

For the Patient: GIGAVFFOXN

Other Names: First-Line Treatment of Locally Advanced or Metastatic Esophageal, Gastroesophageal, or Gastric Cancer using Oxaliplatin, Fluorouracil, Leucovorin and Nivolumab

GI = GastroIntestinal
GAV = Gastroesophageal, **Advanced**
FFOXN = Fluorouracil, **F**olinic Acid, **Ox**aliplatin, **N**ivolumab

ABOUT THIS MEDICATION

What are these drugs used for?

- Fluorouracil (5FU), folinic acid (leucovorin), oxaliplatin and nivolumab are used to treat locally advanced or metastatic cancer of the esophagus, stomach-esophagus junction, or stomach.

How do these drugs work?

- Fluorouracil and oxaliplatin work by interfering with dividing cells and preventing an increase in the number of cancer cells.
- Leucovorin works by enhancing the effect of fluorouracil and strengthening fluorouracil's ability to reduce the number of cancer cells.
- Nivolumab helps the body's immune system target cancer cells to stop them from growing.

INTENDED BENEFITS

- This therapy is being given to destroy and/or limit the growth of cancer cells in your body. This treatment may improve your current symptoms, and delay the onset of new symptoms.
- It may take several treatments before your doctor can judge whether or not this treatment is helping.

TREATMENT SUMMARY

How are these drugs given?

- Fluorouracil, leucovorin, oxaliplatin and nivolumab are given directly into the vein (IV).
- You will receive nivolumab, oxaliplatin and leucovorin at the clinic by a chemotherapy nurse.
- Oxaliplatin and leucovorin are mixed separately into two IV bags, which are then given to you at the same time. You will then receive a dose of fluorouracil given directly into the vein through a syringe.
- You will also be given an additional dose of fluorouracil over 46 hours, or 2 days, using a disposable infusion device called an INFUSOR® or "baby bottle". The infusion device delivers the fluorouracil slowly and continuously to your body over the 46 hour time period. Please see a copy of "*Your INFUSOR® - A Guide for Patients*", available through your chemotherapy nurse.
- The infusion device is connected to your veins by either a peripherally inserted central catheter (PICC Line) or a PORT-A-CATH®. If using a PICC line, this is inserted in your upper arm. If using a PORT-A-CATH®, this is inserted under the skin of the chest using local freezing. The insertion would be done several days before your treatment starts and would be removed once the treatment program is finished.
- The chemotherapy nurse will connect the infusion device to your PICC or PORT-A-CATH® at the clinic and then you can go home while your treatment is delivered over the 2 days.

You may return to the clinic after 2 days for the nurse to disconnect the infusion device, or you will be instructed how to disconnect yourself at home. Some people may be instructed to go to their local hospital to be disconnected, or may have a home care nurse provide this service, if available. You will then have a two week rest period.

- This total 14 days or 2 week period of time is called a “cycle”.
- Each treatment will take **about 4 hours**. This includes a dressing change if you have a PICC line. If you have a PORT-A-CATH®, a dressing change is not needed, so your treatment will take less time. Your first treatment will probably take longer, as the nurse will review information on the chemotherapy and immunotherapy drugs and infusion device with you.

What will happen while I am being treated?

- A blood test is done within one month of starting treatment.
- A blood test is also done before Day 1 of each cycle.
- The dose and timing of your treatment may be changed based on your blood test results and/or other side effects.
- Your very first treatment will take longer than other treatments because a nurse will be reviewing the possible side effects of your treatment plan and will discuss with you how to manage them. It is a good idea to bring someone with you to your first treatment appointment.
- Please bring your anti-nausea drugs with you for each treatment. Your nurse will tell you when to take them. You may also need to take anti-nausea drugs at home after treatment. It is easier to prevent nausea and vomiting than to treat it once it happens, so follow directions closely.

The calendar below outlines your overall treatment plan for each 2 week cycle.

C Y C L E	DATE	TREATMENT PLAN
	1	
		Week 2 → no treatment

C Y C L E	DATE	TREATMENT PLAN
	2	
		Week 2 → no treatment

Treatment may be continued as long as you are benefiting from it and not having too many side effects from treatment and for a maximum of 2 years for nivolumab, as determined by your oncologist.

OTHER INSTRUCTIONS

It is very important to report side effects immediately to your doctor. Do not manage side effects at home without first speaking with your doctor. Be aware that symptoms may be delayed and can develop months after your last dose.

INSTRUCTIONS FOR THE PATIENT

- Tell your doctor if you have ever had an unusual or **allergic reaction** to the following drugs before starting this treatment:
 1. oxaliplatin, cisplatin (PLATINOL®) or carboplatin (PARAPLATIN®)
 2. fluorouracil (5FU, ADRUCIL®) or capecitabine (XELODA®)
 3. leucovorin
 4. nivolumab
- The **drinking of alcohol** (in small amounts) does not appear to affect the safety or usefulness of nivolumab, fluorouracil, oxaliplatin or leucovorin.
- Nivolumab, fluorouracil may cause **sterility** in men and **menopause** in women. If you plan to have children, discuss this with your doctor before beginning treatment.
- Nivolumab, fluorouracil and oxaliplatin may damage sperm and may harm the baby if used during pregnancy. It is best to use **birth control** while undergoing treatment and for **5 months** after the last dose. Tell your doctor right away if you or your partner becomes pregnant. Do not breast feed during treatment.
- Tell doctors, dentists and other health professionals that you are being treated with nivolumab, oxaliplatin, fluorouracil and leucovorin before you receive any treatment from them.

Other important things to know:

- **Before you are given nivolumab**, talk to your doctor or pharmacist if you:
 - have an active condition where your immune system attacks your body (autoimmune disease), such as ulcerative colitis, Crohn's disease, lupus, rheumatoid arthritis or sarcoidosis.
 - take other medicines that make your immune system weak. Examples of these may include steroids, such as prednisone or dexamethasone.
 - had an organ transplant, such as a kidney transplant.
 - have any other medical conditions.

What other drugs or foods can interact with this treatment?

- Other drugs may **interact** with leucovorin and oxaliplatin. Other drugs such as warfarin (COUMADIN®), phenytoin (DILANTIN®) and fosphenytoin (CEREBYX®) may **interact** with fluorouracil.
- Check with your doctor or pharmacist before you start or stop taking any other drugs including all prescription and nonprescription medicines, steroids or other medicines that lower your immune response, vitamins, and herbal supplements.

Special note:

Heart Problems: Serious heart problems can occur when starting fluorouracil. These can rarely be fatal. Problems such as chest pain, heart attack, abnormal heart rhythm, or heart failure can occur. Having a history of heart problems with capecitabine, a related chemotherapy drug, is a risk factor, as is having a history of prior angina (heart pain) or heart attack. Seek medical attention promptly if you experience feelings of heavy pressure or pain in the chest, trouble breathing, significant worsening leg swelling, or marked lightheadedness. These symptoms can occur within days after starting fluorouracil. If your symptoms are severe, you may need to call for emergency help.

Nivolumab may cause serious immune reactions against your own body (autoimmune) affecting many parts.

What is the most important information I should know about SERIOUS SIDE EFFECTS?

- Nivolumab can cause serious side effects in many parts of your body. These side effects are most likely to begin during treatment; however, side effects can show up months after your last treatment with nivolumab.
- **Tell** your doctor as soon as possible if you have any of serious side effects listed in the table below or your symptoms get worse.
- **Do not try to treat or diagnose symptoms yourself.** Getting medical treatment right away may keep the problem from becoming more serious.

The following side effects were most frequently reported with nivolumab:

Very common (more than 1 in 10 people)

- diarrhea
- itching, rash
- joint pain
- feeling tired
- feeling less hungry
- cough

SERIOUS SIDE EFFECTS	How common is it?
<p>Inflammation of the intestines (colitis) <i>Symptoms may include:</i></p> <ul style="list-style-type: none"> • diarrhea (loose stools) or more bowel movements than usual. Do not treat the diarrhea yourself. • blood or mucus in stools or dark, tarry, sticky stools • severe stomach pain (abdominal pain) or tenderness 	<p>Common</p> <p>(less than 1 in 10 but more than 1 in 100)</p>
<p>Inflammation of the thyroid gland (hyperthyroidism, hypothyroidism) <i>Symptoms may include:</i></p> <ul style="list-style-type: none"> • rapid heart beat • weight loss or gain • increased sweating • hair loss • feeling cold • constipation or diarrhea • your voice gets deeper • muscle aches • changes in sleep patterns 	<p>Common</p> <p>(less than 1 in 10 but more than 1 in 100)</p>
<p>Inflammation of the pituitary gland (hypophysitis, hypopituitarism, including secondary adrenal insufficiency) <i>Symptoms may include:</i></p> <ul style="list-style-type: none"> • weight loss • increased sweating, hot flashes • hair loss (includes facial and pubic) • feeling cold • headaches that will not go away or unusual headache • decreased sex drive • vision problems • excessive thirst and urination 	<p>Common</p> <p>(less than 1 in 10 but more than 1 in 100)</p>
<p>Inflammation of the lungs (pneumonitis) <i>Symptoms may include:</i></p> <ul style="list-style-type: none"> • shortness of breath • chest pain • coughing 	<p>Common</p> <p>(less than 1 in 10 but more than 1 in 100)</p>
<p>Problems with muscles <i>Symptoms may include:</i></p> <ul style="list-style-type: none"> • back pain • spasms • weakness • muscle pain 	<p>Common</p> <p>(less than 1 in 10 but more than 1 in 100)</p>
<p>Skin problems <i>Symptoms may include:</i></p> <ul style="list-style-type: none"> • rash • dry skin 	<p>Common</p> <p>(less than 1 in 10 but more than 1 in 100)</p>

SERIOUS SIDE EFFECTS	How common is it?
<p>Problems in other organs (nervous system, eyes) <i>Symptoms may include:</i></p> <ul style="list-style-type: none"> • tingling, numbness, lack of energy • changes in eyesight • dizziness 	<p>Common</p> <p>(less than 1 in 10 but more than 1 in 100)</p>
<p>Inflammation of the liver (hepatitis) <i>Symptoms may include:</i></p> <ul style="list-style-type: none"> • nausea or vomiting • loss of appetite • pain on the right side of your stomach • yellowing of your skin or the whites of your eyes • dark urine • bleeding or bruise more easily than normal 	<p>Uncommon</p> <p>(less than 1 in 100 but more than 1 in 1000)</p>
<p>Inflammation of the kidneys (nephritis) <i>Symptoms may include:</i></p> <ul style="list-style-type: none"> • changes in the amount or colour of your urine 	<p>Uncommon</p> <p>(less than 1 in 100 but more than 1 in 1000)</p>
<p>Problems in the pancreas <i>Symptoms may include:</i></p> <ul style="list-style-type: none"> • abdominal pain • nausea and vomiting 	<p>Rare</p> <p>(less than 1 in 1000 but more than 1 in 10000)</p>
<p>Blood sugar problems (type 1 diabetes mellitus) <i>Symptoms may include:</i></p> <ul style="list-style-type: none"> • hunger or thirst • a need to urinate more often • weight loss 	<p>Rare</p> <p>(less than 1 in 1000 but more than 1 in 10000)</p>
<p>Infusion reactions <i>Symptoms may include:</i></p> <ul style="list-style-type: none"> • shortness of breath • itching or rash • dizziness • fever • wheezing • flushing • feeling like passing out 	<p>Rare</p> <p>(less than 1 in 1000 but more than 1 in 10000)</p>

Management of Other Side Effects

SERIOUS SIDE EFFECTS DURING TREATMENT	MANAGEMENT
<p>Tell your nurse if you feel like you have difficulty breathing or swallowing during or immediately after your oxaliplatin infusion. This may occur rarely.</p>	<ul style="list-style-type: none"> • These symptoms will disappear in a few hours, and may not require treatment. • If you have these symptoms with a 2-hour infusion, your next treatment may be given over 6 hours.
<p>Allergic reactions may very rarely occur. Signs of an allergic reaction are dizziness, feeling faint, confusion, shortness of breath, and wheezing. This may occur immediately or several hours after receiving the drugs. It can occur after the first dose, or after many doses.</p>	<p>Tell your nurse if this happens while you are receiving the drugs or contact your doctor immediately if this happens after you leave the clinic.</p>
<p>Oxaliplatin and fluorouracil will burn if it leaks under the skin.</p>	<p>Tell your nurse or doctor immediately if you feel burning, stinging, or any other change while the drug is being given.</p>
<p>Your white blood cells will decrease after your treatment. They usually return to normal after your last treatment. White blood cells protect your body by fighting bacteria (germs) that cause infection. When they are low, you are at greater risk of having an infection.</p>	<p>To help prevent infection:</p> <ul style="list-style-type: none"> • Wash your hands often and always after using the bathroom. • Take care of your skin and mouth. • Call your doctor immediately at the first sign of an infection such as fever (over 100°F or 38°C by an oral thermometer), chills, cough, or burning when you pass urine.
<p>Your platelets may decrease during or after your treatment. They will return to normal after your last treatment. This is common. Platelets help to make your blood clot when you hurt yourself. You may bruise or bleed more easily than usual.</p>	<p>To help prevent bleeding problems:</p> <ul style="list-style-type: none"> • Try not to bruise, cut, or burn yourself. • Clean your nose by blowing gently. Do not pick your nose. • Avoid constipation. • Brush your teeth gently with a soft toothbrush as your gums may bleed more easily. Maintain good oral hygiene. <p>Some medications such as ASA (e.g. ASPIRIN®) or ibuprofen (e.g. ADVIL®) may increase your risk of bleeding.</p> <ul style="list-style-type: none"> • Do not stop taking any medication that has been prescribed by your doctor (e.g. ASA for your heart). • For minor pain, try acetaminophen (e.g. TYLENOL®) first, but occasional use of ibuprofen may be acceptable.

SERIOUS SIDE EFFECTS DURING TREATMENT	MANAGEMENT
<p>Nausea and vomiting may occur after your treatment and may last for 24- 48 hours. If you are vomiting and it is not controlled, you can quickly become dehydrated. Some people have little or no nausea.</p>	<p>You may be given a prescription for an anti-nausea drug(s) to take before your chemotherapy treatment and/or at home. It is easier to prevent nausea than treat it once it has occurred, so follow directions closely.</p> <ul style="list-style-type: none"> • Drink plenty of liquids. • Eat and drink often in small amounts. • Try the ideas in <i>Practical Tips to Help Manage Nausea*</i> <p>Tell your healthcare team if nausea or vomiting continues or is not controlled with your anti-nausea drug(s).</p>
<p>You may feel tingling or a loss of feeling in your hands, feet, nose, or throat. They may be made worse by exposure to cold. This is very common after oxaliplatin treatment. These problems often disappear after a few hours or days.</p>	<ul style="list-style-type: none"> • Avoid cold air if possible. • Protect yourself from the cold, which can cause or worsen these symptoms. Wear gloves, socks, and something that covers your mouth and nose when outside in cold weather. • Do not drink cold beverages or eat cold food for a few days after treatment. • Be careful when walking on uneven surfaces or doing activities that need you to balance or be steady. • Try the ideas in <i>Coping With/Preventing Oxaliplatin Cold Dysesthesias*</i>. <p>Talk to your healthcare team if symptoms continue for more than a week, or you have trouble with buttons, writing, picking up small objects, walking, or have fallen.</p>
<p>Sore mouth may occur during treatment. This is common. Mouth sores can occur on the tongue, the sides of the mouth or in the throat. Mouth sores or bleeding gums can lead to an infection.</p>	<ul style="list-style-type: none"> • Brush your teeth gently after eating and at bedtime with a very soft toothbrush. If your gums bleed, use gauze instead of a brush. Use baking soda instead of toothpaste. • Make a mouthwash with ¼ teaspoon baking soda AND ¼ teaspoon salt in 1 cup warm water and rinse several times a day. • Try soft, bland foods like puddings, milkshakes and cream soups. • Avoid spicy, crunchy or acidic food, and very hot or cold foods. • Try the ideas in <i>Food Ideas to Try with a Sore Mouth.*</i>

OTHER SIDE EFFECTS DURING TREATMENT	MANAGEMENT
Pain or tenderness may occur where the needle was placed.	<ul style="list-style-type: none"> • Apply warm compresses or soak in warm water for 15-20 mins. several times a day.
Fever may occur shortly after treatment. Fever should last no more than 24 hours.	<ul style="list-style-type: none"> • Take acetaminophen (e.g. TYLENOL®) every 3 – 4 hours. • Fever which occurs more than 48 hours after treatment may be the sign of an infection. See “white blood cells” above.
Your skin may sunburn easily.	<p>To help prevent sunburn:</p> <ul style="list-style-type: none"> • Avoid direct sunlight. • Wear a hat, long sleeves and long pants or skirt outside on sunny days. • Apply a sun block lotion with an SPF (sun protection factor) of at least 30. • Refer to Your Medication Sun Sensitivity and Sunscreens* or the BC Health Guide for more information. • After sun exposure, if you have a severe sunburn or skin reaction such as itching, rash, or swelling, contact your doctor.
Loss of appetite and weight loss sometimes occur.	<ul style="list-style-type: none"> • Try the ideas in <i>Food Ideas to Help with Decreased Appetite.</i>* • If loss of appetite is persistent and you have other symptoms of hepatitis, tell your doctor as soon as possible. (see the table for serious side effects during nivolumab treatment)
Tiredness and lack of energy may occur.	<ul style="list-style-type: none"> • Do not drive a car or operate machinery if you are feeling tired. • Try the ideas in the handout titled <i>Fatigue/Tiredness</i>*
Hair loss is uncommon with fluorouracil and rare with oxaliplatin and nivolumab. If you experience hair loss, your hair will grow back once you stop treatment. Colour and texture may change.	<p>If hair loss is a problem, refer to <i>Resources for Hair Loss and Appearance Changes.</i>*</p>
Abnormal heart rhythm (QT prolongation) rarely occurs.	<p>Minimize your risk of abnormal heart rhythm by:</p> <ul style="list-style-type: none"> • Always checking with your pharmacist and doctor about drug interactions when starting a new medication, herbal product, or supplement. • Tell your doctor immediately or get emergency help if your heart is beating irregularly or fast, or if you feel faint, lightheaded, or dizzy.

***Please ask your chemotherapy nurse, pharmacist, or dietitian for a copy.**



Provincial Health Services Authority

**MEDICAL
ALERT**

NAME _____

has received

CHECKPOINT INHIBITOR IMMUNOTHERAPY:
Immune-Mediated Adverse Reactions

**ALWAYS CARRY THIS CARD AND SHOW TO
PHYSICIANS INCLUDING ANESTHETISTS**

**SEVERE IMMUNE-MEDIATED ADVERSE
REACTIONS**

Including enterocolitis, intestinal perforation, hepatitis, dermatitis (including toxic epidermal necrolysis), neuropathy, endocrinopathy, pneumonitis, myositis, myocarditis and toxicities in other organ systems. Duration of risk after treatment is unknown.

FOR MORE INFORMATION:
BC Cancer – Abbotsford



To Whom It May Concern:

RE: _____

Medical Oncologist _____

Immunotherapy Regimen _____

This patient is receiving **immunotherapy** at the BC Cancer and is at risk of **immune-related toxicities** which may be life threatening and require urgent management.

Immunotherapy toxicities are different from those encountered with standard chemotherapy or targeted therapies. The immune system may become dysregulated during immunotherapy treatment, leading to symptoms and findings which mimic autoimmune disorders. Adverse events can occur during or following treatment and can be life threatening. Any organ system in the body is at risk including, but not limited to:

- Lungs (pneumonitis, pleuritis, sarcoidosis)
- Gastrointestinal (colitis, ileitis, pancreatitis)
- Liver (hepatitis)
- Skin (rash, Stevens-Johnson syndrome)
- Endocrine (hypophysitis, adrenal insufficiency, hypo/hyperthyroidism, type 1 diabetes mellitus)
- Renal (interstitial nephritis)
- Blood (hemolytic anemia, thrombocytopenia, neutropenia)
- Neurologic (encephalitis, Guillain-Barré syndrome, meningitis, myasthenia gravis, neuropathy)
- Musculoskeletal (myositis, arthritis)
- Cardiovascular (pericarditis, myocarditis, vasculitis)
- Ophthalmologic (uveitis, scleritis, episcleritis, conjunctivitis, retinitis)

Management of immune-related toxicities necessitates prompt coordination with a medical oncologist with **initiation of high dose corticosteroids**, and may require referral to the appropriate subspecialty. If you suspect your patient is presenting with immune-related toxicity, **please contact the patient's medical oncologist** directly or if after hours contact the on-call physician, or as per your local centre's process (next page). Additional information on immunotherapy toxicity treatment algorithms is located at the end of the above posted protocol at www.bccancer.bc.ca.

BC CANCER CENTRES	CONTACT INFORMATION AND PROCESS
Abbotsford	Contact the patient's medical oncologist immediately by calling the Abbotsford Regional Hospital and Cancer Centre (ARHCC) switchboard at (604) 851-4700 and ask for the on-call medical oncologist (24-hour call system).
Kelowna	Between 8:30 am – 5:00 pm, call (250) 712-3900 (press "8" to speak to the Kelowna Centre receptionist) and have an oncologist paged. Outside these hours, call the Kelowna General Hospital switchboard at (250) 862-4000 and ask for the on-call medical oncologist.
Prince George	Between 8:30 am – 4:00 pm Monday to Friday, call (250) 645-7313. Outside these hours, go to the emergency department at the University Hospital of Northern British Columbia (UHNBC).
Surrey	Between 8:30 am – 4:00 pm Monday to Friday (except Statutory holidays), call the Nursing Phone Line at (604) 930-4053. Outside these hours, call the Surrey Memorial Hospital switchboard at (604) 581-2211 and ask for the Fraser Valley on-call medical oncologist.
Vancouver	Between 8:30 am – 4:30 pm Monday to Friday, call the Patient Nurse Line at (604) 877-6025. Outside these hours, call the inpatient unit at (604) 877-6000 and press 1, and ask for the on-call medical oncologist.
Victoria	Between 8:30 am – 4:30 pm Monday-Friday (except Statutory holidays), call (250) 519-5500, and press 1 then 4 to speak with a registered nurse. Outside these hours, call the Royal Jubilee Hospital switchboard at (250) 370-8000 and ask for the on-call medical oncologist.