BC Cancer Protocol Summary of Treatment for Unresectable, Locoregionally Recurrent or Metastatic Squamous Cell Carcinoma of the Head and Neck Using PACLitaxel and CISplatin or CARBOplatin

Protocol Code	*HNAVPC*
Tumour Group	*Head and Neck*
Contact Physician	*Dr. Cheryl Ho*

ELIGIBILITY:

- Locoregionally recurrent or metastatic squamous cell carcinoma of the head and neck including primary unknown
- Adequate hematologic, hepatic, and renal function
- Age greater than or equal to 18 years
- ECOG performance status 0, 1, or 2

EXCLUSIONS:

- Significant cardiac disease within previous year (CHF, arrhythmia, recent MI)

TESTS:

- Baseline and before each treatment: CBC & differential, platelets, serum creatinine, liver enzymes (alkaline phosphatase, ALT, bilirubin)

PREMEDICATIONS:

- For CISplatin doses greater than or equal to 50 mg, use antiemetic protocol for highly emetogetic chemotherapy (see SCNAUSEA protocol)
- For CARBOplatin use antiemetic protocol for moderately emetogenic chemotherapy (see SCNAUSEA protocol)
- **Paclitaxel must not be started unless the following drugs have been given:**
  45 minutes prior to PACLitaxel:
  - dexamethasone 20 mg IV in 50 mL NS over 15 minutes

  30 minutes prior to PACLitaxel:
  - diphenhydrAMINE 50 mg IV in NS 50 mL over 15 minutes and famotidine 20 mg IV in NS 100 mL over 15 minutes (Y-site compatible)

TREATMENT: (give PACLitaxel first)

Drug	Dose	BC Cancer Administration Guideline
PACLitaxel	175 mg/m² day 1	IV in 250 to 500 mL NS over 3 hours (use non-DEHP bag and non-DEHP tubing with 0.2 micron in-line filter)
CISplatin	75 mg/m^2 day 1	Prehydrate with NS 1000 mL over 1 hour, then give IV in 500 mL NS with potassium chloride 20 mEq, magnesium sulphate 1 g, 30 g mannitol over 1 hour

Repeat every 21 days x 4 to 6 cycles.

Alternatively, CARBOplatin may be used instead of CISplatin:

Drug	Dose	BC Cancer Administration Guideline
CARBOplatin	AUC 5 or 6 day 1 Dose = AUC x (GFR* + 25)	IV in 100 to 250 mL NS over 30 minutes

Determined at discretion of the attending medical oncologist

*Measured GFR (e.g. nuclear renogram) is preferred whenever feasible, *particularly* in circumstances of co-morbidity that could affect renal function (third-space fluid accumulations, hypoproteinemia, potentially inadequate fluid intake, 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

$$GFR = \frac{N^* \times (140 - \text{age in years}) \times \text{wt (kg)}}{\text{serum creatinine (micromol/L)}}$$

*For males in = 1.23; for females N = 1.04

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).

DOSE MODIFICATIONS:

Hematological on treatment day:

ANC (x 10^9/L)		Platelets (x 10^9/L)	Doses (both drugs)
greater than or equal to 1.0	And	greater than or equal to 100	100%
less than 1.0	Or	less than 100	delay until recovery

Renal dysfunction:

Calculated Cr Clearance (mL/min)	PACLitaxelDose	CISplatin Dose
greater than or equal to 60	100%	100%
45-59	100%	80% CISplatin or go to CARBOplatin option
less than 45	100%	HOLD CISplatin, or go to CARBOplatin option

Renal dysfunction: for CARBOplatin
If significant increase (greater than 20%) in creatinine, repeat nuclear renogram (if available) and recalculate CARBOplatin dose using new GFR.

Hepatic dysfunction for PACLitaxel:
Suggested guidelines for first course; subsequent courses should be based on individual tolerance

ALT or AST		bilirubin	dose
<10 X ULN	and	≤1.25 X ULN	175 mg/m²
<10 X ULN	and	1.26-2 X ULN	135 mg/m²
<10 X ULN	and	2.01-5 X ULN	90 mg/m²
≥10 X ULN	or	>5 X ULN	not recommended

Peripheral Sensory Neuropathy: Dose reduction may be required for CISplatin and PACLitaxel (see BC Cancer Drug Manual)

Arthralgia and/or myalgia: If arthralgia and/or myalgia of grade 2 (moderate) or higher is not relieved by adequate doses of NSAIDs or acetaminophen with codeine (e.g., TYLENOL #3®), a limited number of studies report a possible therapeutic benefit using:

- predniSONE 10 mg po bid x 5 days starting 24 hours post-PACLitaxel
- gabapentin 300 mg po on day before chemotherapy, 300 mg bid on treatment day, then 300 mg tid x 7 to 10 days

If arthralgia and/or myalgia persists, reduce subsequent PACLitaxel doses accordingly.

PRECAUTIONS:

1. **Neutropenia**: Fever or other evidence of infection must be assessed promptly and treated aggressively. Refer to BC Cancer Febrile Neutropenia Guidelines.
2. **Extravasation**: PACLitaxel causes pain and tissue necrosis if extravasated. Refer to BC Cancer Extravasation Guidelines.
3. **Hypersensitivity**: Reactions are common with PACLitaxel. Refer to BC Cancer Hypersensitivity Guidelines, SCDRUGRX protocol.

mild symptoms (e.g. mild flushing, rash, pruritus)	▪ complete PACLitaxel infusion. Supervise at bedside ▪ no treatment required
moderate symptoms (e.g. moderate rash, flushing, mild dyspnea, chest discomfort, mild hypotension	▪ stop PACLitaxel infusion ▪ give IV diphenhydrAMINE 25-50 mg and IV hydrocortisone IV 100 mg ▪ after recovery of symptoms resume PACLitaxel infusion at 20 mL/hr for 5 minutes, 30 mL/hr for 5 minutes, 40 mL/hr for 5 minutes, then 60 mL/hr for 5 minutes. If no reaction, increase to full rate. ▪ if reaction recurs, discontinue PACLitaxel therapy
severe symptoms (i.e. *one* or more of respiratory distress requiring treatment, generalized urticaria, angioedema, hypotension requiring therapy)	▪ stop PACLitaxel infusion ▪ give IV antihistamine and steroid as above. Add epinephhrine or bronchodilators if indicated ▪ discontinue PACLitaxel therapy

4. **Renal Toxicity**: Nephrotoxicity is common with CISplatin. Encourage oral hydration. Avoid nephrotoxic drugs such as aminoglycoside

Call Dr. Cheryl Ho or tumour group delegate at (604) 877-6000 or 1-800-663-3333 with any problems or questions regarding this treatment program.

References:

1. Gibson MK, Li Y, Murphy B, et. al. Randomized phase III evaluation of cisplatin plus fluorouracil versus cisplatin plus paclitaxel in advanced head and neck cancer (E1395): An intergroup trial of the Eastern Cooperative Oncology Group. J Clin Oncol 2005 May 20;23(15):3562-3567.
2. Stathopoulos GP, Rigatos S, Papakostas P, et. al. Effectiveness of paclitaxel and carboplatin combination in heavily pretreated patients with head and neck cancers. Eur J Cancer 1997;33(11):1780-1783
3. Clark JI, Hofmeister C, Choudhury A, et. al. Phase II evaluation of paclitaxel in combination with carboplatin in advanced head and neck carcinoma. Cancer 2001;92:2334-2340.