BC Cancer Protocol Summary for Treatment of Hodgkin Lymphoma and Anaplastic Large Cell Lymphoma with Brentuximab Vedotin

Protocol Code: LYBRENTUX

Tumour Group: Lymphoma

Contact Physician: Dr. Laurie H. Sehn

ELIGIBILITY:
- Not previously treated with brentuximab vedotin
- Advanced stage Hodgkin lymphoma
  - relapsed after high dose chemotherapy and autologous stem cell transplant or, if transplant ineligible due to age or co-morbid conditions, have relapsed after standard ABVD or equivalent
  - for consolidation treatment after response to high dose chemotherapy and autologous stem cell transplant, use LYBV protocol
- Advanced stage anaplastic large cell lymphoma
  - have relapsed after primary chemotherapy or after high dose chemotherapy and stem cell transplant or, if transplant ineligible due to age or co-morbid conditions, have relapsed after primary chemotherapy with CHOP or equivalent

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

PREMEDICATIONS:
None.

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>brentuximab vedotin</td>
<td>1.8 mg/kg on Day 1*</td>
<td>IV in 100 mL NS over 30 minutes</td>
</tr>
</tbody>
</table>

Repeat every 21 days. Maximum 16 cycles. Discontinue if definite progression at any time.

*The dose for patients weighing greater than 100 kg should be calculated based on a weight of 100 kg.

DOSE MODIFICATIONS:

1. Hematological:

<table>
<thead>
<tr>
<th>ANC (x10^9/L)</th>
<th>Platelets (x10^9/L)</th>
<th>Brentuximab</th>
</tr>
</thead>
<tbody>
<tr>
<td>greater than or equal to 0.6 and greater than or equal to 50</td>
<td>100%</td>
<td></td>
</tr>
<tr>
<td>less than 0.6 or less than 50</td>
<td>Delay until recovery</td>
<td></td>
</tr>
</tbody>
</table>

2. Peripheral Neuropathy:

<table>
<thead>
<tr>
<th>Toxicity</th>
<th>Dose Modification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 1</td>
<td>100%</td>
</tr>
<tr>
<td>Grade 2 or 3</td>
<td>Hold until neuropathy improves to grade 1 or baseline, then decrease dose to 1.2 mg/kg</td>
</tr>
<tr>
<td>Grade 4</td>
<td>Discontinue brentuximab</td>
</tr>
</tbody>
</table>

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. Peripheral neuropathy: Brentuximab treatment causes peripheral sensory neuropathy. Cases of peripheral motor neuropathy have also been reported. Brentuximab-induced peripheral neuropathy is cumulative. Monitor patients for symptoms of neuropathy, such as hypoesthesia, hyperesthesia, paresthesia, discomfort, a burning sensation, neuropathic pain or weakness and institute dose modifications accordingly.
5. Infusion reactions: Infusion-related reactions, including anaphylaxis, have occurred with brentuximab. Monitor patients during infusion. If an infusion reaction occurs, stop the infusion. See BC Cancer Hypersensitivity Guidelines.
6. **Tumor lysis syndrome**: Patients with rapidly proliferating tumor and high tumor burden are at risk of tumor lysis syndrome and these patients should be monitored closely.

7. **Progressive multifocal leukoencephalopathy (PML)**: JC virus infection resulting in PML and death has been reported in brentuximab-treated patients. Consider the diagnosis of PML in any patient presenting with new-onset signs and symptoms of central nervous system abnormalities. Hold brentuximab if PML is suspected.

8. **Stevens-Johnson syndrome**: Stevens-Johnson syndrome has been reported with brentuximab. If Stevens-Johnson syndrome occurs, discontinue brentuximab.

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

**REFERENCES:**


