

For the Patient: GIATZB

Other Names: First-Line Treatment of Advanced Hepatocellular Carcinoma using Atezolizumab and Bevacizumab

GI = GastroIntestinal
ATZ = ATeZolizumab
B = Bevacizumab

ABOUT THIS MEDICATION

What is this drug used for?

- Atezolizumab and bevacizumab are intravenous (through the vein) drugs given to treat a type of advanced liver cancer (hepatocellular carcinoma).

How does this drug work?

- Atezolizumab and bevacizumab are monoclonal antibodies, a type of protein designed to target and interfere with the growth of cancer cells in your body.

INTENDED BENEFITS

- This treatment is being given to slow down the growth of your cancer cells in your body. This treatment can help to control some of the symptoms that cancer may be causing and may delay or prevent new symptoms from starting.

TREATMENT SUMMARY

How is this drug given?

- Both atezolizumab and bevacizumab are clear liquids, given as an infusion directly into the vein (IV).
- You will receive atezolizumab and bevacizumab at the clinic by a nurse, for one day only. Each treatment will last about 60-120 minutes. Your first treatment will probably take longer, as the nurse will review information on the chemotherapy drug with you. *It is a good idea to bring someone with you to your first treatment appointment.*
- The treatment is repeated every 3 weeks. This 3 week period of time is called a “cycle”. This treatment will continue as long as you are benefiting from treatment and not having too many side effects, as determined by your oncologist.

The calendar below shows how the medication is given each 3 week cycle.

C Y C L E 1	DATE	TREATMENT PLAN
		▶ Week 1 → atezolizumab IV on day 1 only Bevacizumab IV on day1 only
		▶ Weeks 2 + 3 → no treatment

C Y C L E 2	DATE	TREATMENT PLAN
		▶ Week 1 → atezolizumab IV on day 1 only Bevacizumab IV on day1 only
		▶ Weeks 2+3 → no treatment

Treatment is continued as long as you are benefiting from treatment and not having too many side effects.

What will happen while I am being treated?

- A blood test is done before starting each treatment cycle, usually at the time you see your oncologist.
- Your blood pressure will be checked by a nurse before each treatment and a urine test will be done before each 2nd treatment, on even numbered cycles.
- Your treatment may be interrupted based on your blood test results 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 drug in your treatment plan.

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

Atezolizumab 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?

- Atezolizumab 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 atezolizumab.
- **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 TREATMENT	How Common is it?
<p>Inflammation of the nerves <i>Symptoms may include:</i></p> <ul style="list-style-type: none"> • weakness of the legs, arms or face • numbness or tingling in hands or feet • lack of energy or dizziness 	<p>Very Common (more than 1 in 10)</p>
<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 (less than 1 in 10 but more than 1 in 100)</p>
<p>Inflammation of the skin <i>Symptoms may include:</i></p> <ul style="list-style-type: none"> • rash on your skin, mouth blisters, dry or peeling skin 	<p>Common (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 (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 (less than 1 in 10 but more than 1 in 100)</p>

SERIOUS SIDE EFFECTS DURING TREATMENT	How Common is it?
<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 (less than 1 in 10 but more than 1 in 100)</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, chills and may sometimes occur during the first pembrolizumab infusion. • Reactions are less common with later treatments. • Tell your nurse or doctor immediately 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. 	<p>Common (less than 1 in 10 but more than 1 in 100)</p>
<p>Problems in the pancreas <i>Symptoms may include:</i></p> <ul style="list-style-type: none"> • abdominal pain • nausea and vomiting 	<p>Uncommon (less than 1 in 100 but more than 1 in 1000)</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>Uncommon (less than 1 in 100 but more than 1 in 1000)</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 (less than 1 in 100 but more than 1 in 1000)</p>
<p>Problems with muscles <i>Symptoms may include:</i></p> <ul style="list-style-type: none"> • rash • dry skin 	<p>Rare (less than 1 in 1000 but more than 1 in 10000)</p>

SERIOUS SIDE EFFECTS DURING TREATMENT	How Common is it?
<p>Inflammation of the eyes Symptoms may include:</p> <ul style="list-style-type: none"> • changes in eyesight, blurry vision, double vision, or other vision problems • eye pain or redness 	<p>Rare (less than 1 in 1000 but more than 1 in 10000)</p>
<p>Inflammation of the kidneys (nephritis) Symptoms may include:</p> <ul style="list-style-type: none"> • changes in the amount or colour of your urine 	<p>Rare (less than 1 in 1000 but more than 1 in 10000)</p>

OTHER SIDE EFFECTS DURING TREATMENT	MANAGEMENT
<p>Pain or tenderness may occur where the needle was placed.</p>	<p>Apply cool compresses or soak in cool water for 15 – 20 minutes several times a day.</p>
<p>Nausea and vomiting may occur after your treatment.</p>	<p>You may be given a prescription for 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 fluids. • Eat and drink often in small amounts. • Try the ideas in <i>Practical Tips to Help Manage Nausea*</i> • If nausea and vomiting is persistent and you have other symptoms of hepatitis, tell your doctor as soon as possible. (see the table above for serious side effects.)
<p>Constipation may sometimes occur.</p>	<ul style="list-style-type: none"> • Exercise if you can. • Drink plenty of fluids. • Try ideas in <i>Suggestions for Dealing with Constipation.*</i> • If you have other symptoms of colitis, tell your doctor as soon as possible. (see the table above for serious side effects.)
<p>Diarrhea may sometimes occur.</p>	<p>If diarrhea is a problem:</p> <ul style="list-style-type: none"> • Drink plenty of liquids. • Eat and drink often in small amounts • Avoid high fibre foods as outlined in <i>Food Ideas to Help Manage Diarrhea*</i> • If you have other symptoms of colitis, tell your doctor as soon as possible. (see the table above for serious side effects.)
<p>You may sometimes have trouble sleeping.</p>	<ul style="list-style-type: none"> • Talk to your doctor if you continue to have trouble sleeping. • This will return to normal when you stop taking atezolizumab.

OTHER SIDE EFFECTS DURING TREATMENT	MANAGEMENT
Hair loss is rare with atezolizumab or bevacizumab. If you lose hair, it will grow back once you stop treatment. Colour and texture may change.	<ul style="list-style-type: none"> • If hair loss is a problem, refer to <i>Resources for Hair Loss and Appearance Changes</i>.*
Your blood pressure may rise during treatment. This is common.	The nurse will check your blood pressure before each chemotherapy treatment to make sure it is within a range acceptable for treatment. If too high, you may be given medication to lower your blood pressure, or your treatment may be stopped.
Headache may sometimes occur.	<ul style="list-style-type: none"> • Take acetaminophen (e.g., TYLENOL®) every 4-6 hours, to a maximum of 4 g (4000 mg) per day. • If headache is persistent and you have other symptoms of inflammation of glands or inflammation of the nerves, tell your doctor as soon as possible. (see the table above for serious side effects.)
Muscle or joint pain may sometimes occur.	<ul style="list-style-type: none"> • You may take acetaminophen (e.g., TYLENOL®) every 4-6 hours to a maximum of 4 g (4000 mg) per day. • Tell your doctor if the pain interferes with your activity
Loss of appetite and weight loss are common.	<ul style="list-style-type: none"> • Try the ideas in <i>Food Ideas to Help with Decreased Appetite</i>.*
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. • <i>Try the ideas in the handout titled Fatigue/Tiredness</i>* • If tiredness is persistent and you have other symptoms of hepatitis or inflammation of glands, tell your doctor as soon as possible. (see the table above for serious side effects.)
Minor bleeding , such as nosebleeds, may occur.	<ul style="list-style-type: none"> • Sit up straight and tip your head slightly forward. Tilting your head back may cause blood to run down your throat. • Pinch your nostrils shut between your thumb and forefinger or apply firm pressure against the bleeding nostril for 10 full minutes. • After 10 minutes, check to see if your nose is still bleeding. If it is, hold it for 10 more minutes. • Stay quiet for a few hours and do not blow your nose for at least 12 hours after the bleeding has stopped. • Get emergency help if a nosebleed lasts longer than 20 minutes.

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

Special notes:

Wound Healing: Bevacizumab may slow the healing process when recovering from surgery. See the instructions below under “Instructions for Patient” to prevent any problems with wound healing after surgery.

Bowel Perforation, a small hole in the wall of part of your intestine, can rarely occur with Bevacizumab. Symptoms may include sudden abdominal pain or tenderness, sometimes with constipation and vomiting.

INSTRUCTIONS FOR THE PATIENT

- Other drugs may interact with atezolizumab and bevacizumab. Check with your doctor or pharmacist before you start or stop taking any other drugs including all prescription and non-prescription medicines, steroids or other medicines that lower your immune response, vitamins, and herbal supplements.
- If you are planning to have surgery, bevacizumab may be stopped approximately 4 weeks before surgery and not restarted until approximately 4 weeks after surgery and only if the surgical wound is well healed. This helps to lower the risk of bleeding and may prevent problems with wound healing after surgery.
- The drinking of alcohol (in small amounts) does not appear to affect the safety or usefulness of this treatment.

Other important things to know:

- **Before you are given atezolizumab,** 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.
- Atezolizumab may affect fertility in women. If you plan to have children, discuss this with your doctor before being treated with atezolizumab.
- Both atezolizumab and bevacizumab may cause harm to the baby if used during pregnancy. It is best to use birth control while you are undergoing treatment and for **6 months** after the last dose. Tell your doctor right away if you or your partner becomes pregnant. Do not breast feed during treatment.
- Tell all doctors including dentists you see that you are being treated with atezolizumab and bevacizumab before you receive treatment of any form.

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), shaking chills; severe sore throat, productive cough (coughing up thick or green sputum); cloudy or foul smelling urine; painful, tender, or swollen red skin wounds or sores.
- Diarrhea or changes in bowel habits; black, tarry stools; blood or mucous in the stool; severe abdominal pain.

- Changes in eyesight, eye pain, or redness.
- Signs of a stroke such as sudden onset of: severe headache, eyesight changes, slurred speech, loss of coordination, weakness or numbness in arm or leg.
- Signs of a blood clot such as tenderness or hardness over a vein, calf swelling and tenderness, sudden onset of cough, chest pain, or shortness of breath.
- Signs of heart or lung problems such as new or worsening cough, chest pain, shortness of breath, difficulty in breathing, irregular heartbeat, coughing blood, swelling of feet or lower legs, or fainting.
- Signs of liver problems such as yellow eyes or skin, white or clay-coloured stools
- 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.
- Signs of bleeding problems such as black, tarry stools; blood in urine; pinpoint red spots on skin, extensive bruising.
- Persistent bleeding, such as nosebleeds lasting more than 20 minutes
- Sudden abdominal pain or tenderness, with or without nausea, vomiting, or high fever.
- Severe headache that does not go away, or occurs with vomiting, confusion or changes in eyesight.
- Seizures.

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

- Signs of anemia such as unusual tiredness or weakness.
- Easy bruising or minor bleeding
- Numbness or tingling in feet or hands.
- Skin rash, blisters, or itching
- Signs of thyroid problems such as unusual weight gain or loss, feeling hot or cold, deepened voice, or unusual tiredness or weakness
- Signs of kidney problems such as swelling of feet or lower legs. • Sores that do not heal or are slow to heal.
- Changes in eyesight, eye pain, or redness.

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

- Headache not controlled with acetaminophen (e.g., TYLENOL®).
- Redness, swelling, pain, or sores on your lips, tongue, mouth, or throat.
- Loss of appetite or weight loss.
- Uncontrolled nausea, vomiting, diarrhea, or abdominal pain.
- Irritability or forgetfulness, or trouble sleeping.
- Decreased sex drive.
- Runny or stuffy nose (without other cold symptoms) that does not go away, or occurs with bleeding or crusting of the nose.
- Skin rash or itching.

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: _____



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 - Abbotsford604-851-4710
- BC Cancer - Kelowna250-712-3900
- BC Cancer - Prince George.....250-645-7300
- BC Cancer - Surrey604-930-4055
- BC Cancer - Vancouver.....604-877-6000
- BC Cancer - Victoria.....250-519-5500

www.bccancer.bc.ca/health-professionals/professional-resources/cancer-drug-manual

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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.