

Certification of Completion of the Informed Consent

IRB #

Title:

I have discussed the “Informed Consent for Participation in Research Activities” in its entirety for the above referenced research study, with the research participant listed below (or the research participant’s legally authorized representative). During the review of the consent form, the possible benefits, risks and discomforts involved in his/her participation on the study, as well as potential alternatives were reviewed.

The research participant has been encouraged to ask questions, and all questions asked by the participant have been answered. The research participant affirmed that he/she has received all information that he/she desires at this time, and a copy of the signed consent form has been provided to the participant.

PRINTED NAME of Person Obtaining Informed (Consenter)	SIGNATURE	TITLE	DATE	TIME

City of Hope National Medical Center
1500 East Duarte Road, Duarte, CA 91010

Consenter Certification of the Informed Consent

Version Date: 09-15-2020

Patient Identification / Label

Name :	Last name, First name
DOB :	mm/dd/yyyy
MRN # :	MRN Number

ADULT INFORMED CONSENT

COH Protocol #: 20742

TITLE: A Phase 2 Trial of Neoadjuvant Chemoradiation with Pembrolizumab followed by pembrolizumab with lenvatinib in esophageal/gastroesophageal junction squamous cell and adenocarcinomas

Version date: 11/30/2022

PRINCIPAL INVESTIGATOR: Vincent Chung, M.D.

24-HOUR TELEPHONE NUMBER: (626) 218-7133

DAY TIME TELEPHONE NUMBER FROM THE HOURS OF 8:00 AM TO 5:00 PM: (626) 218-9200

EXPERIMENTAL PARTICIPANT'S BILL OF RIGHTS

The rights below are the rights of every person who is asked to be in a research study, also known as an experiment or research study. As a research participant, you have the following rights:

1. To be told what the research study is trying to find out.
2. To be told what will happen to you and whether any of the procedures to be used are different from what would be used in standard practice.
3. To be told about the discomforts, side effects and risks of the things that will happen to you as part of the research study.
4. To be told if you can expect any benefit from participating in the research study.
5. To be told of the other choices you have and how they may be better or worse than being in the research study.
6. To be told what medical treatment is available if any complications arise.
7. To be allowed to ask any questions concerning the research study, both before agreeing to be in the study and during the course of the study.
8. To refuse to participate in the research study or to change your mind about participation after the study is started. To be informed that this decision will not affect your right to receive the care you would receive if you were not in the study.
9. To receive a copy of the signed and dated research study consent form.
10. To be free of pressure when considering whether you wish to agree to be in the research study.

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IRB NUMBER: 20742

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IRB APPROVED TO: 12/12/2023

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PRINCIPAL INVESTIGATOR: Vincent Chung, M.D.

You are invited to take part in a clinical trial, a type of research study, because you have esophageal cancer. We hope to learn if combining the immunotherapy drug pembrolizumab and a targeted therapy drug lenvatinib after you have finished radiation and chemotherapy is an effective treatment. Pembrolizumab will also be given during chemotherapy and radiation treatment. This research study is looking at combining pembrolizumab and lenvatinib therapy as a possible future treatment for this diagnosis.

Participants in this study will receive the above immunotherapy and targeted therapy and undergo surgery as part of their usual treatment or repeat endoscopies if surgery is not done. We will also obtain small samples of your tumor and some blood samples for laboratory tests to study the effects of this treatment on cancer cells and the immune system.

Participation is expected to last 10 weeks, as long as your cancer is not growing and you are not having any unmanageable side effects. The total duration of preparatory and follow up appointments for this study can encompass up to 3 years.

The major risks associated with study include possible additional side effects from pembrolizumab immunotherapy and lenvatinib targeted therapy such as fatigue, skin itching, rash, high blood pressure, shortness of breath, diarrhea, liver or kidney inflammation, and rarely low thyroid levels or blood clots.

You do not have to join this research study. You can choose to receive standard methods to treat esophageal cancer instead of participating on this study. If you are interested in learning more about this study, please continue to read below.

INTRODUCTION

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You are invited to take part in a clinical trial, a type of research study, because you have esophageal cancer. We hope to learn if this new treatment of pembrolizumab and lenvatinib being added to usual treatment can increase the effectiveness of inducing a complete remission for this cancer. This research study is looking at pembrolizumab and lenvatinib as a possible future treatment for this diagnosis.

This research study is sponsored by City of Hope and Merck. Merck is the company that makes the drugs being tested, pembrolizumab and lenvatinib, and is providing these drugs for the study.

It is expected that about 24 people will take part in this research study.

We encourage you to take some time to think this over, to discuss it with other people and your primary doctor, and to ask questions now and at any time in the future. Please take as much time as you need to read the consent form. If you find any of the language difficult to understand, please ask questions. If you decide to participate, you will be asked to sign this form. We will give you a copy so that you can refer to it while you are involved in this research study. If you choose not to participate in this research study, the research doctors will discuss other treatment options with you and/or refer you back to your primary doctor.

A. WHY IS THIS RESEARCH STUDY BEING DONE?

This research study is a Phase II clinical trial. Phase II clinical trials test the safety and effectiveness of an investigational (experimental) intervention to learn whether the intervention works in treating a specific disease. "Investigational" means that the intervention is being studied.

The current recommended treatment, or standard of care, for esophageal cancer that has not spread to other organs, is to give radiation therapy combined with chemotherapy prior to undergoing surgery. In certain cases and certain subtypes of esophageal cancer, if the cancer completely shrinks and becomes undetectable after radiation and chemotherapy, then surgery may not be needed and you will be monitored closely. However, not all esophageal cancers respond completely to radiation and chemotherapy. Some research studies suggest that radiation and chemotherapy may activate the immune system to attack the cancer, but esophageal cancers are able to evade or shield themselves from the immune system.

Pembrolizumab is an immunotherapy drug that works by harnessing the immune system to attack cancer. It has been found to be effective and is FDA approved for advanced melanoma, lung cancer, head and neck cancer, bladder cancer, Hodgkin lymphoma, stomach cancer, and cancers with high levels of the microsatellite instability (MSI) biomarker. Lenvatinib is another anti-cancer drug that works by stopping or slowing down the growth of cancer cells. It is currently FDA approved for thyroid

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cancer, kidney cancer, liver cancer, and endometrial cancer without high levels of the microsatellite instability (MSI) biomarker. Once daily dosing of lenvatinib combined with pembrolizumab is currently being developed for the treatment of relapsed breast cancer, ovarian cancer, gastric cancer, colorectal cancer, glioblastoma, and biliary tract cancers.

We are conducting this research study (which is a Phase II study) to determine if combining pembrolizumab and lenvatinib after chemotherapy with the addition of pembrolizumab and radiation therapy can be an effective treatment for esophageal cancer. We will also obtain small samples of your tumor and some blood samples for laboratory tests to study the effects of this treatment on cancer cells and the immune system. Your treatment on this study is expected to last 10 weeks, as long as your cancer is not growing and you are not having any unmanageable side effects.

B. WHAT IS INVOLVED IN THE STUDY?

If you decide to take part, this is what will happen:

Before the research starts (screening):

After signing this consent form, you will be asked to undergo some screening tests or procedures to find out if you can be in the research study. Many of these tests and procedures are likely to be part of regular cancer care and may be done even if it turns out that you do not take part in the research study. If you have had some of these tests or procedures recently, they may or may not have to be repeated.

- **A medical history**, which includes questions about your health, current medications, and any allergies.
- **Performance status**, which evaluates how you are able to carry on with your usual activities.
- **An assessment of your tumor** by one or more of the following standard assessment tools: X-ray, CT (Computerized Tomography) scan, MRI (Magnetic Resonance Imaging) or PET (Positron Emission Tomography) scans
- **Blood tests** to check your blood counts and organ function (about 2 teaspoons of blood will be drawn from a vein in your arm or port-a-cath if you have one)
- **Blood tests** to check the status of your disease (about 1 teaspoon of blood will be drawn from a vein in your arm or port-a-cath)
- **Urine test.** Urine will be collected from you for routine laboratory testing to monitor your general health.
- **Pregnancy test** if you are a woman of childbearing potential by drawing about ½ teaspoon of blood usually from a vein in your arm if a urine test is inconclusive.
- **An EKG (electrocardiogram)** to look at the electrical activity and rhythm of your heart.
- **An endoscopy and tumor biopsy** for research purposes to study the cancer and the immune system prior to start of treatment. The endoscopy can be performed during an endoscopic ultrasound that you will already need to complete staging and confirm the location of your

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esophageal cancer. You will sign a separate consent form for this procedure with the gastroenterologist.

If these tests show that you are eligible to participate in the research study, you will begin the study treatment. If you do not meet the eligibility criteria, you will not be able to participate in this research study.

Additional research procedures to be performed at the time of screening but not required to determine eligibility:

- **Blood tests** for research purposes to study the immune system and develop new blood markers to study the cancer (about 5 teaspoons of blood will be drawn from a vein in your arm or port-a-cath)
- **A stool test** for research purposes will be used to study the normal bacteria that live in your intestines and how they may impact the immune system. You will be provided a collection bag and swab kit by the research staff and instructed on how to swab some stool from a toilet hat during your screening visit.

Study Procedures:

If you are eligible to participate in this research study, the following test and procedures will occur. A chart summarizing the timing of these tests and procedures is also provided below. Some tests and procedures may be part of your standard of care. A research nurse and/or study coordinator will assist with scheduling these appointments.

- **Radiation therapy:** You will receive radiation therapy as a standard of care treatment as determined by your treating physicians. Radiation will be given once a day for up to 30 days on a weekday.
- **Chemotherapy with immunotherapy:** You will receive the chemotherapy drugs carboplatin and paclitaxel as a standard of care treatment as determined by your treating physicians. This usually occurs once a week given into your vein (intravenous infusion) for up to 5 infusions. Additionally, you will also receive 1 dose of the immunotherapy drug pembrolizumab, given once into your vein (via intravenous infusion) over about 30 minutes.
- **Tumor biopsies:** A second endoscopy to perform a biopsy to study the cancer and immune system after you completed radiation and chemotherapy will be performed.
- **Receive Pembrolizumab Study Drug:** Two weeks after you finish chemotherapy and radiation, you will be given the study drug, pembrolizumab, once into your vein (by intravenous infusion) over about 30 minutes.
- You may be pre-medicated with drugs to reduce the chance of having a sensitivity reaction to the study treatment. If you tolerate the study treatment without a reaction, then pre-medications may be changed by your doctor.
- **Take Lenvatinib Study Drug:** You will be provided and take the study drug, lenvatinib by mouth, or dissolved in water if you are unable to swallow, once a day starting on the same day

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as the first pembrolizumab infusion. You will continue this medication every day for up to 4 weeks and stopping the last dose 15 days prior to surgery or a follow up endoscopy if you are not undergoing surgery.

- **Clinical Exams:** During this visit you will have a physical exam and you will be asked questions about your general health and specific questions about any problems that you might be having and any medications you may be taking.
- **Performance status,** which evaluates how you are able to perform your daily usual activities.
- **Scans (or Imaging tests):** We will assess your tumor towards the end of the immunotherapy treatment by repeating a PET/CT scan.
 - **Blood tests** to check your blood counts and organ function (about 2 teaspoons of blood per blood draw will be drawn from a vein in your arm or a port-a-cath if you have one)
 - **Blood tests** to check the status of your disease (about 1 teaspoon of blood per blood draw will be drawn from a vein in your arm or port-a-cath)
 - **Blood tests** for research purposes to study the immune system and develop new blood markers to study the cancer (about 5 teaspoons of blood will be drawn from a vein in your arm or port-a-cath)
- **Urine test.** Urine will be collected from you for routine laboratory testing to monitor your general health.
- **Stool test:** You will be asked to provide a stool sample two more times during the study. You can provide the sample during the scheduled clinic visit or be given a collection bag and swab kit by the research staff and instructed on how to swab some stool from a toilet hat 1-2 days ahead of the scheduled day of treatment.

Other Medications: While you are receiving study treatment, you should not take other medications without first discussing them with the study doctor. These include high doses of steroid medications such as prednisone and dexamethasone, as well as herbal medications. The reason you should not take other medications is it may interfere with your study treatment.

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Research Study Calendar:

	Before starting treatment	Study treatment	Rest	Study Treatment			Surgery or Follow-up endoscopy	Follow-up of your health status
	Screening	6 weeks	Weeks 1-2	Week 3-6	Week 7	Week 8		
Medical History	X							
Physical Exam	X	X	X	X	X	X	X	X
Blood Tests	X	X	X	X	X	X	X	X
Research Blood Tests	X		X			X	X	X
Research Stool	X		X			X	X	
PET/CT scan	X				X			
Tumor Biopsy (for research purposes)	X		X				X	
Pregnancy Test	X							
Urine Test	X							
EKG	X							
Chemotherapy and Radiation treatment		X						
Receive Pembrolizumab		X		X				
Take Lenvatinib				X				

Planned Follow-up:

We would like to keep track of your medical condition for the rest of your life. We would like to do this by calling you on the telephone once every 3 months to see how you are doing. Keeping in touch with you and checking your condition every 3 months helps us look at the long-term effects of the research study.

C. HOW LONG WILL I BE IN THIS RESEARCH STUDY?

You will be on study treatment for about 10 weeks provided your cancer is not growing and you are not having any unmanageable side effects from treatment. The total duration of preparatory and follow up appointments for this study can encompass up to 3 years. However, these appointments are inclusive of standard of care check-ups and tests to monitor your disease.

D. WHAT ARE THE POSSIBLE RISKS AND DISCOMFORTS?**INFORMED CONSENT AND AUTHORIZATION**

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All cancer treatments can have side effects, which can range from mild and reversible to severe, long lasting and possibly life-threatening. There is a great deal of variability among side effects of different cancer treatments and between individuals. In a research study, all of the risks or side effects may not be known before you start the study. **You need to tell your doctor or a member of the study team immediately if you experience any side effects.**

Everyone in the research study will be watched carefully for side effects. You will be monitored during the administration of study drugs to keep track of your blood counts and organ function, particularly your kidney, liver, and thyroid function. If you experience side effects, they may go away after you stop taking the study drug. Some side effects can be mild; but others can be long lasting and may never go away as noted below. Some may be life-threatening or fatal and are noted below.

Possible risks and discomforts you could experience during this study include:

Risks associated with taking pembrolizumab and lenvatinib together:

Commonly Occurring Side Effects (in at least 1 in 10 research participants)

- Having any treatment-related side effects as listed below
- High blood pressure

Occasional Side Effects (less than 1 in 10 research participants)

- Fatigue
- Diarrhea (loose stool)
- Increase in a pancreatic enzyme, lipase, that catalyzes the breakdown of fats to fatty acids and glycerol or other alcohols
- Weakness
- Severe skin reaction
- Low sodium levels
- Protein in urine
- Feeling confused or forgetful
- Condition where a clot of material (usually blood) blocks blood from getting to the lungs; usually caused by a blood clot that starts somewhere else in the body and travels to the lungs
- Nausea
- Liver damage [hepatotoxicity and hepatitis]
- Severe loss of blood from ruptured blood vessel [hemorrhage]
- Condition in which the adrenal glands do not produce adequate amounts of steroid hormones, primarily cortisol; but may also include impaired production of aldosterone (a

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mineralocorticoid), which regulates sodium conservation, potassium secretion, and water retention

- Joint pain [arthralgia]
- Decreased weight
- Low magnesium levels
- Stomach pain
- Cardiac dysfunction and QT prolongation, where the heart muscle takes longer than normal to recharge between heartbeats
- Inflammation of kidneys [nephritis]
- Increase in amylase, a protein made by the pancreas and by glands in and around your mouth and throat to help break down carbohydrates and starches into sugar
- Inflammation of the inner lining of the colon
- Feeling lightheaded
- Diminished blood flow providing insufficient oxygen for the cells in the digestive system, causing pain and possible damage to the colon [ischemic colitis]

Rarely Seen Serious Side Effects (less than 1 in 100 research participants)

- Low thyroid levels [hypothyroidism]
- Muscle pain
- Dehydration (body doesn't have as much water as it needs)
- Shortness of breath
- Mouth pain
- Low potassium levels
- Lack of enough healthy red blood cells to carry adequate oxygen to your body's tissues [anemia]
- Inflammation of the pancreas
- Low blood pressure
- Sudden interruption of blood flow to an organ or body part due to a clot (usually blood) that has come from another part of the body
- High potassium levels
- Complete blockage of the small intestine
- Hole in the wall of any part of the gastrointestinal tract (which includes the esophagus, stomach, small intestine, and large intestine), causing severe stomach pain and tenderness
- Inflammation of gallbladder
- Slurred speech
- Low calcium levels
- Severe infection that causes your immune system to attack your body; as a result of that attack, septic shock can occur and result in death
- Acute or chronic inflammation of the pituitary gland
- Low count of white blood cells called neutrophils, increasing susceptibility of infection

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- Condition where air leaks into the space between your lung and chest wall; as a result, this air pushes on the outside of your lung and makes the lung collapse
- Sores developing inside the rectum
- Decreased appetite
- Swelling of mouth and lips [stomatitis]
- Change in voice quality [dysphonia]
- Vomiting
- Headache
- High fat levels in your blood

Since the effect of the study treatment taken with other medications may not be known, it is important that you tell the research doctor about all prescription and non-prescription drugs, herbal preparations and nutritional supplements that you are taking or planning to take. There may also be some foods that you should avoid while on this research study and your research doctor will review this information with you.

Risks Associated with Blood Draw

Risks of blood draws include mild pain or discomfort, bruising and swelling around the puncture site, dizziness or fainting, or infection (rare).

Cancer research often includes biopsies, scans, x-rays that are also provided as routine care. The following describes the side effects of procedures done only for the purposes of research.

Risks Associated with Biopsies:

Biopsies are normally performed with direct visualization during endoscopy. Each procedure requires a separate consent prior to the biopsy. The risks may include:

- Pain and discomfort. The amount of pain and discomfort will vary, depending on the location of the biopsy site. These risks can be discussed with the study doctor.
- Minor bleeding at the biopsy site.
- Tenderness at the biopsy site.
- Scarring at the biopsy site.
- Rarely, an infection at the biopsy site.

Uncommonly, complications from biopsies can be life threatening. As with any interventional procedure, other potentially serious complications from bleeding or organ damage may occur. These might require additional surgical intervention.

Risks Associated with Contrast Agents Used During Scans:

There is a small risk with using a contrast agent that is injected into a vein during the CT scan or MRI if you are unable to undergo a CT scan. The contrast agent is a special dye that highlights organs, blood

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vessels or tissue to make them more visible. Depending on the type of contrast agent that is used, it may cause decreased kidney function or worsen kidney function in people who already have decreased kidney function. Therefore, we will monitor your kidney function closely while you participate in this study. If there is any change in your kidney function, we may have to remove you from the study.

Uncommonly, some people have allergic reactions (such as hives and itching) to the contrast agent. Serious reactions (for example, drop in blood pressure, difficulty breathing or severe allergic reaction and death) are rare.

Incidental Findings:

It is possible the research procedures could find a medical problem unrelated to the purpose of this study that you did not know about before. If during the research procedures we learn information that may be important for you to know about, such as the possibility of a previously unknown medical condition, we will tell you. You may authorize the release and communication of the findings to your personal doctor. These findings may require additional testing or treatment. You will be responsible for the cost of any additional tests or related treatment.

Reproductive Risks:

The drugs used in this research study may affect a fetus. While participating in this research study, you should not become pregnant or father a baby, and should not nurse a baby. We can provide counseling about preventing pregnancy for either male or female study participants. Let your doctor know immediately if you become pregnant or find out that you are going to be the father of a child.

In the event that partner becomes pregnant, it is critical to share information regarding your participation in this research study with that person. Your research doctor should also be told if this happens. The study sponsor may want to collect data on your partner's pregnancy.

You must use birth control while on this study. These are some birth control measures that you can use: hormonal contraceptives (birth control pills, patches, implants, rings, or injections), barrier methods (such as a condom or diaphragm) used with a spermicide, an intrauterine device (IUD), or surgical sterilization (hysterectomy or tubal ligation for women, vasectomy for men).

If you are breastfeeding and do not want to stop, you may not take part in this study.

Other Risks:

This study will involve analyzing the genes in the cancer and may lead to incidental discoveries of your genetic information. A new federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:

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- Health insurance companies and group health plans may not request your genetic information that we get from this research.
- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.
- Employers with 15 or more employees may not use your genetic information that we get from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment.

Be aware that this new federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

Some people may find it upsetting to learn that they have certain mutations or errors in genes that could lead to future health problems for themselves or their children.

E. WILL YOU RECEIVE NEW INFORMATION ABOUT THIS STUDY?

During the research study, you will be notified of newly discovered side effects or significant findings, which may affect your health or willingness to participate. You may be asked to sign a new consent form that shows that you have been informed of new information relating to this research study.

F. HOW WILL YOUR INFORMATION BE KEPT CONFIDENTIAL?

We will take measures to protect the confidentiality and security of all your personal information, but we cannot guarantee complete confidentiality of study data. However, it is impossible to guarantee that information about you will not be mistakenly released. If information learned from this study is published, you will not be identified by name.

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 and 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.

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.

G. WHAT ARE THE POSSIBLE BENEFITS OF TAKING PART IN THIS RESEARCH STUDY?

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We cannot and do not guarantee that you will receive any benefits from this study. The possible benefit of the study drug in the treatment of esophageal and stomach cancer is not fully known. If you decide to participate in this study, your health will be monitored very closely. By being in this study, you will give doctors more information about how well the study drug works. It may help doctors understand your condition better and may help future patients with this medical condition.

H. WHAT OTHER OPTIONS ARE THERE?

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

- You may choose to have the usual approach for your cancer,
- You may choose to take part in a different study, if one is available, or
- You may choose not to be treated for cancer but you may want to receive comfort care to relieve symptoms.

I. ARE THERE ANY PAYMENTS TO YOU FOR TAKING PART IN THE STUDY?

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

J. WHAT ARE THE COSTS?

The investigational drugs, pembrolizumab and lenvatinib, will be provided free of charge by City of Hope and Merck.

Chemotherapy and radiation therapy to treat your cancer is a standard of care procedure and will be the responsibility of you and/or your insurance carrier.

Other standard of care procedures provided to you will be the responsibility of you and/or your insurance carrier. You will be responsible for all copayments, deductibles, and other costs of treatment and diagnostic procedures as set forth by your insurance carrier. You and/or your insurance carrier will be billed for the costs of treatment and diagnostic procedures in the same way as if you were not in a research study.

However, neither you nor your insurance carrier will be responsible for the research procedures related to this study.

Financial counselors are available Monday through Friday, 8:00 a.m. to 5:00 p.m. For additional questions, please call City of Hope Financial Support Services: 626-256-HOPE (4673), extension: 80258.

The National Cancer Institute provides an online resource to help people participating in cancer clinical trials understand which services their insurance company is required by law to pay. This can be found at the website below or can be provided by the study team:
www.cancer.gov or 1-800-4-CANCER (1-800-422-6237)

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K. WHAT HAPPENS IF YOU GET INJURED AS A RESULT OF THIS STUDY?

If you think you have been hurt by taking part in this study, tell the person in charge of this research study as soon as possible. The research doctor's name and phone number are listed in this consent form. City of Hope will offer you the care needed to treat injuries directly resulting from taking part in this research. This care will be billed to you or your insurance company. You will be responsible for deductible and co-payments, or any costs not paid by your insurer. There are no plans to pay you or give you other compensation for the injury. You do not give up your legal rights by signing this form.

L. WHAT ARE YOUR RIGHTS IF YOU TAKE PART IN THIS STUDY AND WHAT WILL HAPPEN IF YOU DECIDE NOT TO PARTICIPATE?

Your participation in this research study is voluntary. You are free to withdraw your consent for participation in this study without any loss of benefits, penalty, or interference with any future treatment at City of Hope.

You can decide to stop at any time and you may still be treated at your hospital or clinic. Tell your study doctor if you are thinking about stopping or decide to stop. You should talk to the doctor about leaving the study before you decide so that he/she can find out if you are having any side effects from study treatment. Another reason to tell your doctor that you are thinking about stopping is so that he/she can talk to you about any other treatments that could be helpful to you.

If you decide to stop being in this study, you will still be asked to come back to the hospital or clinic for the end of treatment tests described above. You may also be asked to take part in the follow-up phone calls and/or visits. This information is important to make sure that there are no lasting side effects from the study treatment and to see if your cancer got better, stayed the same, or got worse after treatment.

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M. CAN YOU BE REMOVED FROM THE STUDY?

You may be removed from this study without your consent for any of the following reasons: you do not follow the investigator's instructions, at the discretion of the investigator or the sponsor, your disease gets worse, or the sponsor closes the study. If this happens, the investigator will discuss other options with you.

N. WHOM DO YOU CALL IF YOU HAVE QUESTIONS OR CONCERNS?

The principal investigator, Dr. Vincent Chung or a colleague, Dr. _____, responsible for your care or treatment, has offered to and has answered any and all questions regarding your participation in this research study. If you have any further questions or in the event of a research related injury, you can contact Dr. Vincent Chung at (626) 471-9200 or Dr. _____ at (626) 256-HOPE (4673) ext. _____.

This study has been reviewed and approved by the Institutional Review Board (IRB). If you have any questions regarding your rights as a research participant, you may contact a representative of that Board, from the Office of Human Research Subjects Protection, at (626) 256-HOPE (4673) ext. 62700.

O. OPTIONAL BIOBANKING OF YOUR LEFTOVER SAMPLES:

As mentioned above, we will be collecting samples (blood and tissue) from you. There may be leftover (unused) samples at the end of the study. We would like to ask you what to do with any leftover samples that you provided to the study.

Your leftover tissue samples from this study may be used for future research, including genetic research, to learn about health and disease. The future research that may be done is unknown at this time and neither you nor your doctors would be informed of the results from research use of your samples. Storing tissue samples for future research is called "biobanking". When samples are stored in a biobank, some medical information about you is also stored. Samples and information are linked together and labeled with a code that does not include your name or other direct identifiers. The key to the code will stay here at City of Hope. The results from these future research studies will not become part of your medical record.

Coded samples and medical information may be shared with researchers at other institutions. Researchers will not be given your name or any other information that could directly identify you. Researchers are trying to learn more about cancer, diabetes, and other health problems. Much of this research is done using samples from your tissue, blood, urine, or other fluids. Through these studies, researchers hope to find new ways to prevent, detect, treat, or cure health problems.

If you choose to take part, a sample of tissue from your previous biopsy will be collected. The researchers ask your permission to store and use your samples and related health information (for example, your response to cancer treatment, results of study tests and medicines you are given) for

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medical research. The research that may be done is unknown at this time. Storing samples for future studies is called “biobanking”.

WHAT IS INVOLVED?

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

- 1) A sample from the tissue that was collected at the time of your surgery will be sent to the Biorepository (Biobank).
- 2) Your sample, and possibly specimens left over from diagnostic and clinical tests and some related health information may be stored in the Biorepository (Biobank), along with samples and information from other people who take part. The samples will be kept until they are used up. Information from your medical record will be updated from time to time.
- 3) Qualified researchers can submit a request to use the materials stored in the Biorepository (Biobank). An ethics committee review will be done 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.
- 4) 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.
- 5) Some of your genetic and health information may be placed in central databases that may be public, along with information from many other people. Information that could directly identify you will not be included.

WHAT ARE THE POSSIBLE RISKS?

- 1) 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.
- 2) 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.
- 3) 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.

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:

- 1) 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.

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- 2) The list that links the unique code to your name will be kept separate from your sample and health information. Any Biorepository (Biobank) staff with access to the list must sign an agreement to keep your identity confidential.
- 3) Researchers to whom City of Hope 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.
- 4) Information that identifies you will not be given to anyone, unless required by law.
- 5) If research results are published, your name and other personal information will not be used.

WHAT ARE THE POSSIBLE BENEFITS?

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.

Some of this research may result in new inventions or discoveries that may be of potential commercial value and may be patented and licensed for the development of new products. Donors of blood, tissue and other biological materials do not retain any property rights to the materials. Therefore, you would not share in any money or other benefits that any entity might receive for these inventions or discoveries. Your decision not to allow storage or future use of your tissue or specimens will not affect your ability to participate in this study.

WHAT IF I CHANGE MY MIND?

If you agree to allow your leftover specimens to be used for future research, you can change your mind at any time. Your decision not to allow storage or future use of your tissue or specimens will not affect your ability to participate in this study. If you change your mind, please ask for the “Withdrawal of Informed Consent for Use of Leftover Specimens for Future Research” for COH Protocol #20742: A Phase 2 Trial of Neoadjuvant Pembrolizumab in Combination with Lenvatinib in Patients with Non-Metastatic Esophageal/Gastroesophageal Squamous Cell and Adenocarcinomas Treated with Neoadjuvant Chemoradiation: A Window-Of-Opportunity Study. Please sign the withdrawal form and send it to the principal investigator of this study at City of Hope. Once City of Hope processes your signed withdrawal of informed consent, your leftover specimens will not be used in any new research. At that time, any of your existing leftover samples and/or genetic material will be destroyed. Samples and medical information from the biobank that have already been used for research cannot be retrieved.

WHAT IF I HAVE MORE QUESTIONS?

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If you have questions about the use of your samples for research, contact the study doctor, Dr. Vincent Chung, at (626) 218-9200

Please circle your answer to show whether or not you would like to take part in this option

Samples for Future Research Studies:

My leftover samples from this study and related information may be kept in a biobank at City of Hope for use in future medical research.

YES _____ NO _____

This is the end of the section about optional studies.

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P. SIGNATURE SECTION

SIGNATURE FOR CONSENT: By signing this consent form, you are making a decision to participate in this research study. Your signature on this informed consent form indicates that you:

1. Have read and understood the information in this form.
2. Have had the information in this form explained to you.
3. Have had a chance to ask questions and these questions were answered to your satisfaction.
4. Have been informed that you will receive a copy of this signed consent form, which includes the "Experimental Subject's Bill of Rights."

I hereby agree to be a research participant in this research study:

Research Participant's Signature	Date	Time
(Date and time must be in research participant's handwriting)		

Print Research Participant's Name

INDIVIDUAL OBTAINING CONSENT SIGNATURE

Signature of Individual Obtaining Consent	Date	Time

Print Name of Individual Obtaining Consent

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NOTE: To determine who should sign below, review the guidance document, *Consenting Non English Speaking Research Participants (Pediatric or Adult) – Who Signs What?*

Interpreter: By signing here, I attest that I have acted as interpreter and facilitated this consent process.

Interpreter's Signature

Date

Time

Print Interpreter's Name

FOR USE WHEN A WITNESS IS REQUIRED:

Witness: By signing here, I attest that I witnessed the consent process and that the entire consent form was discussed.

Witness' Signature

Date

Time

Print Witness' Name

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A Phase 2 Trial of Neoadjuvant Chemoradiation with Pembrolizumab followed by pembrolizumab with lenvatinib in esophageal/gastroesophageal junction squamous cell and adenocarcinomas

AUTHORIZATION TO USE AND DISCLOSURE OF YOUR PROTECTED HEALTH INFORMATION (PHI) FOR PURPOSES OF THIS STUDY:

- I. **Purpose of this Authorization:** The information about your health is something that is protected by law and cannot, except for certain purposes, be disclosed (shared) without your permission. As part of this research, you are agreeing to allow City of Hope to use and share with others your protected health information ("PHI"), as needed for the research. If you agree to participate in the study named above (called the "Study"), you must sign this authorization in addition to the *Study Consent Form*.

- II. **The Information About You that is Covered By this Authorization:** PHI refers to information that we maintain about you that identifies you and includes the information contained in your medical record. Your medical record consists of information related to your health and the treatment we provide to you, such as your medical history, the results of physical exams, blood tests, x-rays and other diagnostic and medical procedures. If you sign this authorization, you are allowing City of Hope and the individuals indicated below to use and share any PHI we maintain about you that is required for your participation in the Study.

- III. **Purposes for Uses and Sharing of your PHI; Who Will Use, Share and Receive your PHI:** Your PHI will be used and shared with others for the purpose of doing this research as described in the *Study Consent Form*. Your PHI will also be used to keep the research sponsor informed about this Study, for reporting to those individuals and authorities responsible for overseeing our research activities to make sure that the activities are properly conducted, and to report to regulatory agencies as required by the Study.

The people authorized to use and share your PHI for purposes of the Study include the Principal Investigator and the research staff supporting the Study; your City of Hope physicians and the health care team; and the Health Information

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Management Services Department (i.e., Medical Records Department). This also includes any agents or contractors used by these individuals or groups for purposes of conducting or managing this Study. At the City of Hope, the Institutional Review Board (“IRB”), and other City of Hope research regulatory committees will have access to your PHI as necessary to monitor research.

You are also allowing your PHI to be shared with the Office for Human Research Protections (“OHRP”) and with any person or agency as required by law. In addition, certain other regulatory agencies, including, the Food and Drug Administration (“FDA”) and the National Cancer Institute (“NCI”), will have access to your PHI.

Use and disclosure of your PHI may also continue for as long as the sponsor needs to maintain the PHI for purposes of obtaining approval of the drug from the FDA or for other FDA reporting.

Your information will also be shared, with City of Hope and Merck, the “Research Sponsor” and its employees, agents or contractors who are involved in the administration of the Study.

This study also involves tissue banking (storing your specimens such as blood or tumor tissue). The tissue banked as part of this study will be kept at City of Hope. The banked tissue will be stored indefinitely.]

This authorization will allow us to use and share your PHI for the Study. No other additional uses and disclosures other than for the purposes of the Study is included in this authorization. City of Hope’s Notice of Privacy Practices will continue to protect your non-Study information. If necessary, another separate permission will be obtained from you for any non-Study uses or sharing of your PHI.

- IV. Expiration of this Authorization:** This authorization to use and share your PHI will expire twenty-five (25) years from the date that you sign this authorization.
- V. Further Sharing of Your PHI:** Your privacy is important and this is the reason for having rules which control who can use or see your PHI. City of Hope maintains control over your PHI at present, but once we share this information with a third

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party (for example, an individual or agency outside of the City of Hope), then it is no longer possible to maintain the same level of protection. The persons outside our control may not be governed by federal or state privacy laws and it is possible that they could share your PHI with others for whom you have not given permission.

The information from this Study may be published in scientific journals or presented at scientific meetings but your identity will be kept confidential.

- VI. Your Rights Under this Authorization:** You may cancel this permission to use and share your PHI at any time by contacting City of Hope's Privacy Officer at (626) 256-HOPE (4673) ext. 64025. You should ask for the form, *Revocation (Cancellation) of Authorization for Use of Protected Health Information for Research*. Fill this form out and return it as the form instructs. Your cancellation begins when the Health Information Management Department of City of Hope receives this form. If you cancel this authorization to use and share your PHI, you will no longer be able to participate in the Study. This is because the research under this Study cannot be conducted without your PHI.

Once you cancel your permission to use and share your PHI, the researchers and others involved in conducting the Study will no longer be able to use or share your PHI for this research. PHI already used and shared up to this point as part of this Study will continue to be used for purposes of this research. This means that any uses of your PHI and any PHI shared about you by City of Hope prior to receiving your cancellation (revocation) form cannot be taken back. While no further PHI about you will be shared for the Study, your PHI already shared will continue to be used in the overall Study.

- VII. Signing this Authorization is Your Choice:** Your ability to obtain care at the City of Hope will not be affected by your decision to sign this authorization form. You will be able to continue to receive health care at City of Hope if you choose not to sign this authorization form or if you sign this form and later cancel your permission to use and share your PHI.

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If you agree to the use and sharing of your PHI, please sign below. You will be given a copy of this authorization form.

Research Participant's Signature Date Time
(date and time must be in research participant's handwriting)

Print Research Participant's Name

INDIVIDUAL OBTAINING CONSENT SIGNATURE

Signature of Individual Obtaining Consent Date Time

Print Name of Individual Obtaining Consent

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Interpreter: By signing here, I attest that I have acted as interpreter and facilitated this consent process.

Interpreter's Signature

Date

Time

Print Interpreter's Name

Witness: By signing here, I attest that I witnessed the consent process and that the entire consent form was discussed.

Witness' Signature

Date

Time

Print Witness' Name

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