**BC Cancer Protocol Summary for Treatment of Non-Hodgkin Lymphoma with Bendamustine**

**Protocol Code**

LYBEND

**Tumour Group**

Lymphoma

**Contact Physician**

Dr Laurie H. Sehn

**ELIGIBILITY:**

- Patients with relapsed or refractory indolent non-Hodgkin lymphoma (follicular, marginal zone, lymphoplasmacytic)
- Patients with mantle cell lymphoma
- Advanced stage symptomatic disease requiring therapy

**EXCLUSIONS:**

- Hodgkin’s lymphoma, diffuse large B-cell lymphoma
- Creatinine clearance (CrCl) less than 40 mL/min
- AST or ALT greater than 2.5 x upper limit of normal and total bilirubin greater than 1.5 x upper limit of normal

**TESTS:**

- Baseline, then as indicated:
  - Required before first treatment: CBC & diff, platelets, creatinine, ALT, bilirubin
  - 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
- Before day 1 of each treatment cycle: CBC & diff, platelets
- If clinically indicated: creatinine, ALT, bilirubin

**PREMEDICATIONS:**

Antiemetic protocol for moderately emetogenic chemotherapy (see protocol SCNAUSEA)

**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>
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</thead>
<tbody>
<tr>
<td>bendamustine</td>
<td>90 mg/m²* on days 1 and 2</td>
<td>IV in 250 to 500 mL NS over 1 hour (concentration range = 0.2 to 0.6 mg/mL)</td>
</tr>
</tbody>
</table>

* May escalate dose to 120 mg/m²

Repeat every 28 days. Maximum 6 cycles. Discontinue if definite progression at any time.

DOSE MODIFICATIONS:

1. Hematological, day 1 only

<table>
<thead>
<tr>
<th>ANC (x10⁹/L)</th>
<th>Platelets (x10⁹/L)</th>
<th>Bendamustine</th>
</tr>
</thead>
<tbody>
<tr>
<td>greater than or equal to 1.0 and greater than or equal to 75</td>
<td>100%</td>
<td></td>
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<tr>
<td>less than 1.0 or less than 75</td>
<td>Delay until recovery</td>
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</tr>
</tbody>
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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. **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.
4. **Infusion Reactions and Hypersensitivity**: Bendamustine can cause allergic type reactions during the IV infusion such as fever, chills, pruritus and rash. Severe anaphylactic and anaphylactoid reactions have occurred rarely, particularly in the second and subsequent cycles of therapy. If an allergic reaction occurs, stop the infusion and the physician in charge should determine a safe time and rate to resume the infusion. Consider pre-treatment with antihistamines, antipyretics and corticosteroids for patients experiencing Grade 1 or 2 infusion reactions; consider discontinuing treatment for patients experiencing Grade 3 or 4 infusion reactions. See BC Cancer Hypersensitivity Guidelines.
5. **Tumour Lysis Syndrome**: Tumor lysis syndrome has been associated with bendamustine, possibly leading to acute renal failure and death. Usual onset occurs during the first cycle. Maintain adequate volume status and monitor blood chemistry, including potassium and uric acid levels. Allopurinol has been used, but the concomitant use of bendamustine and allopurinol can cause increased risk of severe skin toxicity.
6. **Drug Interactions**: CYP1A2 inhibitors can potentially decrease plasma concentration of bendamustine. CYP1A2 inducers can potentially increase plasma concentration of bendamustine.
7. **Skin Reactions**: Rash, toxic skin reactions and bullous exanthema have been reported. They may be progressive and increase in severity with further treatment. Monitor closely. If skin reactions are severe or progressive, consider withholding or discontinuing bendamustine.
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: