

For the Patient: BRPCTAC

Other Names: Neoadjuvant Therapy for Triple Negative Breast Cancer Using Pembrolizumab with Carboplatin and Weekly Paclitaxel Followed by Doxorubicin and Cyclophosphamide

BR	BR east
P =	P embrolizumab
C =	C arboplatin
T =	T axol (TAXOL®)
A =	A driamycin (ADRIAMYCIN®)
C =	C yclophosphamide

ABOUT THIS MEDICATION

What are these drugs used for?

- Pembrolizumab, carboplatin, paclitaxel, doxorubicin, and cyclophosphamide are drugs given before breast cancer surgery (called neoadjuvant chemotherapy), in the hope of destroying breast cancer cells that may have spread to other parts of your body and shrinking the breast cancer in the breast and/or lymph nodes.

How do these drugs work?

- Pembrolizumab (pem" broe liz' ue mab) is a monoclonal antibody, a type of protein designed to help your own body's immune system target cancer cells to stop them from growing.
- Carboplatin (KAR-boe-plat-in), doxorubicin (dox-oh-ROO-biss-in), and cyclophosphamide (sigh-kloe-FOSS-fa-mide) work by interfering with the genetic material of replicating cells and preventing an increase in the number of cancer cells.
- Paclitaxel (pak" li tax' el) works by interfering with dividing cells and preventing an increase in the number of cells.

INTENDED BENEFITS

- This treatment may reduce the chance of your breast cancer coming back and may improve your overall survival or chance of a cure.

TREATMENT SUMMARY

How are these drugs given?

- Each medication will be given directly into the vein, intravenously (IV).
- The treatment will be given in 'cycles'. Each cycle length is 3 weeks.
- There will be two parts to this treatment.
 - In the first part, you will receive 4 cycles of pembrolizumab, paclitaxel, and carboplatin. Paclitaxel will be given once weekly for 12 weeks (=4 cycles) for the

first 4 cycles, while pembrolizumab and carboplatin will be given once every 3 weeks for the first 4 cycles.

- In the second part of your treatment, you will receive 4 cycles of pembrolizumab, doxorubicin, and cyclophosphamide. All three medications will be given together on day 1, once every three weeks.

The calendar below outlines your overall treatment plan.

Cycles 1 to 4:

C Y C L E	DATE	TREATMENT PLAN
		▶ Week 1 → pembrolizumab, paclitaxel, and carboplatin on day 1
		Week 2 → paclitaxel on day 8
	1	Week 3 → paclitaxel on day 15

Cycles 5 to 8:

C Y C L E	DATE	TREATMENT PLAN
		▶ Week 1 → pembrolizumab, doxorubicin, and cyclophosphamide on day 1
		Week 2 → no treatment
	2	Week 3 → no treatment

This treatment will continue for 8 cycles. Surgery and further treatment with pembrolizumab will follow.

What will happen when I get my drugs?

- You will see your clinician and will need to have a blood test before each treatment.
- The dose and timing of your treatment may be changed based on your blood counts and/or other side effects.
- Your clinician will be assessing whether your cancer is improving with each treatment.
- 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 chemotherapy appointment.*
- You will be given a prescription for anti-nausea medications (to be filled at your regular pharmacy). Please bring your anti-nausea medications with you for each treatment. Your nurse will tell you when to take the anti-nausea medication.
- You may also need to take your anti-nausea drugs at home after therapy. It is easier to prevent nausea than to treat it once it has occurred, so follow directions closely.
- You will be given some intravenous medications before paclitaxel to prevent or lessen the chance of an allergic reaction.

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. If other doctors are involved in your care it is important they know you are on these treatments and the autoimmune side effects they can cause.

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. Pembrolizumab
 2. Carboplatin or cisplatin
 3. Paclitaxel
 4. Doxorubicin, daunorubicin, epirubicin, idarubicin, mitomycin or mitoxantrone
 5. Cyclophosphamide
- The **drinking of alcohol** (in small amounts) does not appear to affect the safety or usefulness of treatment.
- Pembrolizumab, carboplatin, paclitaxel, doxorubicin, and cyclophosphamide may damage sperm and may harm the baby if used during pregnancy. It is best to use **birth control** while being treated these drugs, and for at least 4 months after the last dose of pembrolizumab. Tell your doctor right away if you or your partner becomes

pregnant. **Do not breastfeed** during treatment and for at least 4 months after the last dose of pembrolizumab.

- Tell doctors, dentists and other health professionals that you are being treated with pembrolizumab, carboplatin, paclitaxel, doxorubicin, and cyclophosphamide before you receive any treatment from them. You should carry the BC Cancer **wallet card** for pembrolizumab to alert health providers.
- **Do not receive any immunizations before discussing with your doctor**

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 significant medical conditions.

Medication Interactions:

- Other drugs may **interact** with pembrolizumab, carboplatin, paclitaxel, doxorubicin, and cyclophosphamide. Tell a member of your healthcare team if you are taking any other drugs as you may need extra blood tests or your dose(s) may need to be changed. Check with your doctor or pharmacist before you start or stop taking any new drugs including all prescription and non-prescription medicines, steroids or other medicines that lower your immune response, vitamins, and herbal supplements.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

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

Are there any risks?

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.

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.

The following side effects were most frequently reported:

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 (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>
<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>

SERIOUS SIDE EFFECTS	How common is it?
Inflammation of the lungs (pneumonitis) <i>Symptoms may include:</i> <ul style="list-style-type: none"> • shortness of breath • chest pain • coughing 	Common (less than 1 in 10 but more than 1 in 100)
Problems with muscles <i>Symptoms may include:</i> <ul style="list-style-type: none"> • back pain • spasms • weakness • muscle pain 	Common (less than 1 in 10 but more than 1 in 100)
Skin problems <i>Symptoms may include:</i> <ul style="list-style-type: none"> • rash • dry skin 	Common (less than 1 in 10 but more than 1 in 100)
Problems in other organs (nervous system, eyes) <i>Symptoms may include:</i> <ul style="list-style-type: none"> • tingling, numbness, lack of energy • changes in eyesight • dizziness 	Common (less than 1 in 10 but more than 1 in 100)
Blood sugar problems (type 1 diabetes mellitus) <i>Symptoms may include:</i> <ul style="list-style-type: none"> • hunger or thirst • a need to urinate more often • weight loss 	Common (less than 1 in 10 but more than 1 in 100)
Inflammation of the liver (hepatitis) <i>Symptoms may include:</i> <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 	Uncommon (less than 1 in 100 but more than 1 in 1000)
Inflammation of the kidneys (nephritis) <i>Symptoms may include:</i> <ul style="list-style-type: none"> • changes in the amount or colour of your urine 	Uncommon (less than 1 in 100 but more than 1 in 1000)
Problems in the pancreas <i>Symptoms may include:</i> <ul style="list-style-type: none"> • abdominal pain • nausea and vomiting 	Rare (less than 1 in 1000 but more than 1 in 10000)

SERIOUS SIDE EFFECTS	How common is it?
<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

SIDE EFFECTS DURING TREATMENT	MANAGEMENT
<p>Allergic reactions to pembrolizumab may rarely occur. Signs of an allergic reaction may include flushing, rash, itching, dizziness, swelling or breathing problems. This can occur immediately or several hours after receiving pembrolizumab.</p>	<p>Tell your nurse if this happens while you are receiving pembrolizumab or contact your oncologist <i>immediately</i> if this happens after you leave the clinic.</p>
<p>Allergic reactions commonly occur to paclitaxel. Signs of an allergic reaction may include flushing, rash, dizziness, breathing problems, abdominal or back pain. This can occur immediately or several hours after receiving paclitaxel and usually only with the first or second dose.</p>	<p>Tell your nurse if this happens while you are receiving paclitaxel or contact your oncologist <i>immediately</i> if this happens after you leave the clinic.</p>
<p>Allergic reactions may rarely occur to carboplatin. Signs of an allergic reaction may include rash, itching, fever, dizziness, or breathing problems. This can occur immediately or several hours after receiving carboplatin.</p>	<p>Tell your nurse if this happens while you are receiving carboplatin or contact your oncologist <i>immediately</i> if this happens after you leave the clinic.</p>
<p>Paclitaxel and doxorubicin burn if they leak under the skin.</p>	<p>Tell your nurse or doctor <i>immediately</i> if you feel burning, stinging, or any other change while the drug is being given.</p>

SIDE EFFECTS DURING TREATMENT	MANAGEMENT
<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. • Avoid crowds and people who are sick. • Call your healthcare team immediately at the first sign of an infection such as fever (over 38°C or 100°F 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. 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). <p>For minor pain, try acetaminophen (e.g., TYLENOL®) first, to a maximum of 4 g (4000 mg) per day, but occasional use of ibuprofen may be acceptable.</p>
<p>Nausea and vomiting may occur after your treatment. If you are vomiting and it is not controlled, you can quickly become dehydrated.</p>	<p>You will be given a prescription for antinausea drug(s) to take before your 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 Practical Tips to Help Manage Nausea* <p>Tell your healthcare team if nausea or vomiting continues or is not controlled with your antinausea drug(s).</p>

SIDE EFFECTS DURING TREATMENT	MANAGEMENT
<p>Fever may sometimes occur shortly after treatment with paclitaxel. Fever should last no more than 24 hours.</p>	<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. <p>Fever (over 100°F or 38°C by an oral thermometer) which occurs more than a few days after treatment may be a sign of an infection. Report this to your doctor immediately.</p>
<p>Your urine may be pink or reddish for 1- 2 days after your treatment.</p>	<p>This is expected as doxorubicin is red and is passed in your urine.</p>
<p>Sore mouth may sometimes occur a few days after treatment. 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 the ideas in Food Ideas to Try with a Sore Mouth.*
<p>Pain or tenderness may occur where the needle was placed.</p>	<ul style="list-style-type: none"> • Apply cool compresses or soak in cool water for 15-20 minutes, several times a day.
<p>Muscle or joint pain may commonly occur a few days after your treatment</p>	<p>You may take acetaminophen (e.g., TYLENOL®) every 4-6 hours to a maximum of 4 g (4000 mg) per day or ibuprofen (e.g., ADVIL®) for mild to moderate pain. Tell your healthcare team if the pain interferes with your activity.</p>
<p>Tiredness and lack of energy may occur.</p>	<ul style="list-style-type: none"> • Do not drive a car or operate machinery if you are feeling tired. • Try the ideas in Fatigue/Tiredness-patient handout*

SIDE EFFECTS DURING TREATMENT	MANAGEMENT
<p>Hair loss is common with paclitaxel, doxorubicin, and cyclophosphamide, and rare with carboplatin and pembrolizumab. It may begin within a few days or weeks of treatment. Your hair may thin or you may lose it completely. Your scalp may feel tender. Hair loss may occur on your face and body. Hair will grow back once your treatments are over and sometimes between treatments. Colour and texture may change.</p>	<p>Refer to <i>Resources for Hair Loss and Appearance Changes – Patient Handout.*</i> You may also want to:</p> <ul style="list-style-type: none"> • Apply mineral oil to your scalp to reduce itching. • If you lose your eyelashes and eyebrows, protect your eyes from dust and grit with a broad-brimmed hat and glasses.
<p>Numbness or tingling of the fingers or toes may commonly occur. This will slowly return to normal once your treatments are over. This may take several months.</p>	<ul style="list-style-type: none"> • Be careful when handling items that are sharp, hot, or cold. • Be careful when walking on uneven surfaces or doing activities that need you to balance or be steady. • Tell your healthcare team at your next visit if you have trouble with buttons, writing, picking up small objects, walking, or have fallen.
<p>Swelling of hands, feet, or lower legs may sometimes occur if your body retains extra fluid.</p>	<p>If swelling is a problem:</p> <ul style="list-style-type: none"> • Elevate your feet when sitting. • Avoid tight clothing.
<p>Your skin may darken in some areas such as your nails, soles or palms.</p>	<p>This will slowly return to normal once you stop treatment with doxorubicin.</p>
<p>Loss of appetite and weight loss may occur, and may persist after discontinuation of treatment.</p>	<ul style="list-style-type: none"> • Try the ideas in <i>Food Ideas to Help with Decreased Appetite.*</i>
<p>Constipation may sometimes occur.</p>	<ul style="list-style-type: none"> • Exercise if you can. • Drink plenty of fluids. • Try the ideas in <i>Food Choices to Manage Constipation.*</i>

* Please ask a member of your healthcare team for a copy.

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 heartbeat, face swelling or breathing problems.
- Signs of an **infection** such as fever (over 38°C or 100°F by an oral thermometer); chills, cough, pain or burning when you pass urine.
- **Diarrhea** or **changes in bowel habits**; black, tarry stools; blood or mucous in the stool; severe abdominal pain
- Signs of **bleeding problems** such as black, tarry stools, blood in urine, pinpoint red spots on skin, extensive bruising.
- 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 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.

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.