BC Cancer Protocol Summary for Adjuvant Treatment of Squamous Cell Carcinoma of the Head and Neck using Pembrolizumab and Concurrent CISplatin and Radiation Therapy

Protocol Code: *HNAJPMBPRT*

Tumour Group: *Head and Neck*

Contact Physicians: *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

EXCLUSIONS:

Patient must not have:

- Distant metastases
- Tumours outside the oropharynx, larynx, hypopharynx or oral cavity
- Contraindication to CISplatin (e.g. deafness, intolerance to fluid load, neuropathy)

CAUTIONS:

- Active uncontrolled autoimmune disease
- Known active hepatitis B, C or HIV
- Patients with long term immunosuppressive therapy or systemic corticosteroids (requiring more than 10 mg predniSONE/day or equivalent)
- Pre-existing motor or sensory neuropathy greater than Grade 2

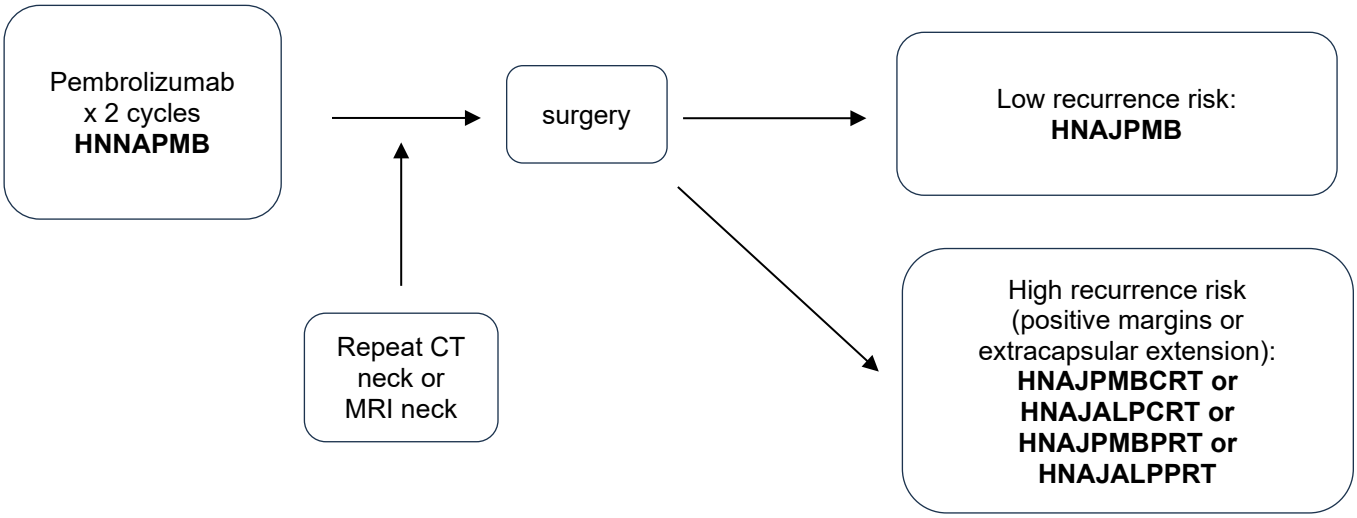
TESTS:

- 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 2 (and Cycle 3 if CISplatin ordered): antiemetic protocol for highly emetogenic chemotherapy (see protocol SCNAUSEA).
- For Cycle 3 and onwards (if only pembrolizumab ordered): 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 for Cycles 1 to 3: Since CISplatin 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 CISplatin that day: postpone until radiation therapy resumes. Pembrolizumab may be continued during CISplatin 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
CISplatin	100 mg/m^2	IV in NS 1000 mL with mannitol 30 g and potassium chloride 10 mmol over 2 hours

*Select dose per Dose Banding Table (appendix).

- Repeat every 21 days for 2 cycles

Cycle 3: starts 21 days after Cycle 2

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
CISplatin	100 mg/m^2 (optional)**	IV in NS 1000 mL with mannitol 30 g and potassium chloride 10 mmol over 2 hours

*Select dose per Dose Banding Table (appendix).

**If radiation therapy is planned for longer than 6.5 weeks, CISplatin may be ordered.

Hydration:

Pre-CISplatin:	D5W-1/2NS 1000 mL with potassium chloride 20 mmol plus magnesium sulphate 2 g over 60 minutes.
Post-CISplatin:	D5W-1/2NS 1000 mL with potassium chloride 20 mmol plus magnesium sulphate 2 g at 500 mL/h for 2 hours.

Alternative hydration for inpatients:

Pre-CISplatin:	D5W-1/2NS 1000 mL with potassium chloride 20 mmol plus magnesium sulphate 2 g IV over 3 hours. Prior to beginning **CISplatin**, urine output must be greater than or equal to 300 mL in 3 hours. May repeat prehydration x 1000 mL to ensure urine output greater than 300 mL in 3 hours. If urine output not adequate after 2000 mL, notify physician.
Post-CISplatin:	D5W-1/2NS with potassium chloride 20 mmol/L plus magnesium sulphate 2 g/L IV at 200 mL/h for 12 hours. Measure intake/output every 3 hours while on IV: • If output less than 300 mL during a 3-hour period, increase IV to 300 mL/h for 3 hours. • If urine output still less than 300 mL in a subsequent 3-hour period, give **furosemide** 20 mg IV x 1. • If output still not adequate, notify physician. May discontinue IV and discharge after post- hydration if urine output adequate and patient not vomiting.

Cycles 4 and onwards: start 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).

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. **Hematological:** for CISplatin

ANC (x 10^9/L)		Platelets (x 10^9/L)	Dose
Greater than or equal to 1.5	and	Greater than or equal to 100	100%
1.0 to less than 1.5	or	75 to less than 100	75%
Less than 1.0	or	Less than 75	Delay one week

3. **Renal dysfunction:** for CISplatin

Creatinine clearance (mL/minute)	Dose
Greater than or equal to 60	100%
45 to less than 60	80% CISplatin
Less than 45	Hold CISplatin or delay with additional fluids

4. **Gastrointestinal:** for CISplatin

Grade	Dysphagia or Stomatitis	Dose
0 to 2		100%
3	Requiring [initiation of] feeding tube, IV hydration or hyperalimentation	Delay until improvement and proceed at 75%
4	Complete obstruction (cannot swallow saliva); ulceration with bleeding not induced by minor trauma or abrasion or perforation	Discontinue

Weight Loss from Baseline	Dose
Less than or equal to 10%	100%
Greater than 10%	Consider 75% if hyperalimentation instituted, otherwise discontinue (at physician's discretion)

5. **Neuropathy**: Dose modification or discontinuation of CISplatin may be required (see BC Cancer Cancer Drug Manual).

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. **Renal Toxicity:** Nephrotoxicity is common with CISplatin. Encourage oral hydration. Avoid nephrotoxic drugs such as aminoglycosides.
4. **Ototoxicity:** CISplatin is ototoxic and its use must be cautioned in individuals with existing hearing loss.
5. **Neutropenia**: Fever or other evidence of infection must be assessed promptly and treated aggressively.

Contact 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**