ELIGIBILITY:
- Previously untreated patients with Stage IIIB or IV disease.
  - May be used as second- or third-line therapy if prior treatment with immunotherapy or targeted agents
- Also:
  - Previously untreated stage IIIA disease not amenable to combined modality therapy
  - Inoperable early stage disease
  - Recurrent disease, including individuals treated with adjuvant chemotherapy following resection of early stage disease or individuals treated with combined modality therapy for locally advanced disease
- Adequate hematologic, hepatic and renal function
- Age greater than or equal to 18 years
- ECOG performance status 0, 1 or 2

TESTS:
- Baseline: CBC & differential, platelets, creatinine, alkaline phosphatase, ALT, total bilirubin, LDH, chest X-ray, camera nuclear renogram for GFR (if available)
  - C-reactive protein and albumin (optional, and results do not have to be available to proceed with first treatment)
- Before each treatment: CBC & differential, platelets, creatinine, any initially elevated tumor marker
- If clinically indicated: alkaline phosphatase, ALT, total bilirubin and LDH prior to each cycle

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 and Ranitidine 50 mg IV in 50 mL NS over 20 minutes (compatible up to 3 hours when mixed in bag)
Antiemetic protocol for High emetogenic chemotherapy (see protocol SCNAUSEA)

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>200 mg/m²</td>
<td>IV in 500 mL NS over 3 hours (use non-DEHP bag and non-DEHP tubing with 0.22 micron or smaller in-line filter)</td>
</tr>
<tr>
<td>CARBOplatin</td>
<td>AUC 6</td>
<td>IV in 250 mL NS over 30 minutes</td>
</tr>
</tbody>
</table>

Repeat every 21 days x 4-6 cycles

*GFR preferably from nuclear renogram, if not possible use:

\[
GFR = \frac{N \times (140 - \text{age in years}) \times \text{wt (kg)}}{\text{serum creatinine (micromol/L)}} \quad N = 1.04 \text{ (women)} \text{ or } 1.23 \text{ (men)}
\]

The estimated GFR 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.

DOSE MODIFICATIONS:

1. Hematology (on treatment day):

<table>
<thead>
<tr>
<th>ANC (x 10⁹/L)</th>
<th>Platelets (x 10⁹/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>less than 1.0 or less than 100</td>
<td>100% delay until recovery</td>
</tr>
</tbody>
</table>

2. 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:
   - predni SONE 10 mg PO bid x 5 days starting 24 hours post-PACLtaxel
   - 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 to 175 mg/m².
3. **Neuropathy**: Dose modification or discontinuation may be required (see BC Cancer Drug Manual).

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

5. **Hepatic dysfunction**: Dose reduction may be required for PACLItaxel (see BC Cancer Drug Manual)

**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 epinephrine 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. Christopher Lee or tumour group delegate at (604) 930-2098 or 1-800-523-2885 with any problems or questions regarding this treatment program.

**References:**
