BC Cancer Protocol Summary for Palliative Therapy for Germ Cell Cancers Using PACLitaxel and Gemcitabine

**Protocol Code**: UGUTAXGEM

**Tumour Group**: Genitourinary

**Contact Physician**: Dr. Christian Kollmannsberger

**Dr. Bernie Eigl**

**ELIGIBILITY**:
- Relapsed germ cell cancers not amenable to cure with surgery or chemotherapy
- Cisplatin-refractory (failed during 1st-line EP/BEP or after 2nd-line VIP/VEIP)
- Patients relapsed after BMT are potentially eligible
- A BC Cancer "Compassionate Access Program (CAP)" approval

**EXCLUSIONS**:
- PS 3-4
- Motor neuropathy
- ANC less than 1.5, Platelet less than 100, ALT or AST greater than 4xULN, bilirubin greater than 35, or creatinine greater than 180

**TESTS**:
- Weekly CBC; monitor creatinine, LFTs, AFP, serum HCG, neuropathy each cycle
- Relevant imaging for response every 8 weeks (baseline and alternate cycles)

**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)
- Additional antiemetics not usually required.

**TREATMENT**:
- Cycle length four weeks, repeat every 28 days x 2 - 6 cycles.
- Discontinue if no response after 2 cycles.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>BC Cancer Administration Guideline</th>
</tr>
</thead>
<tbody>
<tr>
<td>PACLitaxel</td>
<td>110 mg/m² (d1, 8, 15)</td>
<td>IV in 500 mL NS over 1 hour (use non-DEHP bag and non-DEHP tubing with 0.22 micron or smaller in-line filter)</td>
</tr>
<tr>
<td>gemcitabine</td>
<td>1,000 mg/m² (d1, 8, 15)</td>
<td>IV in 250 mL NS over 30 min</td>
</tr>
</tbody>
</table>

*use 250 mL for doses less than 150 mg*
DOSE MODIFICATIONS:

1. **Hematological**

<table>
<thead>
<tr>
<th>ANC (x10⁹/L)</th>
<th>Platelets (x10⁹/L)</th>
<th>Dose (both drugs)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>greater than or equal to 1.5 and greater than or equal to 75</td>
<td></td>
<td>100% of previous cycle</td>
</tr>
<tr>
<td>1.0 to less than 1.5 and/or 50 to less than 75</td>
<td></td>
<td>75% of previous cycle</td>
</tr>
<tr>
<td>0.5 to less than 1.0 and/or 25 to less than 50</td>
<td></td>
<td>50% of previous cycle</td>
</tr>
<tr>
<td>less than 1.0 and/or less than 25</td>
<td></td>
<td>Omit (d8) or delay (d1)**</td>
</tr>
</tbody>
</table>

*a dose reduction for granulocytopenic fever or thrombocytopenia within a cycle results in a reduction of 25% in the start dose of the next cycle*

**if day 15, omit and start next cycle on day 22 instead of day 29**

2. **Gastrointestinal Toxicities**

<table>
<thead>
<tr>
<th>Grade</th>
<th>Stomatitis</th>
<th>Diarrhea</th>
<th>Dose Gemcitabine</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Painless ulcers, erythema or mild soreness</td>
<td>Increase of 2-3 stools/day or mild increase in loose watery colostomy output</td>
<td>100%</td>
</tr>
<tr>
<td>2</td>
<td>Painful erythema, edema, or ulcers but can eat</td>
<td>Increase of 4-6 stools, or nocturnal stools or mild increase in loose watery colostomy output</td>
<td>Omit until toxicity resolved then resume at 100%</td>
</tr>
<tr>
<td>3</td>
<td>Painful erythema, edema, or ulcers and cannot eat</td>
<td>Increase of 7-9 stools/day or incontinence, malabsorption; or severe increase in loose watery colostomy output</td>
<td>Omit until toxicity resolved then resume at 75%</td>
</tr>
<tr>
<td>4</td>
<td>Mucosal necrosis, requires parenteral support</td>
<td>Increase of 10 or more stools/day or grossly bloody diarrhea, or grossly bloody colostomy output or loose watery colostomy output requiring parenteral I support; dehydration</td>
<td>Omit until toxicity resolved then resume at 50%.</td>
</tr>
</tbody>
</table>

3. **Other Non-Hemtological Toxicities**: dose modifications recommended for
- LFTs greater than or equal to 2 x ULN
- nausea Grade 4
- myalgia/rash Grade 3
- other toxicities of Grade 2-4 severity (excluding alopecia)

For more details, consult Table 2 of the referenced article.

PRECAUTIONS:

1. **Hypersensitivity**: Reactions are common with PACLitaxel. See BC Cancer Hypersensitivity Guidelines.
2. **Extravasation**: PACLitaxel causes pain and 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.
4. **Thrombocytopenia**: platelet support may be required as per local guidelines.
5. **Renal Dysfunction**: Irreversible renal failure associated with hemolytic uremic syndrome may occur with gemcitabine (rare). Use caution with pre-existing renal dysfunction.
6. **Pulmonary Toxicity**: Acute shortness of breath may occur. Discontinue treatment if gemcitabine-induced pneumonitis is suspected.
7. **Arthralgia and/or Myalgia**: if unrelieved by acetominophen + codeine, try
   - 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 7-10 days
8. **Neuropathy**: Dose modification or discontinuation may be required (see BC Cancer Drug Manual).

Contact Dr. Christian Kollmannsberger, Dr. Bernie Eigl or tumour group delegate at (604) 877-2730 or 1-800-663-3333 with any problems or questions regarding this treatment program.

Reference: