug Risks

Rarely, there are problems getting enough supplies of the study agent. If that happens, your doctor will talk with you about your options.

Possible Side Effects of Radiation to the Esophagus

COMMON, SOME MAY BE SERIOUS In 100 people receiving Radiation Therapy to the esophagus, more than 20 and up to 100 may have:
• Swelling and redness of the esophagus, which can cause a sore throat and painful swallowing • Narrowing of the esophagus, which can cause problems with swallowing • Fatigue • Decrease in blood counts, which can cause infection, bleeding, and bruising • Tanning and redness of the skin in the treatment area • Nausea/vomiting • Stomach pain

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Radiation Therapy to the esophagus, from 4 to 20 may have:
• Growth of fibrous tissues underneath your skin • Diarrhea • Loss of appetite, weight loss

RARE, AND SERIOUS In 100 people receiving Radiation Therapy to the esophagus, 3 or fewer may have:
• Swelling of the muscle tissue of the heart • Swelling and/or scarring of the lung tissue • Bleeding from the esophagus and stomach

What are my responsibilities in this study?

If you choose to take part in this study you will need to:

- Keep your study appointments.
- Avoid receiving live vaccines with 30 days of telomelysin injection and for 30 days after last injection. Inactivated vaccines such as the flu vaccine are allowed.
- Tell your doctor about:
    - all medications and supplements you are taking
    - any side effects
    - any doctors' visits or hospital stays outside of this study
    - if you have been or are currently in another research study.

For women: Do not get pregnant or breastfeed while taking part in this study. **For men:** Do not father a baby while taking part in this study. **For all:** You must use an effective method of birth control (which includes oral contraceptives, implantable hormone contraception, double barrier method or intrauterine device) while taking part during the duration of study treatment as well as (6 months) if you are a woman or (12 months)if you are a man after your last dose of the study drug. Tell your study doctor right away if you think that you or your partner have become pregnant during the study or within 6 or 12 months after your last dose of study agent.

What are the costs of taking part in this study?

You and/or your insurance plan will need to pay for the costs of medical care you get as part of the study, just as you would if you were getting the usual care for your cancer. This includes:

- the costs of tests, exams, procedures, and drugs (including paclitaxel, carboplatin and radiation therapy) that you get during the study to monitor your safety, and prevent and treat side effects.
- the costs of getting the telomeylsin ready and giving it to you.
- your insurance co-pays and deductibles.

Talk to your insurance provider and make sure that you understand what your insurance pays for and what it doesn't pay for if you take part in this clinical trial. Also, find out if you need approval from your plan before you can take part in the study.

Ask your doctor or nurse for help finding the right person to talk to if you are unsure which costs will be billed to you or your insurance provider.

You and/or your insurance provider will not have to pay for exams, tests, and procedures done for research purposes only or that are covered by the study. These include:

- The endoscopy procedures in this study done at each study agent injection

You or your insurance provider will not have to pay for telomelysin while you take part in this study.

Taking part in this study may mean that you need to make more visits to the clinic or hospital than if you were getting the usual approach to treat your cancer. You may:

- Have more travel costs.

- Need to take more time off work.
- Have other additional personal costs.

You will not be paid for taking part in this study. The research may lead to new tests, drugs, or other products for sale. If it does, you will not get any payment.

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

If you are injured as a result of taking part in this study and need medical treatment, please talk with your study doctor right away about your treatment options. The study sponsors will not pay for medical treatment for injury. Your insurance company may not be willing to pay for a study-related injury. Ask them if they will pay. If you do not have insurance, then you would need to pay for these medical costs.

If you feel this injury was caused by medical error on the part of the study doctors or others involved in the study, you have the legal right to seek payment, even though you are in a study. Agreeing to take part in this study does not mean you give up these rights.

Who will see my medical information?

Your privacy is very important to us. The study doctors will make every effort to protect it. The study doctors have a privacy permit to help protect your records if there is a court case. However, some of your medical information may be given out if required by law. If this should happen, the study doctors will do their best to make sure that any information that goes out to others will not identify who you are.

Some of your health information, such as your response to cancer treatment, results of study tests, and medicines you took, will be kept by the study sponsor in a central research database. However, your name and contact information will not be put in the database. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

There are organizations that may look at or receive copies of some of the information in your study records. Your health information in the research database also may be shared with these organizations. They must keep your information private, unless required by law to give it to another group.

Some of these organizations are:

- NRG Oncology and any company supporting the study now or in the future. This would include any organization helping the company with the study.
- The NCI Central IRB, which is a group of people who review the research with the goal of protecting the people who take part in the study.
- The FDA and the groups it works with to review research.
- The NCI and the groups it works with to review and conduct research, including the Cancer Trials Support Unit (CTSU) and the Imaging and Radiation Oncology Core (IROC).

In addition to storing data in the study database, data from studies that are publicly funded may also be shared broadly for future research with protections for your privacy. The goal of this data sharing is to make more research possible that may improve people's health. Your study records may be stored and shared for future use in public databases. However, your name and other personal information will not be used.

Some types of future research may include looking at your information and information from other patients to see who had side effects across many studies or comparing new study data with older study data. However, right now 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.

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.

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 the study doctor **(*insert name of study doctor[s]*)** at **(*insert telephone number, and email address if appropriate*).**

For questions about your rights while in this study, call the **(*insert name of organization or center*)** Institutional Review Board at **(*insert telephone number*).**

Optional studies that 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. They are separate from the main study described above. These optional studies will not benefit your health. 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.

Taking part in this optional study is your choice. You can still take part in the main study even if you say "no" to this study. There is no penalty for saying "no." You and your insurance company will not be billed for this optional study. If you sign up for, but cannot complete this study for any reason, you can still take part in the main study.

Circle your choice of "yes" or "no" for the following study.

Optional sample collections for known laboratory studies

Researchers are trying to learn more about cancer and other health problems using blood and tissue samples from people who take part in clinical trials. By studying these samples, researchers hope to find new ways to prevent, detect, treat, or cure diseases.

Some of these studies may be about how genes affect health and disease. Other studies may look at how genes affect a person's response to treatment. Genes carry information about traits that are found in you and your family. Examples of traits are the color of your eyes, having curly or straight hair, and certain health conditions that are passed down in families. Some of the studies may lead to new products, such as drugs or tests for diseases.

Known future studies

If you choose to take part in this optional study, researchers will collect tumor tissue and blood for research on the biomarkers response to the treatment

What is involved in this optional sample collection?

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

1. About 1-1.5 tablespoons of blood will be collected from a vein in your arm during each telomelysin injection procedure and 6-8 weeks after radiation therapy if needed. A sample from the tissue that was collected at the time of your diagnostic biopsy will be sent to the biobank. A sample of tissue will be collected during each telomelysin injection procedure and 6-8 weeks after radiation therapy if needed.
2. Your sample will be stored in the biobank. There is no limit on the length of time we will keep your samples and research information. The samples will be kept until they are used for research or destroyed.
3. Researchers can only get samples from the biobank after their research has been approved by experts. Researchers will not be given your name or contact information.
4. Some of your genetic and health information may be placed in central databases for researchers to use. The databases will not include your name or contact information.

What are the risks in this optional sample collection?

- The most common risks related to drawing blood from your arm are brief pain and maybe a bruise.
- Generally, hospitals will keep some of your tissue. This tissue may be used to help treat your cancer in the future. There is a small risk that when this tissue sample is submitted to the biobank for this optional sample collection, your tissue could be used up.
- Your medical and genetic information is unique to you. There is a risk that someone outside of the research study could get access to your study records or trace information in a database back to you. They could use that information in a way that could harm you. Researchers believe the chance that someone could access and misuse your information is very small. However, the risk may increase in the future as people find new ways of tracing information.

- In some cases, this information could be used to make it harder for you to get or keep a job and get or keep health insurance. There are laws against the misuse of genetic information, but they may not give full protection. For more information about the laws that protect you, ask your study doctor or visit: https://www.genome.gov/10002328/

How will information about me be kept private?
Your privacy is very important to the study researchers and biobank. They will make every effort to protect it. Here are just a few of the steps they will take:

1. They will remove identifiers, such as your initials, from your sample and information. They will replace them with a code number. There will be a master list linking the code numbers to names, but they will keep it separate from the samples and information.
2. Researchers who study your sample and information will not know who you are. They also must agree that they will not try to find out who you are.
3. Your personal information will not be given to anyone unless it is required by law.
4. If research results are published, your name and other personal information will not be used.

What are the benefits to taking part in this optional sample collection?
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 to this optional sample collection?
There are no costs to you or your insurance. You will not be paid for taking part in this study. The research may lead to new tests, drugs, or other products for sale. If it does, you will not get any payment.

What if I change my mind about this optional sample collection?
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 biobank know. Then, any sample that remains in the biobank will be destroyed or returned to your study doctor. This will not apply to any samples or related health information that have already been given to or used by researchers.

What if I have questions about this optional sample collection?
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 answer below to show if you would or would not like to take part in each optional study:

Samples for known future studies:

I agree that my samples and related health information may be used for the laboratory (*study or studies*) described above.

YES NO

This is the end of the section about optional studies.

Contact for Future Research

I agree that my study doctor, or someone on the study team, may contact me or my doctor to see if I wish to participate in other research in the future.

YES NO

My signature agreeing to take part in the 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 and dated copy of this form. I agree to take part in the main study. I also agree to take part in any additional studies where I circled "yes".

Participant's signature

Date of signature

Signature of person(s) conducting the informed consent discussion

Date of signature