

For the Patient: PROTOCOL SMAVALIPNI

Other Names: Treatment of Unresectable or Metastatic Melanoma Using Alternative Dosing Regimen of Ipilimumab and Nivolumab

SM = Skin and Melanoma

AV = Advanced

AL = ALternative

IP = IPilimumab

NI = Nivolumab

ABOUT THIS MEDICATION

What is this drug used for?

- Ipilimumab (ip" i lim' ue mab) and Nivolumab (nye vol' ue mab) is an immunotherapy drug combination that is used to treat a type of cancer called melanoma, that has spread to other parts of the body (metastatic melanoma) or cannot be removed by surgery.
- Alternative dosing of these medications is used in patients who are unable to tolerate the standard doses.

How does this drug work?

- Ipilimumab and nivolumab are a type of therapy called immunotherapy. They are antibodies designed to help your own body's immune system target cancer cells to stop them from growing.

INTENDED BENEFITS

- Ipilimumab and nivolumab are being given to destroy and/or limit the growth of melanoma cells. It may improve your current symptoms, delay or prevent the onset of new ones and prolong your life expectancy
- It may take several treatments before your doctor can judge whether or not this treatment is helping. Treatment is continued as long as there is benefit and side effects are tolerable.

TREATMENT SUMMARY

How is this drug given?

- Nivolumab will be given as an infusion (a drip) into a vein (intravenously, IV) over a period of 30 minutes, followed by ipilimumab, which will be given IV over 30 minutes.
- You will be treated with nivolumab and ipilimumab once every 3 weeks. This 3 weeks period is called a "cycle". The cycle is repeated up to a total of 4 times.

- You will then receive nivolumab alone every 2 weeks **or** 4 weeks.

What will happen while I am being treated?

- A blood test (lab work) and other tests are done before starting each treatment cycle .
- Treatment may be interrupted based on your test results and/or side effects.

INSTRUCTIONS FOR THE PATIENT

- ***It is very important to report side effects immediately to your healthcare team. Do not manage side effects at home without speaking with your healthcare team. 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.***

What other drugs or foods can interact with ipilimumab and nivolumab?

- Other drugs may interact with ipilimumab and nivolumab. 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.
- The drinking of alcohol (in small amounts) does not appear to affect the safety or usefulness of ipilimumab or nivolumab.

Other important things to know:

- **Before you are given ipilimumab or nivolumab**, talk to your doctor if you:
 - have an active condition where your immune system attacks your body (autoimmune disease), such as ulcerative colitis, Crohn's disease, rheumatoid arthritis, multiple sclerosis, lupus 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 liver damage from diseases or drugs.
 - have any other medical conditions.
- In some cases your tumour may grow before it shrinks.
- Ipilimumab and nivolumab may cause fetal harm if used during pregnancy. It is best to use **birth control** while being treated with ipilimumab and nivolumab and for at least **5 months** after the last dose. Tell your doctor right away if you or your partner becomes pregnant.
- Ipilimumab and nivolumab may pass into your breast milk. **Do not breastfeed** during treatment.
- **Tell** doctors or dentists that you are being treated with ipilimumab and nivolumab before you receive any treatment from them. You should carry the BC Cancer **wallet card** for ipilimumab and nivolumab to alert health providers.
- ***Do not receive any immunizations before discussing with your doctor***

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Ipilimumab and nivolumab 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 drugs in your treatment plan.

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

- Ipilimumab and 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.
- **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
- feeling nauseous
- fever

| SERIOUS SIDE EFFECTS | How common is it? |
|--|--|
| Inflammation of the INTESTINES (colitis) <i>Symptoms may include</i> <ul style="list-style-type: none"> • diarrhea (loose stools) or more bowel movements than usual. Do not treat the diarrhea yourself. • blood in stools or dark, tarry, sticky stools • stomach pain (abdominal pain) or tenderness • fever | Very Common (more than 1 in 10) |
| Inflammation of the THYROID GLAND (hyperthyroidism, hypothyroidism) <i>Symptoms may include:</i> <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 | Very Common (more than 1 in 10) |
| Inflammation of the SKIN <i>Symptoms may include</i> <ul style="list-style-type: none"> • rash on your skin, mouth blisters, dry or peeling skin | Very Common (more than 1 in 10) |
| Depigmentation of the SKIN (vitiligo) | Common |
| Inflammation of the LUNGS (pneumonitis) <i>Symptoms may include:</i> <ul style="list-style-type: none"> • shortness of breath • chest pain • coughing | Very Common (more than 1 in 10) |

| SERIOUS SIDE EFFECTS | How common is it? |
|--|--|
| Problems with MUSCLES <i>Symptoms may include:</i> <ul style="list-style-type: none"> • back pain • spasms • weakness • muscle pain | Very Common (more than 1 in 10) |
| Inflammation of the NERVES <i>Symptoms may include</i> <ul style="list-style-type: none"> • weakness of legs, arms or face • numbness or tingling in hands or feet • lack of energy or dizziness | Common (less than 1 in 10 but more than 1 in 100) |
| Inflammation of certain GLANDS (pituitary, adrenal glands so they do not make enough hormone. <i>Symptoms may include:</i> <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 • changes in behavior such as less sex drive, being irritable or forgetful • vision problems, dizziness or fainting • excessive thirst and urination • unusual tiredness or sleepiness | Common (less than 1 in 10 but more than 1 in 100) |
| Inflammation of the EYES <i>Symptoms may include</i> <ul style="list-style-type: none"> • changes in eyesight, blurry vision, double vision, or other vision problems • eye pain or redness | Common (less than 1 in 10 but more than 1 in 100) |

| SERIOUS SIDE EFFECTS | How common is it? |
|--|--|
| 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 | Common (less than 1 in 10 but more than 1 in 100) |
| Infusion reaction. <i>Symptoms may include</i> <ul style="list-style-type: none"> • shortness of breath, wheezing or trouble breathing, cough, chest tightness • dizziness, fainting, rapid or weak heartbeat • itching, rash, hives, or feeling warm or flushed • swelling of the throat, tongue, or face • hoarse voice, throat tightness or trouble swallowing | 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"> • yellowing of your skin or the whites of your eyes, • dark urine, tiredness, nausea or vomiting, loss of appetite, pain on the right side of your stomach, or bruise easily | 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) |
| 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 | Rare (less than 1 in 1000 but more than 1 in 10000) |

| OTHER SIDE EFFECTS | How common is it? | MANAGEMENT |
|---|-------------------|---|
| Pain or tenderness may occur where the needle was placed. | Rare | Apply cool compresses or soak in cool water for 15-20 minutes several times a day. |
| Nausea does not usually occur. | Rare | |
| Fever may sometimes occur. | Common | <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 you have other symptoms of colitis, tell your doctor as soon as possible. (see the table above for serious side effects) |
| Tiredness and lack of energy may sometimes occur. | Very Common | <ul style="list-style-type: none"> Do not drive a car or operate machinery if you are feeling tired. Try the ideas in <i>Your Bank to Energy Savings: Helping People with Cancer Handle Fatigue</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) |
| Headache may sometimes occur. | Common | <ul style="list-style-type: none"> Take acetaminophen (e.g., TYLENOL®) every 4-6 hours if needed, 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) |

| OTHER SIDE EFFECTS | How common is it? | MANAGEMENT |
|---|-------------------|--|
| Constipation may sometimes occur. | Rare | <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) |
| Loss of appetite and weight loss sometimes occur. | Common | <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 above for serious side effects) |
| Hair loss is rare with ipilimumab and nivolumab. | Uncommon | If hair loss is a problem, refer to <i>For the Patient: Hair Loss Due to Chemotherapy</i> .* |

***Please ask your nurse or pharmacist for a copy.**

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

**IPILIMUMAB: 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 - Surrey.....604-930-4055
BC Cancer - Vancouver.....604-877-6000
BC Cancer - Victoria.....250-519-5500

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

Rev May 2019



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. Additional information on immunotherapy toxicity treatment algorithms is located at the end of the above posted protocol at www.bccancer.bc.ca.

Provincial Systemic Therapy Program
Developed: 28 Nov 2017 Revised: