BC Cancer Protocol Summary for Treatment of Recurrent or Metastatic Nasopharyngeal Carcinoma with CARBOplatin and PACLitaxel

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

ELIGIBILITY:
- Recurrent or metastatic nasopharyngeal carcinoma
- Adequate hematologic, hepatic and renal function.
- Age greater than or equal to 18 years.
- ECOG performance status 0, 1 or 2.

TESTS:
- Baseline and before each treatment: CBC & differential, platelets, creatinine, liver function tests (ALT, Bilirubin)

PREMEDICATIONS:
- **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)
- Antiemetic protocol for High emetogenic chemotherapy (see protocol SCNAUSEA)

TREATMENT: (Give PACLitaxel first)

Drug	Dose	BC Cancer Administration Guideline
PACLitaxel	175 mg/m^2	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)
CARBOplatin	AUC 6 Dose = AUC x (GFR* + 25)	IV in 100 to 250 mL NS over 30 minutes

- Repeat every 21 days x 4-6 cycles

*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:

Hematology (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

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

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 accordingly.

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

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

PRECAUTIONS:

1. **Hypersensitivity**: Reactions are common. See BC Cancer Hypersensitivity Guidelines

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

2. **Extravasation**: PACLitaxel causes pain and may, rarely, cause tissue necrosis if extravasated. Refer to BC Cancer Extravasation Guidelines.
3. **Neutropenia**: Fever or other evidence of infection must be assessed promptly and treated aggressively.

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

References:

1. Ciuleanu TE, Fountzilas G, Ciuleanu E, et al. Paclitaxel and carboplatin in relapsed or metastatic nasopharyngeal carcinoma: a multicenter phase II study. J BUON. 2004;9(2):161-5.
2. Yeo W, Leung TW, Chan AT, et al. A phase II study of combination paclitaxel and carboplatin in advanced nasopharyngeal carcinoma. Eur J Cancer 1998;34(13):2027-31.
3: Tan EH, Khoo KS, Wee J, et al. Phase II trial of a paclitaxel and carboplatin combination in Asian patients with metastatic nasopharyngeal carcinoma. Ann Oncol 1999;10(2):235-7.
4: Airoldi M, Pedani F, Marchionatti S, et al. Carboplatin plus taxol is an effective third-line regimen in recurrent undifferentiated nasopharyngeal carcinoma. Tumori 2002;88(4):273-6.