BC Cancer Protocol Summary for First-line Palliative Chemotherapy for Advanced Gallbladder Cancer and Cholangiocarcinoma using Gemcitabine and CISplatin

**Protocol Code**  
GIAVPG

**Tumour Group**  
Gastrointestinal

**BCCA Contact Physician**  
GI Systemic Therapy

**ELIGIBILITY:**
- Metastatic or unresectable gallbladder cancer or cholangiocarcinoma
- ECOG performance status 0 to 2
- Adequate marrow reserve (ANC greater than or equal to 1.5 x 10^9/L, platelets greater than 100 x 10^9/L)
- For metastatic or unresectable pancreatic adenocarcinoma, a BC Cancer “Compassionate Access Program” request must be approved prior to treatment

**EXCLUSIONS:**
- Patients with inadequate renal function (creatinine clearance less than 60 ml/min by GFR measurement or Cockcroft formula) unless treated with carboplatin.

**TESTS:**
- Baseline: CBC & differential, platelets, creatinine, liver function tests, bilirubin. Optional : CA 19-9
- Prior to each treatment:
  - Day 1: CBC & differential, platelets, creatinine, bilirubin
  - Day 8: CBC & differential, platelets, creatinine
- Optional day 1: CA 19-9

**PREMEDICATIONS:**
- Antiemetic protocol for high moderate emetogenic chemotherapy protocols (see protocol SCNAUSEA).

**TREATMENT:**
A Cycle equals -

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>BC Cancer Administration Guideline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gemcitabine</td>
<td>1000 mg/m² on days 1 and 8</td>
<td>IV in 250 mL NS over 30 min</td>
</tr>
<tr>
<td>CISplatin</td>
<td>25 mg/m² on days 1 and 8</td>
<td>IV in 100 mL NS over 30 min</td>
</tr>
</tbody>
</table>

Repeat every 21 days for 8 cycles unless disease progression or toxicity. If there is continued evidence of response or stable disease by imaging or tumour markers, may apply for additional cycles via Compassionate Access Program (CAP).
DOSE MODIFICATIONS:

1. Hematology:

<table>
<thead>
<tr>
<th>ANC (x 10^9 /L)</th>
<th>Platelets (x 10^9 /L)</th>
<th>Day 1</th>
<th>Day 8</th>
</tr>
</thead>
<tbody>
<tr>
<td>greater than or equal to 1.0</td>
<td>greater than or equal to 100</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>0.5 to less than 1.0</td>
<td>75 to less than 100</td>
<td>75%</td>
<td>100%</td>
</tr>
<tr>
<td>less than 0.5</td>
<td>less than 75</td>
<td>Delay</td>
<td>Delay</td>
</tr>
</tbody>
</table>

2. Renal Dysfunction:

<table>
<thead>
<tr>
<th>Creatinine Clearance (mL/min)</th>
<th>Day 1</th>
<th>Day 8</th>
</tr>
</thead>
<tbody>
<tr>
<td>greater than or equal to 60</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>45 to 59</td>
<td>100%</td>
<td>50%</td>
</tr>
<tr>
<td>less than 45</td>
<td>Delay</td>
<td>Delay</td>
</tr>
</tbody>
</table>

Alternatively, CARBOplatin may be used instead of CISplatin:

<table>
<thead>
<tr>
<th>DRUG</th>
<th>DOSE</th>
<th>BC Cancer Administration Guidelines</th>
</tr>
</thead>
<tbody>
<tr>
<td>CARBOplatin</td>
<td>AUC 5 DAY 1 only Dose = AUC x (GFR* +25)</td>
<td>IV in 250mL NS over 30 minutes.</td>
</tr>
</tbody>
</table>

* 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

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

*For males N = 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).

PRECAUTIONS:
1. **Neutropenia**: Fever or other evidence of infection must be assessed promptly and treated aggressively.

2. **Renal Toxicity**: Nephrotoxicity is common with CISplatin. Encourage oral hydration. Avoid nephrotoxic drugs such as aminoglycoside antibiotics. Irreversible renal failure associated with hemolytic uremic syndrome may occur (rare) with gemcitabine. Use caution with pre-existing renal dysfunction.

3. **Pulmonary Toxicity**: Acute shortness of breath may occur. Discontinue treatment if drug-induced pneumonitis is suspected.

4. **Drug Interaction**: Possible interaction between gemcitabine and warfarin has been reported and may occur at any time. Close monitoring is recommended (monitor INR weekly during gemcitabine therapy and for 1 to 2 month after discontinuing gemcitabine treatment).

Call the GI Systemic Therapy physician at your regional cancer centre or the GI Systemic Therapy Chair Dr. Janine Davies at (604) 877-6000 or 1-800-663-3333 with any problems or questions regarding this treatment program.

**References**:

