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 emetogenic 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)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>BC Cancer Administration Guideline</th>
</tr>
</thead>
<tbody>
<tr>
<td>PACLitaxel</td>
<td>175 mg/m²  day 1</td>
<td>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)</td>
</tr>
<tr>
<td>CISplatin</td>
<td>75 mg/m²  day 1</td>
<td>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</td>
</tr>
</tbody>
</table>

Repeat every 21 days x 4 to 6 cycles.

Alternatively, CARBOplatin may be used instead of CISplatin:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>BC Cancer Administration Guideline</th>
</tr>
</thead>
<tbody>
<tr>
<td>CARBOplatin</td>
<td>AUC 5 or 6 day 1</td>
<td>Dose = AUC x (GFR* + 25) IV in 100 to 250 mL NS over 30 minutes</td>
</tr>
</tbody>
</table>

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:

<table>
<thead>
<tr>
<th>ANC (x 10^9/L)</th>
<th>Platelets (x 10^9/L)</th>
<th>Doses (both drugs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>greater than or equal to 1.0 And greater than or equal to 100</td>
<td>100%</td>
<td></td>
</tr>
<tr>
<td>less than 1.0 Or less than 100</td>
<td>delay until recovery</td>
<td></td>
</tr>
</tbody>
</table>

Renal dysfunction:

<table>
<thead>
<tr>
<th>Calculated Cr Clearance (mL/min)</th>
<th>PACLitaxel Dose</th>
<th>CISplatin Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>greater than or equal to 60</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>45-59</td>
<td>100%</td>
<td>80% CISplatin or go to CARBOplatin option</td>
</tr>
<tr>
<td>less than 45</td>
<td>100%</td>
<td>HOLD CISplatin, or go to CARBOplatin option</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>ALT or AST</th>
<th>bilirubin</th>
<th>dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;10 X ULN and ≤1.25 X ULN</td>
<td>175 mg/m²</td>
<td></td>
</tr>
<tr>
<td>&lt;10 X ULN and 1.26-2 X ULN</td>
<td>135 mg/m²</td>
<td></td>
</tr>
<tr>
<td>&lt;10 X ULN and 2.01-5 X ULN</td>
<td>90 mg/m²</td>
<td></td>
</tr>
<tr>
<td>≥10 X ULN or &gt;5 X ULN</td>
<td>not recommended</td>
<td></td>
</tr>
</tbody>
</table>

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 epinephrine 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: