BC Cancer Protocol Summary for Treatment of Locally Advanced Non-Small Cell Lung Cancer Using 4-Weekly Durvalumab

Protocol Code	*ULULADUR4*
Tumour Group	*Lung*
Contact Physician	*Dr. Angela Chan*

ELIGIBILITY:

- Stage III unresectable NSCLC
- No disease progression following prior treatment with at least 2 cycles of platinum-based chemotherapy given concurrently with radiation (e.g., LULAPERT, LULAPE2RT, LULACATRT)
- ECOG 0-1
- Adequate hepatic and renal function
- Access to a treatment centre with expertise to manage immune-mediated adverse reactions of durvalumab
- *BC Cancer Compassionate Access Program (CAP) approval must be obtained. CAP approval is not required for switch to ULULADUR4 if prior approval is in place for ULULADUR.*
- *Note: patients may have subsequent checkpoint inhibitors provided the last dose of durvalumab was > 6 months. They are not eligible if they progressed on durvalumab.*

EXCLUSIONS:

- ECOG performance status ≥ 2
- Active or previous autoimmune disease (within the past 2 years)
- Unresolved toxic effects of Grade ≥ 2 from prior treatment
- Grade ≥ 2 pneumonitis from prior chemoradiotherapy
- Use with caution in patients with long term immunosuppressive therapy or systemic corticosteroids (requiring more than 10 mg predniSONE/day or equivalent)

TESTS:

- Baseline: CBC & differential, platelets, creatinine, alkaline phosphatase, ALT, total bilirubin, LDH, sodium, potassium, TSH, morning serum cortisol, chest x-ray
- Before each treatment: CBC & differential, platelets, creatinine, alkaline phosphatase, ALT, total bilirubin, LDH, sodium, potassium, TSH
- If clinically indicated: chest x-ray, ECG, morning serum cortisol, lipase, glucose, serum or urine hCG (required for women of child bearing potential if pregnancy suspected), free T3 and free T4, serum ACTH levels, testosterone, estradiol, FSH, LH
- Weekly telephone nursing assessment for signs and symptoms of side effects while on treatment (optional)

Warning: The information contained in these documents are a statement of consensus of BC Cancer professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is at your own risk and is subject to BC Cancer's terms of use available at www.bccancer.bc.ca/legal.htm

PREMEDICATIONS:

- Antiemetics are not usually required
- Antiemetic protocol for low emetogenicity (see SCNAUSEA)
- If prior infusion reactions to durvalumab: diphenhydrAMINE 50 mg PO, acetaminophen 325 to 975 mg PO, and hydrocortisone 25 mg IV 30 minutes prior to treatment

TREATMENT:

Drug	Dose	BC Cancer Administration Guideline
durvalumab	20 mg/kg (maximum 1500 mg)	IV in 100 mL NS over 60 minutes *Using a 0.2 micron in-line filter*

- Repeat **every 4 weeks** for 1 year of treatment (including doses given as ULULADUR), unless disease progression or unacceptable toxicity

DOSE MODIFICATIONS:

No specific dose modifications. Toxicity managed by treatment delay and other measures (see SCIMMUNE for management of immune-mediated adverse reactions to checkpoint inhibitor immunotherapy: http://www.bccancer.bc.ca/chemotherapy-protocols-site/Documents/Supportive%20Care/SCIMMUNE_Protocol.pdf).

PRECAUTIONS:

1. **Serious immune-mediated reactions**: can be severe to fatal and usually occur during the treatment course, but may develop months after discontinuation of therapy. They may include enterocolitis, intestinal perforation or hemorrhage, hepatitis, dermatitis, neuropathy, endocrinopathy, pneumonitis, as well as toxicities in other organ systems. Early diagnosis and appropriate management are essential to minimize life-threatening complications (see SCIMMUNE for management of immune-mediated adverse reactions to checkpoint inhibitor immunotherapy: http://www.bccancer.bc.ca/chemotherapy-protocols-site/Documents/Supportive%20Care/SCIMMUNE_Protocol.pdf).
2. **Infusion-related reactions:** isolated cases of severe infusion reactions have been reported. For mild or moderate infusion reactions, decrease the infusion rate to 50% or temporarily interrupt infusion until the reaction has resolved. Consider premedication for subsequent infusions. Permanently discontinue durvalumab for severe reactions.
3. **Infections:** severe infections such as sepsis, necrotizing fasciitis, and osteomyelitis have been reported. Treat suspected or confirmed infections as indicated. Withhold durvalumab for severe infections.

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Contact Dr. Angela Chan or tumour group delegate at (604) 930-2098 or 1-800-523-2885 with any problems or questions regarding this treatment program.

REFERENCES:

1. Antonia SJ, Villegas A, Daniel D, et al. Durvalumab after Chemoradiotherapy in Stage III Non-Small Cell Lung Cancer. N Engl J Med 2017; 377:1919-29.
2. Antonia SJ, Villegas A, Daniel D, et al. Overall Survival with Durvalumab After Chemoradiotherapy in Stage III NSCLC. N Engl J Med 2018; 379;24:2342-50.
3. AstraZeneca Canada Inc. IMFINZI® product monograph. Mississauga, Ontario; 23 August 2019.
4. Baverel PG, Dubois V, Jin C, et al. Population Pharmacokinetics of durvalumab in cancer patients and association with longitudinal biomarkers of disease status. Clin Pharmacol Therapeut 2018;103:631-642.
5. Nehra J, Bradbury PA, Ellis PM, et al. A Canadian cancer trials group phase IB study of durvalumab (anti-PD-L1) plus tremelimumab (anti-CTLA-4) given concurrently or sequentially in patients with advanced, incurable solid malignancies. Invest New Drugs (Epub February 4, 2020, DOI: 10.1007/s10637-020-00904-7).
6. Ogasawara K, Newhall K, Maxwell S, et al. Population pharmacokinetics of an anti-PD-L1 antibody, durvalumab in patients with hematologic malignancies Clin Pharmacokinet 2020;59:217-227.
7. Paz-Ares L, Dvorkin M, Chen, Y, et al. Durvalumab plus platinum-etoposide versus platinum-etoposide in first-line treatment of extensive-stage small-cell lung cancer (CASPIAN): a randomized, controlled, open-label, phase 3 trial. Lancet 2019;394:1929-39.

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