BC Cancer Protocol Summary for Adjuvant Treatment of Squamous Cell Carcinoma of the Head and Neck using Pembrolizumab and Concurrent 3-Weekly CARBOplatin and Radiation

Protocol Code	*HNAJPMBCRT*
Tumour Group	*Head and Neck*
Contact Physician	*HN Systemic Therapy*

ELIGIBILITY:

Patients must have:

- Resected locally advanced squamous cell carcinoma of the head and neck (HNSCC) at high risk of recurrence (with positive margins or extracapsular extension)
- PD-L1 CPS score greater than or equal to 1%,
- Completed neoadjuvant treatment with HNNAPMB prior to resection,
- Ineligibility for CISplatin, such as:
  - Renal insufficiency, creatinine clearance less than 45 mL/min
  - Cardiac disease that results in an intolerance to fluid load
  - Severe neuropathy
  - Marked hearing loss
  - Other significant risk factors that render patient ineligible for concurrent CISplatin, however the risk of disease is sufficient to warrant concurrent treatment

Patients should have:

- Access to a treatment centre with expertise to manage immune-mediated adverse reactions of pembrolizumab

EXCLUSIONS:

Patient must not have:

- Distant metastases
- Tumours outside the oropharynx, larynx, hypopharynx or oral cavity

CAUTIONS:

- Active, known or suspected autoimmune disease
- Patients with long term immunosuppressive therapy or systemic corticosteroids (requiring more than 10 mg predniSONE/day or equivalent)

SUPPORTIVE CARE:

- Prior to initiation of treatment, patients will be referred for consultation to Dentistry and Nutrition Services
- Placement of a feeding gastrostomy tube prior to treatment is encouraged if there has been significant weight loss (i.e., greater than 10% from baseline)
- Standard oral hygiene and care during treatment (sodium bicarbonate mouth rinse, nystatin/fluconazole for fungal infections, antibiotics for documented infections)

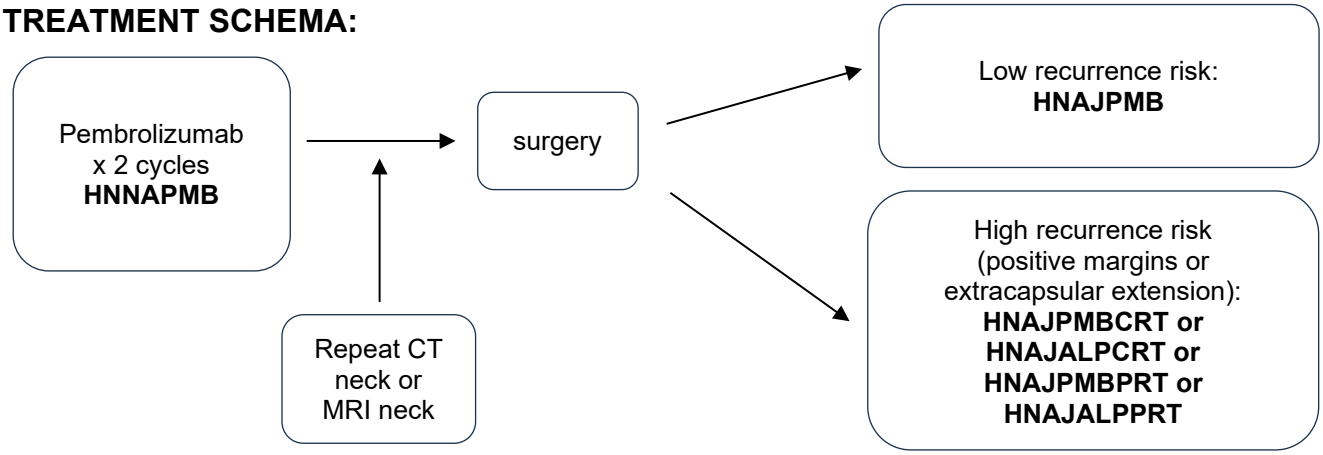
TESTS:

- Baseline: CBC & Diff, creatinine, ALT, total bilirubin, alkaline phosphatase, sodium, potassium, urea, albumin, magnesium, calcium, phosphate, serum or urine HCG (required for women of childbearing potential if pregnancy suspected)
- Cycles 1 to 3, prior to each cycle: CBC & Diff, creatinine, alkaline phosphatase, ALT, total bilirubin, LDH, sodium, potassium, calcium, albumin, magnesium, TSH
- Cycle 4 and onwards, before each treatment: CBC & Diff, creatinine, alkaline phosphatase, ALT, total bilirubin, LDH, sodium, potassium, TSH
- If clinically indicated: chest x-ray, morning serum cortisol, lipase, random glucose, serum or urine HCG (required for women of childbearing potential if pregnancy suspected), free T3 and free T4, serum ACTH levels, testosterone, estradiol, FSH, LH, ECG
- Weekly telephone nursing assessment for signs and symptoms of side effects while on treatment (optional).

PREMEDICATIONS:

- For Cycles 1 to 3, antiemetic protocol for highly emetogenic chemotherapy (see protocol SCNAUSEA).
- For Cycle 4 and onwards: Antiemetics are not usually required. If required, antiemetic protocol for low emetogenicity (see SCNAUSEA).
- If prior infusion reactions to pembrolizumab: diphenhydrAMINE 50 mg PO, acetaminophen 325 to 975 mg PO, and hydrocortisone 25 mg IV 30 minutes prior to treatment

TREATMENT SCHEMA:



TREATMENT:

- Note: Since CARBOplatin is a radio-sensitizing as well as an active agent, it is to be administered on a day on which radiation therapy is delivered. If radiation therapy is cancelled, do not give CARBOplatin that day: postpone until radiation therapy resumes. Pembrolizumab may be continued during CARBOplatin or radiation therapy delay.

Cycles 1 and 2: Treatment to start on Day 1 of radiation therapy

Drug	Dose	BC Cancer Administration Guideline
pembrolizumab	2 mg/kg* (maximum 200 mg)	IV in 50 mL NS over 30 minutes using a 0.2 micron in-line filter
CARBOplatin	Dose = AUC 5 x (GFR*+ 25)	IV in 100 to 250 mL NS over 30 minutes

*Select dose per Dose Banding Table (appendix).

- Repeat every 21 days x 2 cycles

Cycle 3: Treatment to start 21 Days after Cycle 2 Day 1

Drug	Dose	BC Cancer Administration Guideline
pembrolizumab	2 mg/kg* (maximum 200 mg)	IV in 50 mL NS over 30 minutes using a 0.2 micron in-line filter
CARBOplatin	Dose = AUC 5 x (GFR+ 25) (optional)**	IV in 100 to 250 mL NS over 30 minutes

*Select dose per Dose Banding Table (appendix).
**If radiation therapy is planned for longer than 6.5 weeks, CARBOplatin should be ordered.

*Measured GFR (e.g. nuclear renogram) is preferred in circumstances of co-morbidity that could affect renal function (third-space fluid accumulations, hypoproteinemia, potentially inadequate fluid intake, age greater than 70, etc.). The lab reported GFR (MDRD formula) may be used as an alternative to the Cockcroft-Gault estimate of GFR; the estimated GFR reported by the lab or calculated using the Cockcroft-Gault equation should be capped at 125 mL/min when it is used to calculate the initial carboplatin dose. When a nuclear renogram is available, this clearance would take precedence.

Cockcroft-Gault Formula

$$CrCl = \frac{N\ (140 - age) \times weight\ (kg)}{serum\ creatinine\ (micromol/L)}$$

Where N = 1.04 for females, and 1.23 for males

Note: The *same* method of estimation should be used throughout the treatment course (i.e. if lab reported GFR was used initially, this should be used for dosing in all subsequent cycles and not the Cockcroft- Gault estimate).

Recalculate GFR if creatinine increases by greater than 20% or rises above the upper limit of normal.

Cycles 4 and onwards: starts 21 days after Cycle 3

Drug	Dose	BC Cancer Administration Guideline
pembrolizumab	2 mg/kg* (maximum 200 mg)	IV in 50 mL NS over 30 minutes using a 0.2 micron in-line filter

*Select dose per Dose Banding Table (appendix).

- Repeat every 21 days until disease progression, unacceptable toxicity up to a maximum of 17 cycles of 3-weekly dosing (or equivalent combination of 3-weekly and 6-weekly doses), including doses given as part of HNNAPMB. Patients may have treatment breaks for reasons other than progression (e.g. toxicities).

OR

Drug	Dose	BC Cancer Administration Guideline
pembrolizumab	4 mg/kg* (maximum 400 mg)	IV in 50 mL NS over 30 minutes using a 0.2 micron in-line filter

*Select dose per Dose Banding Table (appendix).

- Repeat every 42 days until disease progression, unacceptable toxicity up to a equivalent maximum of 17 cycles of 3-weekly dosing (equivalent combination of 3-weekly and 6-weekly doses), including doses given as part of HNNAPMB. Patients may have treatment breaks for reasons other than progression (e.g. toxicities).

DOSE MODIFICATIONS:

1. **For pembrolizumab:** No specific dose modifications for pembrolizumab. Toxicity managed by treatment delay and other measures (see SCIMMUNE protocol for management of immune-mediated adverse reactions to checkpoint inhibitors immunotherapy).

2. **Hematology:** for CARBOplatin

ANC ($x10^9$/L)		Platelets ($x10^9$/L)	Dose
Greater than or equal to 1.0	and	Greater than or equal to 100	100%
Less than 1.0	or	Less than 100	Delay 1 week or until recovery

2. **Renal dysfunction:** If significant increase (greater than 20% or rises above the upper limit of normal) in creatinine, recheck/recalculate GFR and recalculate CARBOplatin dose using new GFR.

3. **Neutropenic fever**: If febrile neutropenia occurs at any point during treatment, reduce subsequent CARBOplatin doses to 80%.

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 protocol for management of immune-mediated adverse reactions to checkpoint inhibitors immunotherapy).
2. **Infusion-related reactions:** isolated cases of severe infusion reactions have been reported. Discontinue pembrolizumab with severe reactions (Grade 3 or 4). Patients with mild or moderate infusion reactions may receive pembrolizumab with close monitoring, reduced rates of administration and use of premedication.
3. **Neutropenia**: Fever or other evidence of infection must be assessed promptly and treated aggressively.
4. **Hypersensitivity**: Reactions to CARBOplatin may develop in patients who have been extensively pre-treated with this agent. See BC Cancer Protocol Summary for Management of Infusion-Related Reactions to Chemotherapeutic Agents – SCDRUGRX.

Call the HN Systemic therapy physician at your regional cancer centre or the HN Systemic Therapy Chair with any problems or questions regarding this treatment program.

REFERENCES:

1. Uppaluri R, Haddad RI, Tao Y et al. Neoadjuvant and Adjuvant Pembrolizumab in Locally Advanced Head and Neck Cancer. N Engl J Med 2025;393:37-50.
2. Pembrolizumab (Keytruda) Canada's Drug Agency (CDA-AMC) Reimbursement Recommendation. Canadian Journal of Health Technologies. October 2025; 5(10): 1-21.

Appendix. Dose Bands

PEMBROLIZUMAB DOSE BANDING TABLE (2 mg/kg capped 200 mg)

Ordered Dose (mg)		Rounded dose (mg)
From:	To:	
Less than 70		**Pharmacy prepares specific dose**
70	80.49	**75**
80.5	92.49	**85**
92.5	110.49	**100**
110.5	137.49	**125**
137.5	162.49	**150**
162.5	187.49	**175**
187.5	200	**200**

PEMBROLIZUMAB DOSE BANDING TABLE (4 mg/kg capped 400 mg)

Ordered Dose (mg)		Rounded dose (mg)
From:	To:	
Less than 137.5		**Pharmacy prepares specific dose**
137.5	162.49	**150**
162.5	187.49	**175**
187.5	221.49	**200**
221.5	242.49	**225**
242.5	264.49	**250**
264.5	284.49	**275**
284.5	332.49	**300**
332.5	374.49	**350**
374.5	400	**400**