BC Cancer Protocol Summary for Treatment of Lymphoma with Gemcitabine, Dexamethasone and Platinum

**Protocol Code**
LYGDP

**Tumour Group**
Lymphoma

**Contact Physician**
Dr Laurie Sehn

**ELIGIBILITY:**
- Patients with relapsed aggressive non-Hodgkin's lymphomas (B cell and T cell) with good performance status being treated with curative intent (note: patients whose disease responds to LYGDP may be candidates for high dose chemotherapy and hematopoietic stem cell transplant)
- Patients with relapsed or refractory Hodgkin lymphoma with good performance status being treated with curative intent
- For other indications, or for more than 6 cycles, a BC Cancer “Compassionate Access Program” request with appropriate clinical information for each patient must be approved prior to treatment

**EXCLUSIONS:**
- Age greater than 70 years
- Creatinine clearance (CrCl) less than 45 mL/min

**TESTS:**
- Baseline, then as indicated:
  - Required before first treatment: CBC & diff, platelets, creatinine, bilirubin, ALT
  - Required, but results do not have to be available to proceed with first treatment; results must be checked before proceeding with cycle 2: HBsAg, HBCoreAb
  - Recommended but optional: bilirubin, alkaline phosphatase, magnesium, calcium
- Before each treatment:
  - Day 1: CBC & diff, platelets, creatinine
  - Day 8: CBC & diff, platelets
  - Creatinine (if cisplatin dose is given day 1 and 8)
- Before each treatment cycle: Use calculated creatinine clearance and serum creatinine to determine CISplatin dose, see dose modifications below.

**PREMEDICATIONS:**
For cisplatin use antiemetic protocol for highly emetogenic chemotherapy (see protocol SCNAUSEA)

For CARBOplatin use antiemetic protocol for moderately emetogenic chemotherapy (see SCNAUSEA protocol)

**SUPPORTIVE MEDICATIONS:**
If HBsAg or HBCoreAb positive, start lamivUDine 100 mg/day PO for the duration of chemotherapy and for six months afterwards.
TREATMENT:

<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 day 1 &amp; 8</td>
<td>IV in 250 mL NS over 30 min*</td>
</tr>
<tr>
<td>dexamethasone</td>
<td>40 mg/d days 1 to 4</td>
<td>Oral daily in am with food (Note: The anti-emetic premedication is separate from the Dexamethasone given as part of the protocol; both should be prescribed separately.)</td>
</tr>
<tr>
<td>CISplatin*</td>
<td>75 mg/m² days 1</td>
<td>Prehydrate with 1000 mL NS over 1 hour, then CISplatin IV in 500 mL NS with 20 mEq potassium chloride, 1 g MgSO4, 30 g mannitol over 1 hour</td>
</tr>
</tbody>
</table>

* gemcitabine may be given during prehydration for CISplatin

* Alternatively carboplatin may be used instead of cisplatin. See Renal Dysfunction under Dose Modifications. Note: it is acceptable for physicians to substitute CARBOplatin for CISplatin for reasons other than reduced GFR (for example, concerns around ototoxicity with CISplatin).

Estimate calculated creatinine clearance (CrCl) with following formula:

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

(N=1.04 for females, N=1.23 for males)

Borderline cases (CrCl 60 to 70 mL/min): perform nuclear renogram for GFR, if available

Repeat every 21 days. Maximum prior to high dose chemotherapy and stem cell transplant, 3 cycles; otherwise 6 cycles. Discontinue if definite progression at any time. A Compassionate Access Program approval is required to continue beyond 6 cycles.
DOSE MODIFICATIONS:

1. Hematological on Day 1

<table>
<thead>
<tr>
<th>ANC (x10^9/L)</th>
<th>Platelets (x10^9/L)</th>
<th>Dose (all drugs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>greater than or equal to 1.0 and greater than or equal to 75</td>
<td></td>
<td>100%</td>
</tr>
<tr>
<td>greater than or equal to 1.0 and less than 75</td>
<td></td>
<td>Delay 1 week*</td>
</tr>
<tr>
<td>less than 1.0 and greater than or equal to 75</td>
<td></td>
<td>Delay 1 week*</td>
</tr>
<tr>
<td>less than 1.0 and less than 75</td>
<td></td>
<td>Delay 1 week*</td>
</tr>
</tbody>
</table>

*If counts presumed to be low due to marrow involvement, treat after 1 week delay (i.e at 4 weeks) despite counts

** filgrastim should be given prophylactically for all future cycles.
Hematological on Day 8:

<table>
<thead>
<tr>
<th>ANC (x10^9/L)</th>
<th>Platelets (x10^9/L)</th>
<th>Dose (all drugs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>greater than or equal to 1.0 and greater than or equal to 75</td>
<td>100% gemcitabine (and cisplatin) and start filgrastim* OR Reduce gemcitabine (and cisplatin) dose to 75% of current cycle’s day 1 dose</td>
<td></td>
</tr>
<tr>
<td>greater than or equal to 0.5 and less than 1.0 and greater than or equal to 75</td>
<td>Reduce gemcitabine (and cisplatin) to 75% of current cycle’s day 1 dose</td>
<td></td>
</tr>
<tr>
<td>greater than or equal to 0.5 and less than 1.0 and less than 50</td>
<td>Omit gemcitabine (and cisplatin) and start filgrastim**</td>
<td></td>
</tr>
</tbody>
</table>

*if counts presumed to be low due to marrow involvement, treat after 1 week delay (i.e at 4 weeks) despite counts

** filgrastim should be given prophylactically for all future cycles

2. Renal Dysfunction

Delay for one week if serum creatinine greater than 3 x ULN where ULN = local upper limit of normal range. If serum creatinine less than 3 x ULN adjust CISplatin dose as follows

<table>
<thead>
<tr>
<th>Creatinine Clearance (ml/min)</th>
<th>CISplatin dose</th>
<th>Gemcitabine dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>greater than or equal to 60</td>
<td>75 mg/m^2 on Day 1</td>
<td>100%</td>
</tr>
<tr>
<td>45 to 59</td>
<td>37.5 mg/m^2 on Days 1 and 8 or go to CARBOplatin option</td>
<td>100%</td>
</tr>
<tr>
<td>less than 45</td>
<td>Delay</td>
<td>Delay/Omit*</td>
</tr>
</tbody>
</table>

*Delay if day 1; if day 8, omit if serum creatinine greater than 3 x ULN where ULN = local upper limit of normal range.
Alternatively CARBOplatin can be used instead of CISSplatin per physician discretion for reasons other than reduced GFR (for example, concerns around ototoxicity).

<table>
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<tr>
<th>Drug</th>
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<tr>
<td>CARBOplatin</td>
<td>AUC 5 on Day 1 only Dose= AUC x (GFR+25)</td>
<td>IV in 250 mL NS over 30 minutes</td>
</tr>
</tbody>
</table>

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.

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).

Consider re-calculation of CARBOplatin dose if serum creatinine changes ± 20% from baseline.

Prehydration is not needed if carboplatin is given.

**PRECAUTIONS:**

1. **Neutropenia:** Fever or other evidence of infection must be assessed promptly and treated aggressively.
2. **Thrombocytopenia:** Support with platelet transfusion may be required.
3. **Renal Toxicity:** Nephrotoxicity is common with CISSplatin. 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.
4. **Pulmonary Toxicity:** Acute shortness of breath may occur. Discontinue treatment if drug-induced pneumonitis is suspected.
5. **Hepatitis B Reactivation:** All lymphoma patients should be tested for both HBsAg and HBcoreAb. If either test is positive, such patients should be treated with lamivUDine during chemotherapy and for six months afterwards. Such patients should also be monitored with frequent liver function tests and hepatitis B virus DNA at least every two months. If the hepatitis B virus DNA level rises during this monitoring, management should be reviewed with an appropriate specialist with experience managing hepatitis and consideration given to halting chemotherapy.

Call Dr. Laurie Sehn or tumor group delegate at (604) 877-6000 or 1-800-663-3333 with any problems or questions regarding this treatment program.

**References:**