Official Title:	**A Phase 1 Study of Talimogene Laherparepvec and Panitumumab in Patients with Locally Advanced Squamous Cell Carcinoma of the Skin (SCCS)**
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[redacted]

SUBJECT CONSENT TO TAKE PART IN A RESEARCH STUDY

TITLE OF STUDY: A Phase I Study of Talimogene Laherparepvec and Panitumumab in Patients with Locally Advanced Squamous Cell Carcinoma of the Skin (SCCS)

PROTOCOL NUMBERS: [redacted]

Principal Investigator: [redacted]

STUDY SUMMARY: This consent form is part of an informed consent process for a research study and it will provide information that will help you decide whether you want to take part in this study. It is your choice to take part or not.
The purpose of the research is to determine the safety and benefit of the combined treatment with talimogene laherparepvec (also known as IMLYGIC®) and panitumumab in patients with advanced squamous cell cancer of the skin.
If you take part in the research, you will be asked to sign this document, go through laboratory and medical tests to verify your eligibility to enter this study, receive the experimental combination of drugs (Talimogene laherparepvec and panitumumab) and undergo laboratory tests and study procedures on specified days during the study period, complete end of study evaluations and tests, and participate in post-study follow up every 12 weeks for 2 years. Your

time in the study will take approximately 4-6 hours during pre-study, study and end of study visits.
Possible harms or burdens of taking part in the study may be many side effects or toxicities known and/or unknown for the drugs you take in this study (details provided later in the document). You may feel discomfort and/or pain during some of the tests or procedures in the study. Your condition may not improve and could even worsen if you take part in this study.
Possible benefits of taking part may be improvement in your condition and slowing or stopping the growth of your cancer, if the drugs work. Information learned from the study may help other people in the future. However, it is possible that you might receive no direct personal benefit from taking part in this study.
Alternatives to taking part in the research study are a marketed drug or treatment with a different investigational drug, other chemotherapy regimens, surgery to relieve distressing symptoms or radiation treatment, or comfort care (pain medication and other support) or non-traditional medical care.
Your alternative to taking part in the research study is not to take part in it and pursue other available treatment options as described above after talking with your physician.

The information in this consent form will provide more details about the research study and what will be asked of you if you choose to take part in it. If you have any questions now or during the study, if you choose to take part, you should feel free to ask them and should expect to be given answers you completely understand. After all of your questions have been answered and you wish to take part in the research study, you will be asked to sign this consent form. You are not giving up any of your legal rights by agreeing to take part in this research or by signing this consent form.

Who is conducting this research study?

[redacted]

Sponsor of the study:
Amgen, Inc. is the external sponsor of this research study. As a sponsor, [redacted].

The costs that are usually covered include things such as research laboratory tests required by the study and the costs of collecting all of the information required by the study.

Why is this study being done?
The purpose of this study is to:

- Primary:
  - To determine the safety of the combined treatment of Talimogene laherparepvec and panitumumab.
  - To determine the preliminary effectiveness (also known as efficacy) of the combined treatment of Talimogene laherparepvec and panitumumab, in comparison to single-drug panitumumab (historical effectiveness).
- Secondary:
  - To assess the effectiveness of panitumumab in combination with intratumoral Talimogene laherparepvec in terms of non-advancing or growing (progression-free) survival at 12 months.
  - To measure the improvement in conditions, signs and symptoms of your disease (including whether disease has had a complete response) to panitumumab combined with Talimogene laherparepvec.
  - Assess the response of injected and non-injected tumor sites after panitumumab and Talimogene laherparepvec.
  - See the time it takes to first-time (initial) response.
  - See how long responses to the drugs last.

This is a research study to test drugs (panitumumab and Talimogene laherparepvec) that have been approved for use in certain types of cancer. Panitumumab is FDA-approved for use in patients with wild-type RAS (defined as wild-type in both KRAS and NRAS as determined by an FDA-approved test for this use) in metastatic colorectal cancer (mCRC). The safety and optimal dosing of Talimogene laherparepvec was established in melanoma, and it is an FDA-approved agent for metastatic melanoma. However, these drugs have not been approved for your cancer, and are therefore, experimental. "Experimental" means that the study drug is currently being tested. These drugs are not approved by the U.S. Food and Drug Administration (FDA) for treatment of your condition.

Who may take part in this study? And who may not?
If you decide that you want to be in this study and you sign this consent form, you will have some procedures done to see if you are eligible to be in this study. If you are eligible, you will be enrolled in the study.

In order to be eligible for participation in this trial, you must/have

1) Be willing and able to provide written informed consent/assent for the trial.
2) Age 18 years or greater.
3) Microscopically confirmed skin cancer (a type known as SCCS) that is a) locally advanced or metastatic for which curative surgery or radiation would be difficult or impossible, or b) recurrent after initial surgery, chemotherapy, or radiation therapy, or c)

considered to have aggressive features.

4) Tumor suitable for direct or ultrasound-guided injection (more than 10 mm in diameter).
5) Cancer disease with daily working performance of fully active or restricted to light work (known as ECOG Performance Status 0, or 1, or 2).
6) No prior treatment with panitumumab or Talimogene laherparepvec for advanced disease.
7) Adequate organ function
8) Female patients of childbearing potential should have a negative pregnancy test within 72 hours prior to receiving the first dose of study medication.
9) Female patients of childbearing potential should be willing to use 2 methods of birth control or be surgically sterile, or abstain from heterosexual activity for the course of the study through 120 days after the last dose of study medication.
10) Male patients should agree to abstinence or use of an adequate method of contraception starting with the first dose of study therapy through 120 days after the last dose of study therapy.

There may be reasons why you are not allowed to take part in this study. Some of these reasons include:

1) Age <18 years.
2) Pregnant women.
3) Tumor not suitable for direct or ultrasound-guided injection.
4) Prior treatment with Talimogene laherparepvec for advanced disease.
5) Patients with active, uncontrolled infections including active herpetic infections or chronic herpetic infections requiring anti-viral therapy (e.g., acyclovir).
6) Patients without adequate organ function.
7) History of allergic reactions attributed to compounds of similar chemical or biologic composition to panitumumab or Talimogene laherparepvec.

The study doctor or staff will discuss these and any other reasons why you may not be allowed to enter the study.

Why have I been asked to take part in this study?
You are being asked to take part in this study because it is believed that you have a type of tumor that may respond to treatment with Panitumumab and Talimogene laherparepvec.

How long will the study take and how many subjects will participate?
Up to 30 people may enroll in the study. The estimated duration of the study will be 24 to 30 months. You may receive study treatment for up to two years, as long as your disease is not getting worse or you do not have serious side effects.

Upon study completion or early withdrawal, it is important for you to speak with your study doctor to arrange follow-up care.

What will I be asked to do if I take part in this research study?

Before you begin study treatment:
If you agree to take part in this study, you will first sign this "Subject Consent to take part in a research study" before any study-related procedures are performed, including stopping use of medication not allowed in this study.

Before you are enrolled in the study, you will undergo certain tests to ensure that it is safe for you to go on the study. Most of these exams, tests, or procedures are part of regular cancer care and may be done even if you do not take part in this study. If you have had some of these tests recently, they may not need to be repeated. These tests and procedures, for example baseline laboratory, blood tests, and EKG (electrocardiogram), need to be done within 14 days before you receive your first study treatment. Tests such as tumor assessment (evaluation of cancer disease), radiology scan tests, and first tumor biopsy need to be done within 30 days of your first study treatment.

In addition,

- Tell your study doctor before starting on this study about all of the medicines you are taking or have recently taken (over-the-counter medications, supplements, prescription medications, or illegal drugs).
- If your blood tests show that you have liver lab results that are not normal, the study doctor or staff will ask you to provide additional samples of blood for testing to find out why your liver lab results are not normal. If you do decide to provide the samples, the study staff will discuss with you the amount of the additional samples of blood that will be taken and the tests that will be performed on the blood.
- The results of all of your blood tests, just like all other laboratory test results, will be provided to the Sponsor.
- It is your decision whether you provide the additional samples and have these tests performed. However, if you decide not to provide the additional samples, you may need to leave the study for your own safety (as the cause of your abnormal liver lab results may not be able to be determined without them).

While on study treatment:
When all of the above tests have been completed, you have been found eligible to enter this study, and you agree to participate, you will be scheduled to begin treatment on this study.

- You will receive study drug as below.
  - Talimogene laherparepvec will be administered as a single agent on day 1 (week 1), and thereafter in combination with Panitumumab on day 22 (week 4), and to be continued on weeks 6, and every 2 weeks thereafter.
  - The total volume of Talimogene laherparepvec to be injected will be based on investigator evaluation of injectable lesions and tumor size. The maximum volume of

Talimogene laherparepvec administered at any dose is 4.0 mL (a little less than a teaspoon) for any individual lesion. The maximum dose in any one treatment is 4.0 mL (a little less than a teaspoon).

- The recommended dose of panitumumab, 6 mg/kg, is administered as an intravenous infusion over 60 minutes, every 14 days. If the first infusion is tolerated, subsequent infusions are administered over 30 to 60 minutes. Doses higher than 100 mg will be administered over 90 minutes.
- **Your treatment may be withheld if you experience serious side effects.**

- Study Tests/Procedures
  - These exams, tests, and procedures are being done to evaluate your health and response to the study therapy. At each of these study visits you will be asked how you are feeling, if you have had any side effects, if you may be pregnant, if you have had any medical procedures, and about any medications you are taking.
  - It is important you check with your study doctor before starting any new medications. Taking other drugs (including alcohol, over-the-counter medications, herbal preparations, illegal drugs, or nutritional supplements) may cause additional side effects or even life-threatening reactions when combined with the drugs being used in this study.
  - If you experience side effects, changes in your health and/or changes in medications between study visits, you will be asked to contact your study doctor or a study team member.
  - You will have the following tests, procedures, and assessments done at the timepoints below. The study doctor or staff will discuss with you when and on which days to report to the clinic. It may be necessary to perform these procedures at unscheduled time points if considered clinically necessary by study doctor.

Evaluation	Day 1 (Week 1)	Day 22 (Week 4)	Day 36 (Week 6) & every 2 weeks during Tx Phase	Day 64 +/- 1 week
History & Physical Exam, Medical status, Tumor Site Assessment[1]	X	X	X	
Talimogene laherparepvec Treatment	X	X	X	
Panitumumab Treatment		X	X	
Toxicity Assessment	X	X	X	
Photo of Tumor				X[2]
Surgical evaluation				X[2]
Blood tests	X	X	X	
Cancer Scan Assessments[1]				X[1]
Other Research tests				X[3]

1- Tumor assessments as indicated by study doctor use scans (e.g. PET/CT, CT C/A/P, MRI; these are different scans that evaluate your tumor) and as needed. First assessment to be followed by evaluation by surgery for complete surgical resection. Photos and scans to be completed at each restaging time point. Surgeon will assess optimal timing of procedure once therapy initiated. Patients who did not have surgery will have radiologic scan assessments every 12 weeks.

2- Photo of tumor with restaging time points and Surgical evaluation. Decision may be made to proceed with 3 more cycle of systemic therapy if it is thought tumor will continue to respond.

3- Research tests for blood cells will be done on peripheral blood and tumor tissue. Biopsies of your tumor will be obtained prior to therapy beginning, after therapy is completed at surgery if surgery is recommended, or as a separate biopsy if not; and within 30 days of disease progression if this occurs.

- Overview of Possible Molecular Investigations
  - The laboratory investigations using your blood and/or tumor samples in this study will be detailed. The results of these tests may provide information on how and if your tumor is showing response to therapy or resistance.

- Tumor Evaluations
  - Standard tumor assessments during the study will be performed by the study doctor using various scan studies (e.g. PET/CT, CT C/A/P, MRI). Photos and scans are to be completed at each restaging time point. Surgeon will assess optimal timing of procedure once therapy initiated. Patients who did not have surgery will have cancer scan assessments every 12 weeks.
  - If you discontinue treatment for any reason other than progression, tumor assessments will be done every 12 weeks (± 14 days) for the duration of study and disease monitoring for 24 months.
  - If the scan assessment of your cancer (by CT or MRI) shows that your cancer may have worsened, you may be asked to have another scan assessment performed 4-6 weeks later for confirmation. The study doctor will discuss with you your options during the period between scans, which may include the following:
    1. Continue to receive treatment with the study drug, or
    2. Have study drug held until the time of the confirmatory scan, or
    3. Discontinue from the study and instead receive an approved, licensed drug which may shrink your tumor, delay progression of your cancer, provide symptom relief or prolong survival.
    4. You may also be eligible to receive treatment with a different investigational drug.
    5. If you elect to stay in the study until the confirmatory scan, you will not be eligible to receive any of these other medications until the worsening of your disease is confirmed.

Ending Study Drug:
You will take the study drug for a total of 9 weeks prior to first restaging scans and assessment for therapy. The decision may be made to offer up to 3 more cycles of therapy prior to surgery if it is felt that the tumor may continue to respond.

After day 64 of therapy (about 7 days after or before), you will be evaluated for surgical resection. At the conclusion of treatment, we will collect peripheral blood and tumor tissue again post-treatment, either at the time of surgical resection, if applicable, or by re-biopsy. You will also receive a biopsy at progression, if applicable. If you are not considered a candidate for surgery and/or radiation therapy after the conclusion of 6 cycles, and you are benefitting from treatment with parial or complete response or stable disease, you will be given the option to continue on protocol therapy.

You will discontinue to take the study drug(s):
- If repeat tumor imaging confirms your tumor keeps growing and worsening disease

- If, in the opinion of the study doctor, you develop clinical evidence of any herpes infection (herpes is a common infection).
- If you require treatment with another anticancer drug.
- If you develop serious side effects or allergic reactions attributed to Talimogene laherparepvec that would require a dose delay of greater than 4 weeks from the date of the planned dose (i.e., approximately 6 weeks from the previous dose).
- If you develop any other Talimogene laherparepvec-related toxicities that are severe that, in the opinion of the investigator, would require a dose delay of greater than 4 weeks from the date of the planned dose (i.e., approximately 6 weeks from the previous dose).
- If you become pregnant or fail to use acceptable method(s) of effective contraception.
- If you breast feed while on study treatment.
- If you develop another medical illness that, in the judgment of the study doctor, would make continued treatment with Talimogene laherparepvec dangerous.
- If you develop skin toxicities that are severe.
- If you develop skin or soft tissue toxicity with severe or life-threatening inflammatory or infectious complications.
- If you develop a confirmed Interstitial Lung Disease.
- If you develop serious infusion reactions that are life threatening and/or require hospitalization.
- If you decide to withdraw from the study.
- If you are in noncompliance with treatment plan.

After you have completed study treatment

After you stop taking study therapy or after surgery, you will complete a safety follow-up visit 30 days after the last dose of trial treatment or before the initiation of a new anti-cancer treatment, whichever comes first. Your disease status will be monitored every 12 weeks by scan imaging. Every effort will be made to collect information regarding your disease status until the start of new anti-neoplastic therapy, disease progression, death or end of the study.

You will have the following tests, procedures, and assessments done at 30 days after surgery or 30 Day follow up, Follow up every 12 weeks for 2 years, and at progression. The study doctor or staff will discuss with you when and on which days to report to the clinic. It may be necessary to perform these procedures at unscheduled time points if considered clinically necessary by the study doctor.

Evaluation	Post- surgery or Bx follow up	Follow up (every 12 weeks for 2 years)	At progression
Physical Exam Medical status, Tumor Site Assessment	X	X	X
Toxicity Assessment	X	X	
Photo of Tumor			X
Tumor Biopsy or Resection			X
Lab Tests with Blood		X	
Cancer scan Assessments[1]		X[1]	X

[1]Tumor assessments are by various scans (e.g. PET/CT, CT C/A/P, MRI) every 12 weeks.

What will happen during the study visits?

When you come in for your study visits, the study doctor or staff may do any or all of the following to measure if the drug is working and/or to monitor your health:

- Give you a patient identification card. This pocket card is intended for medical professionals and contains relevant information on the trial as well as contact information to be used in case of an emergency. Please carry this card all the time and show it whenever you consult a health professional.
- Administer study drug and provide instructions.
- Review your medical history.
- Review prior and current medications.
- Perform a physical exam.
- Check your vital signs (including blood pressure, heart rate, temperature, breathing rate).
- Measure your height and weight.
- Collect blood and urine samples.
  - For safety tests.
  - To perform a pregnancy test, if you are a woman able to have children.
- Perform a computerized tomography (CT) scan, magnetic resonance imaging (MRI) of your tumor, or perform additional scans.
- Check your disease status.
- Review any side effects you have had.
- Complete questionnaires about your health status.
- Collect a tumor biopsy and whole blood, if applicable, before the start of study drug.
- With your permission, any samples left over from this study will be stored for future biomedical research. You will be asked to sign the Future Biomedical Research consent if you are willing to allow your samples to be stored.
- Your tumor will be tested by a laboratory to see if features that determine if patients respond to this therapy can be determined. These results do not impact your ability to participate in the study.
- Provide samples to be used for studying biomarkers (DNA, RNA, proteins, and other molecules in your tissues) in the blood. These samples will be used to analyze biomarkers to discover ways that the study drugs do or do not work to shrink tumors. Additional biomarkers which may impact how individuals respond to the study drugs may also be analyzed. Your samples will be retained for 15 years. This allows the Sponsor to fully study biomarkers and answer questions from health authorities about the way the drugs work in this study. Samples will not be retained longer than that or used for other research unless you consent to the optional Future Biomedical Research (FBR) sub-study. These results are for research only. Since these tests are exploratory research, they will have no clear implications with respect to you or your family's medical conditions. The results of the testing will not be returned to you.
- You will also be asked to take part in optional Future Biomedical Research. You will be given a separate document that will describe this research and seek your consent.

What are the risks and/or discomforts I might experience if I take part in this study?

ABOUT THE STUDY DRUG(S)

What is known about this study drug?

Talimogene Laherparepvec
Talimogene Laherparepvec, also known as IMLYGIC, is a viral therapy indicated for the local treatment of advanced disease in patients with melanoma recurrent after initial surgery.

Limitations of use: Talimogene laherparepvec on its own does not improve overall survival for all patients and may not significantly impact tumor spreading to other sites. However, Talimogene laherparepvec combined with other therapies has shown improved antitumor activity. The goal of this study is to understand how Talimogene laherparepvec and panitumumab work together.

As of 26 October 2020, more than 6,055 patients have received talimogene laherparepvec with approximately 1,416 patients having received talimogene laherparepvec in research studies and approximately 4,639 people were prescribed talimogene laherparepvec after it was approved for sale.

The most commonly reported adverse drug reactions (very common, ≥ 10%) in talimogene laherparepvec-treated patients were fatigue, chills, fever, nausea, influenza-like illness, and injection site pain. Adverse events such as vomiting, diarrhea, constipation, muscle pain, joint pain, extremity pain, headache and abdominal pain, were also reported as very common.

Adverse Events related to your immune system
Adverse events related to your immune system, which fights infection, becoming more active have been observed in subjects receiving Talimogene laherparepvec. These included inflammation of the kidney, blood vessels, and lung tissue.

Plasmacytoma
Plasmacytoma (abnormal blood plasma cells) has been observed with the administration of Talimogene laherparepvec. Talimogene laherparepvec will be discontinued permanently if development of abnormal plasma cells is observed.

Injection Site Reactions
Talimogene laherparepvec is administered by direct injection into skin tumor masses. Injection site adverse events may occur, such as reddening of the skin, local skin discoloration, hardening of soft tissue, warmth, and pain. Less frequently, injected skin tumor masses may become open wounds, predisposing you to local and/or systemic infections. Similarly, injected nodes may enlarge or become necrotic death of cells or tissues). Adverse events of "injection site pain" and "injection site reaction" were very common, occurring in ≥10% of Talimogene laherparepvec-

treated subjects. Most events of injection site pain and injection site reaction were mild to moderate in severity.

Cellulitis
Death of body tissue of skin tumor masses and diseased lymph nodes injected with Talimogene laherparepvec may infrequently occur, predisposing to local/regional infection (i.e., cellulitis). In clinical studies to date, cellulitis was common, occurring in $\geq 1\%$ to $< 10\%$ of subjects treated with Talimogene laherparepvec.

Flu-like Symptoms
Symptoms including chills, fatigue, headache, muscle pain, and fever may occur with Talimogene laherparepvec. In clinical studies to date, adverse events "chills", "fatigue", "headache", "influenza like illness", "muscle pain", and "fever" were very common, occurring in $\geq 10\%$ of subjects treated with Talimogene laherparepvec. Most of these events were mild to moderate in severity.

Accidental Exposure
Accidental exposure may lead to transmission of Talimogene laherparepvec and herpetic infection.

Caregivers should wear protective gloves when assisting you in applying or changing occlusive dressings (bandage) and observe safety precautions for disposal of used dressings, gloves, and cleaning materials. Spreading talimogene laherparepvec may be more likely if your close contact has a break in the skin or mucous membranes that comes into contact with your injection site or your body fluids. In patients treated with talimogene laherparepvec in clinical trials, talimogene laherparepvec has been found on the surface of the injected tumors and on the outside of the dressings that covered these injection sites.

Talimogene laherparepvec have also been detected in patients' blood and urine, and in the patient's mucous membranes of the mouth and genitals, no samples had detectable talimogene laherparepvec 30 days after the end of treatment. For patients who had talimogene laherparepvec presence in the surface of injected tumors, no samples had detectable talimogene laherparepvec 60 days after end of treatment.

In the event of an accidental exposure to talimogene laherparepvec, exposed individuals should clean the affected area thoroughly with soap and water and/or a disinfectant. If signs or symptoms of herpetic infection develop, the exposed individuals should contact their healthcare provider for appropriate treatment.

You should avoid touching or scratching injection sites or their occlusive dressings, as doing so could lead to inadvertent transfer of talimogene laherparepvec to other areas of the body.

[redacted]

Panitumumab
Panitumumab, also known as Vectibix®, is useful for certain cancers (as a single drug for the treatment of epidermal growth factor receptor (EGFR)-expressing, metastatic colorectal carcinoma (mCRC) with advancing disease or following some chemotherapy regimens. It has also shown activity in patients with squamous carcinoma of the skin.

The effectiveness of panitumumab as a single agent for the treatment of EGFR-expressing, metastatic colorectal carcinoma is based on progression-free survival.

Safety data are available from 15 clinical trials in which 1467 patients received panitumumab; of these, 1293 received panitumumab monotherapy and 174 received panitumumab in combination with chemotherapy. Toxicities include: Skin reactions (rash, skin acne or eruption, redness, dry skin, itchy skin, skin toxicity of redness and pain), diarrhea, nausea, chemical or mineral disturbances (which can produce irregular or fast heart rate, fatigue, nausea), nail disease, ocular (visual) disorders, interstitial lung disease, infusion-related reactions, vomiting, constipation, abdominal pain, fatigue, fever, painful inflammation and ulcers of lining the digestive tract, and weight loss.

Renal impairment
Mild-to-moderate renal (kidney) dysfunction and mild-to-moderate liver dysfunction were observed in some studies.

Skin Toxicity
Skin toxicities occurred in 90% of patients and were severe in 15% of patients receiving panitumumab. The clinical symptoms included acne like rash, itchy skin, reddening of the skin, rash, skin peeling, nail disease, dry skin, and tear in the skin. You are advised to avoid sun exposure while receiving panitumumab.

Scarring of lung
Scarring of lung may be acute in onset and has been observed in 1.3% of patients, and some cases have been fatal.

Chemical and Mineral Abnormalities
Progressively decreasing serum magnesium levels leading to severe low magnesium (a mineral in your blood) occurred in up to 7% of patients across clinical trials. Other chemical disturbances have also been observed.

Infusion Reactions
In one study, 4% of patients receiving panitumumab experienced infusion reactions, and 1% of patients experienced severe infusion reactions. Infusion reaction symptoms include fevers, chills, difficulty breathing, tightening of the airways in the lungs, and low blood pressure.

Photosensitivity
Exposure to sunlight can worsen skin toxicity. You are advised to wear sunscreen and hats, and limit sun exposure while receiving panitumumab.

Ocular Toxicities
Keratitis (inflamed eye's cornea) and ulcerative keratitis are both known risk factors for corneal tearing, and keratorhexis (corneal perforation) have been reported with panitumumab.

Other Toxicities
Life-threatening and fatal infectious complications including inflammation, collection of pus, and infection have been observed in patients treated with panitumumab.
Life-threatening and fatal blisters, erosions, and skin peeling has also been observed in patients treated with panitumumab.

Your condition may not improve and could even worsen if you take part in this study.
The study does have risks. Because the treatment is investigational, we may not yet know all the side effects: something unexpected could happen.

Are there any other risks?
Other less common side effects have been reported with the use of the drugs in this study. The study doctor or staff can discuss these with you.

There may be other side effects or risks that are not known at this time.

As with all medications, the side effects or risks described may occur more often or be more severe than has been seen before.

What is standard of care?
Several agents including cemiplimab, EGFR inhibitors like tyrosine kinase inhibitors (e.g., erlotinib, gefitinib) and EGFR monoclonal antibodies (e.g., cetuximab, necitumumab, panitumumab alone) or chemotherapy can be employed in locally advanced disease.

Other options include treatment with immunotherapy such as cemiplimab, which can produce responses. Not all patients are candidates for cemiplimab and this needs to be discussed with your doctor. Palliative care options can be considered.

ABOUT TESTS, PROCEDURES, AND INTERVENTION

What effects, risks, and discomfort could the tests have on me?
You may feel discomfort during some of these tests or may experience some inconveniences. Some may also have risks, which may include:

- Blood Samples: drawing blood from your extremity (arm or leg) may cause pain, bruising, lightheaded-ness, and rarely, infection.
  - Estimated Total Blood Draws:
    - Treatment Phase: 200 ml (about 7 ounces)

- IV Line: placement of an intravenous line for infusion of the study drug may cause discomfort, irritation, mild bruising, bleeding, and rarely infection, nausea, and lightheadedness. Because panitumumab is an antibody, there is the possibility that you may experience an acute infusion reaction. These are side effects that develop during or immediately after the administration of panitumumab. Signs and symptoms may include:
  - Blood pressure changes (increase or decrease)
  - Cough
  - Dizziness
  - Fast heart beat
  - Feeling cold
  - Feeling that the tongue is swelling or your airway is closing and you have trouble breathing
  - Fever
  - Headache
  - Joint pains
  - Muscle pains
  - Nausea
  - Rash, hives, or itching
  - Shortness of breath
  - Sweating
  - Tiredness
  - Vomiting
- Tumor Biopsy: A biopsy will be used to determine how your immune system is responding to the treatment. The biopsy will be done at baseline prior to treatment beginning, at completion of therapy (at surgery if surgery is pursued; if surgery is not recommended, a second biopsy will be obtained) and within 30 days of tumor recurrence. The tumor will be sent to a central laboratory for testing and will not be a part of your medical record.

Physical risks of harm:

- From Biopsies, you may experience:
- Pain and discomfort at the biopsy site
- Minor bleeding at the biopsy site
- Tenderness at the biopsy site
- Scarring at the biopsy site
- Rarely, an infection at the biopsy site.

REPRODUCTIVE RISKS

Panitumumab and talimogene laherparepvec may have adverse effects on a fetus in utero. Furthermore, it is not known if panitumumab and talimogene laherparepvec have transient adverse effects on the composition of sperm. It is unknown whether panitumumab and talimogene laherparepvec are excreted in human milk. Since many drugs are excreted in human milk, panitumumab and Talimogene laherparepvec have the potential for serious adverse reactions in the nursing infant.

Females
It is not known if the study drug(s) may affect an unborn or nursing baby. If you are pregnant, trying to become pregnant, or breast-feeding, you may not be in the study. The study doctor will perform a blood or urine pregnancy test before the start of and during the study, if you are able to have a baby.

If you are a female and are not otherwise post-menopausal (a woman who is 45 years old or older and has not had a menstrual cycle for more than one year) and are able to have a baby, you must agree to avoid becoming pregnant, while receiving study drug and for 120 days after the last dose of study drug by complying with one of the following:

- Avoid having sex (abstinence)
  - Acceptable if this is the usual lifestyle and preferred method for you. Your study doctor will be able to answer any questions or provide you further information on whether this is acceptable.

OR

- Use (or have your partner use) acceptable contraception methods

The following contraception methods are acceptable for the study:
Use of two (2) of the following in combination:

- Diaphragm with spermicide (cannot be used in conjunction with cervical cap/spermicide)
- Condom (male or female cannot be used together)
- Contraceptive sponge (only for women who have not given birth)
- Cervical cap with spermicide (only for women who have not given birth)
- Hormonal contraceptives (estrogen/progestin pill or progestin-only pill), contraceptive skin patch, vaginal contraceptive ring, or under the skin contraceptive injection

OR

One (1) of the following:

[redacted]

[redacted]

IRB
Approval Date:
Expiration Date: