

For the Patient: GIGAVFFOXP

Other Names: First-Line Treatment of Locally Advanced or Metastatic Gastroesophageal Cancer using Oxaliplatin, Fluorouracil, Folinic Acid (Leucovorin) and Pembrolizumab

GI	= GastroIntestinal
GAV	= Gastroesophageal, Advanced
FFOXP	= Fluorouracil, Folinic Acid, Ox aliplatin, P embrolizumab

ABOUT THIS MEDICATION

What are these drugs used for?

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

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.
- Pembrolizumab helps 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 pembrolizumab are given directly into the vein (IV).
- You will receive pembrolizumab at the clinic by a chemotherapy nurse on the first day of treatment for **one day only**.
- You will be given oxaliplatin, leucovorin and fluorouracil on **days 1, 15 and 29**. 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" on **days 1, 15 and 29**. 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 IV site 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 42 days or 6 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.

The calendar below outlines your overall treatment plan for each 6 week cycle.

	DATE	TREATMENT PLAN
с		► Week 1 → pembrolizumab, oxaliplatin, leucovorin and fluorouracil IV on Day 1 + fluorouracil infusion over 46 hours starting on Day 1
Y C		Week 2 🗲 no treatment
L E		Week 3 → oxaliplatin, leucovorin and fluorouracil IV on Day 15 + fluorouracil infusion over 46 hours starting on Day 15
1		Week 4 Week 4 Image: A state of the state
		Week 5 → oxaliplatin, leucovorin and fluorouracil IV on Day 29 + fluorouracil infusion over 46 hours starting on Day 29
		Week 6 🗲 no treatment

	DATE	TREATMENT PLAN
с		► Week 1 → pembrolizumab, oxaliplatin, leucovorin and fluorouracil IV on Day 1 + fluorouracil infusion over 46 hours starting on Day 1
Y C		Week 2 🔿 no treatment
L E		Week 3 → oxaliplatin, leucovorin and fluorouracil IV on Day 15 + fluorouracil infusion over 46 hours starting on Day 15
2		Week 4 Week 4 Image: A state of the state
		Week 5 → oxaliplatin, leucovorin and fluorouracil IV on Day 29 + fluorouracil infusion over 46 hours starting on Day 29
		Week 6 🗲 no treatment

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

What will happen when I get my drugs?

• A **blood test** is done each cycle, on or before the first day of each cycle. The dose and timing of your chemotherapy may be changed based on your blood counts and/or other side effects.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Unexpected and unlikely side effects can occur with any drug treatment. The ones listed below are particularly important for you to be aware of as they are directly related to the common actions of the drugs in your treatment plan.

Your doctor will review the risks of treatment and possible side effects with you before starting treatment. The chemotherapy nurse will review possible side effects of the drugs and how to manage those side effects with you on the day you receive your first treatment.

SERIOUS SIDE EFFECTS DURING TREATMENT	MANAGEMENT
Tell your nurse if you feel like you have difficulty breathing or swallowing during or immediately after your oxaliplatin infusion. This may occur rarely.	 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.
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.	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.
Oxaliplatin and fluorouracil will burn if it leaks under the skin.	Tell your nurse or doctor immediately if you feel burning, stinging, or any other change while the drug is being given.
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.	 You may be given a prescription for an antinausea 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. Drink plenty of liquids. Eat and drink often in small amounts. Try the ideas in <i>Practical Tips to Help Manage Nausea</i>* Tell your healthcare team if nausea or vomiting continues or is not controlled with your antinausea drug(s).

SERIOUS SIDE EFFECTS	MANAGEMENT
DURING TREATMENT 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.	 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> Talk to your healthcare team if symptoms
Diarrhea may occur during your treatment. This is very common. If you have diarrhea and it is not controlled, you can quickly become dehydrated.	 continue for more than a week, or you have trouble with buttons, writing, picking up small objects, walking, or have fallen. To help diarrhea: Drink plenty of fluids Eat and drink often in small amounts Eat low fibre foods & avoid high fibre foods as outlined in <i>Food Ideas to Help Manage Diarrhea*</i> If you have an increase of less than 4 stools per day more than normal, or a mild increase in ostomy output, start the following: Loperamide (IMODIUM®) 2 mg, take 2 tablets (4 mg) to start, followed by 1 tablet (2 mg) every 4 hours, or after each unformed stool to a maximum of 8 tablets (16 mg) daily, unless otherwise directed by a physician
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.	 diarrhea for more than 24 hours. 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 ½ teaspoon baking soda or 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 ideas in <i>Food Ideas to Try with a Sore Mouth*</i>

SERIOUS SIDE EFFECTS DURING TREATMENT	MANAGEMENT
Your white blood cells will decrease 7 – 10 days after your treatment. They usually return to normal 2 weeks 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.	 To help prevent infection: 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.

OTHER SIDE EFFECTS DURING TREATMENT	MANAGEMENT
Pain or tenderness may occur where the needle was placed.Fever may occur shortly after treatment with oxaliplatin. Fever should last no more than 24 hours.Your platelets may decrease during or after	 Apply warm compresses or soak in warm water for 15-20 mins. several times a day. 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. To help prevent bleeding problems:
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.	 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. Some medications such as ASA (e.g. ASPIRIN®) or ibuprofen (e.g. ADVIL®) may increase your risk of bleeding. 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.
Skin rashes are uncommon but may occur.	 To help itching: You can use calamine lotion. If very irritating, call your doctor during office hours. Otherwise mention it at your next visit.

OTHER SIDE EFFECTS DURING TREATMENT	MANAGEMENT
Your skin may sunburn easily.	 To help prevent sunburn: 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 is uncommon but may occur and may persist long after discontinuation of fluorouracil.	 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 pembrolizumab treatment)
Tiredness and lack of energy may occur.	 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. If you experience hair loss, your hair will grow back once you stop treatment. Colour and texture may change.	 Use a gentle shampoo and soft brush. Care should be taken with use of hair spray, bleaches, dyes and perms. If hair loss is a problem, refer to <i>Resources for Hair Loss and Appearance Changes</i>.*
Abnormal heart rhythm (QT prolongation) rarely occurs.	 Minimize your risk of abnormal heart rhythm by: 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.

Pembrolizumab 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?

- Pembrolizumab 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 pembrolizumab.
- **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.

SERIOUS SIDE EFFECTS DURING PEMBROLIZUMAB TREATMENT	How Common is it?
Inflammation of the intestines (colitis)	Common
Symptoms may include:	(less than 1 in 10 but
• diarrhea (loose stools) or more bowel movements than usual. Do not treat	more than 1 in 100)
the diarrhea yourself.	
 blood or mucus in stools or dark, tarry, sticky stools 	
 severe stomach pain (abdominal pain) or tenderness 	
Inflammation of the thyroid gland (hyperthyroidism, hypothyroidism)	Common
Symptoms may include:	(less than 1 in 10 but
rapid heart beat	more than 1 in 100)
weight loss or gain	
 increased sweating 	
hair loss • feeling cold	
constipation or diarrhea	
your voice gets deeper	
muscle aches	
changes in sleep patterns	
Inflammation of the pituitary gland (hypophysitis, hypopituitarism,	Common
including secondary adrenal insufficiency)	(less than 1 in 10 but
Symptoms may include:	more than 1 in 100)
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	
Inflammation of the lungs (pneumonitis)	Common
Symptoms may include:	(less than 1 in 10 but
shortness of breath	more than 1 in 100)
chest pain	
coughing	

SERIOUS SIDE EFFECTS	How Common is
DURING PEMBROLIZUMAB TREATMENT	it?
Problems with muscles	Common
Symptoms may include:	(less than 1 in 10 but
• rash	more than 1 in 100)
dry skin	
Problems in other organs (nervous system, eyes)	Common
Symptoms may include:	(less than 1 in 10 but
 tingling, numbness, lack of energy 	more than 1 in 100)
changes in eyesight	
dizziness	
Inflammation of the liver (hepatitis)	Uncommon
Symptoms may include:	(less than 1 in 100
nausea or vomiting	but more than 1 in
loss of appetite	1000)
 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 	
Inflammation of the kidneys (nephritis)	Uncommon
Symptoms may include:	(less than 1 in 100
changes in the amount or colour of your urine	but more than 1 in 1000)
Problems in the pancreas	Rare
Symptoms may include:	(less than 1 in 1000
abdominal pain	but more than 1 in
nausea and vomiting	10000)
Blood sugar problems (type 1 diabetes mellitus)	Rare
Symptoms may include:	(less than 1 in 1000
hunger or thirst	but more than 1 in
a need to urinate more often	10000)
weight loss	
Infusion reactions	Rare
Symptoms may include:	(less than 1 in 1000
• Shortness of breath, itching or rash, dizziness, fever, wheezing, flushing,	but more than 1 in
feeling like passing out, chills and may sometimes occur during the first pembrolizumab infusion.	10000)
 Reactions are less common with later treatments. 	
• Tell your nurse or doctor <i>immediately</i> if you have a reaction during your	
treatment.	
 Your pembrolizumab may be temporarily stopped and then given more slowly. 	
 You may be given other drugs to treat the reaction. 	

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.

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 or capecitabine (XELÓDA®).
 - 3. leucovorin.
- The **drinking of alcohol** (in small amounts) does not appear to affect the safety or usefulness of pembrolizumab, fluorouracil, oxaliplatin or leucovorin.
- Pembrolizumab, fluorouracil may cause **sterility** in men and **menopause** in women. If you plan to have children, discuss this with your doctor before beginning treatment.
- Pembrolizumab, 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 **4 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 pembrolizumab, oxaliplatin, fluorouracil and leucovorin before you receive any treatment from them.

Other important things to know:

- Before you are given pembrolizumab, 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.

Medication Interactions:

• Other drugs may **interact** with leucovorin and oxaliplatin. Other drugs such as warfarin (COUMADIN®), phenytoin (DILANTIN®) and fosphenytoin (CEREBYX®) may **interact** with fluorouracil. Tell your doctor if you are taking this or any other drugs as you may need extra blood test or your dose may need to be changed. Check with your doctor or pharmacist before you start taking any new drugs

THE FOLLOWING INFORMATION IS VERY IMPORTANT

SEE YOUR DOCTOR OR GET EMERGENCY HELP IMMEDIATELY IF YOU HAVE:

- Signs of an **allergic reaction** (rare) soon after a treatment including dizziness, fast heart beat, face swelling or breathing problems.
- Signs of an **infection** such as fever (over 100°F or 38°C by an oral thermometer); chills, cough, pain or burning when you pass urine.
- Signs of **bleeding problems** such as black, tarry stools, blood in urine, pinpoint red spots on skin, extensive bruising.
- Signs of **heart or lung problems** such as fast or uneven heartbeat, chest pain, chest pressure, shortness of breath, or difficulty in breathing, swelling of ankles, or fainting.
- Signs of **kidney problems** such as lower back or side pain, blood in the urine, swelling of feet or lower legs, or change in amount or colour of urine.
- Signs of **blood sugar problems** such as thirst and frequent need to pass urine.
- Sudden abdominal pain or tenderness.
- Seizures or loss of consciousness with or without confusion, headache, or changes in eyesight.
- Uncontrolled nausea, vomiting, or diarrhea.

SEE YOUR DOCTOR AS SOON AS POSSIBLE (DURING OFFICE HOURS) IF YOU HAVE:

- Signs of **anemia** such as unusual tiredness or weakness.
- Signs of liver problems such as yellow eyes or skin, white or clay-coloured stools.
- Signs of **thyroid problems** such as unusual weight gain or loss, feeling hot or cold, deepened voice, or unusual tiredness or weakness.
- Changes in eyesight, eye pain, or redness.
- Severe skin irritation.

CHECK WITH YOUR DOCTOR IF ANY OF THE FOLLOWING CONTINUE OR BOTHER YOU:

- Headache not controlled with acetaminophen (e.g., TYLENOL®).
- Easy bruising or minor bleeding.
- Tingling or a loss of feeling in your hands, feet, nose or throat
- Redness, swelling, pain, or sores where the needle was placed.
- Redness, swelling, pain, or sores on your lips, tongue, mouth, or throat.
- Heartburn; mild to moderate abdominal or stomach pain.
- Dizziness or trouble walking.
- Eye irritation or changes in eyesight.
- Skin rash or itching, Changes in skin colour (lightening)
- Irritability or forgetfulness.
- Decreased sex drive

If you experience symptoms or changes in your body that have not been described above but worry you, or if any symptoms are severe, contact:

_at telephone number:

BCCAR MEDICAL CER ALERT Provincial Health Services Authority NAME	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.
has received CHECKPOINT INHIBITOR IMMUNOTHERAPY: Immune-Mediated Adverse Reactions ALWAYS CARRY THIS CARD AND SHOW TO PHYSICIANS INCLUDING ANESTHETISTS	FOR MORE INFORMATION: BC Cancer - Abbotsford

To Whom It May Cond	cern:	
RE:		
Medical Oncol	ogist	
Immunotherap	by Regimen	
	ng immunotherapy at the BC Cancer and is at risk of imm u be life threatening and require urgent management.	ine-related
or targeted therapies. treatment, leading to events can occur durin	ities are different from those encountered with standard o The immune system may become dysregulated during ir symptoms and findings which mimic autoimmune disorde ng or following treatment and can be life threatening. An ncluding, but not limited to:	nmunotherapy ers. Adverse
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oncologist with initiat appropriate subspecia toxicity, please conta on-call physician, or a	une-related toxicities necessitates prompt coordination wi ion of high dose corticosteroids , and may require referra alty. If you suspect your patient is presenting with immune ct the patient's medical oncologist directly or if after hour s per your local centre's process (next page). Additional in ity treatment algorithms is located at the end of the above <u>incer.bc.ca</u> .	l to the e-related rs contact the nformation on
BC Cancer Systemic Therapy I	Program Revised:	1 / 2



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.

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