BC Cancer Protocol Summary for Treatment of Hodgkin Lymphoma with DOXOrubicin, Bleomycin, vinBLAStine, and Dacarbazine

Protocol Code: LYABVD  
Tumour Group: Lymphoma  
Contact Physician: Dr. Laurie Sehn

ELIGIBILITY:
- Histology: Hodgkin lymphoma, all stages

TESTS:
- Baseline (required before first treatment): CBC & diff, platelets, bilirubin, ALT, creatinine
- Baseline (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 cycle: CBC & diff, platelets, (and bilirubin if elevated at baseline). Note: No tests are required before day 15.
- After cycle #2 (for all patients): PET Scan (ideally performed between day 21 and day 28 of cycle 2)

PREMEDICATIONS:
- Antiemetic protocol for highly emetogenic chemotherapy (see protocol SCNAUSEA)
- If past etoposide drug reactions:
  - hydrocortisone 100 mg IV prior to etoposide
  - diphenhydrAMINE 50 mg IV prior to etoposide

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>DOXOrubicin</td>
<td>25 mg/m² on days 1 and 15</td>
<td>IV push</td>
</tr>
<tr>
<td>vinBLAStine</td>
<td>6 mg/m² on days 1 and 15</td>
<td>IV in 50 mL NS over 15 minutes</td>
</tr>
<tr>
<td>hydrocortisone</td>
<td>100 mg on days 1 and 15</td>
<td>IV in 50 to 100 mL NS over 10 to 15 minutes</td>
</tr>
<tr>
<td>bleomycin*</td>
<td>10 units/m² on days 1 and 15</td>
<td>IV in 50 mL NS over 15 minutes</td>
</tr>
<tr>
<td>dacarbazine</td>
<td>375 mg/m² on days 1 and 15</td>
<td>IV in 250 to 500 mL NS or D5W over 1 to 2 hours</td>
</tr>
</tbody>
</table>

Repeat each treatment cycle every 28 days.

*Discontinue bleomycin after cycle 2 if PET negative on interim PET done after cycle 2. See below for definition of PET negative, which varies according to stage.
PET-based Management According to Stage

(please note definition of PET negative varies according to stage, definitions below)

Limited Stage: ABVD x 2 cycles then PET scan
- If PET negative (Deauville score 1, 2) → AVD x 2 more cycles, omit bleomycin from cycles 3 and 4.
- If PET positive (Deauville score 3, 4, 5) without evidence of progression → no further chemotherapy, proceed to involved site radiation.
  - Obtain end-of-treatment CT.

Advanced Stage: ABVD x 2 cycles then PET scan
- If PET negative (Deauville score 1, 2, 3) → AVD x 4 cycles, omit bleomycin from cycles 3 to 6.
  - Obtain end-of-treatment CT and PET
- If PET positive (Deauville score 4, 5) without evidence of progression → ABVD x 4 more cycles.
  - CT scan after 4 cycles to rule out progression. Obtain both CT and PET at end-of-treatment.
  - If CR after 6 cycles, no further treatment.
  - If PET positive after 6 cycles and without evidence of progression → consider consolidative radiation to PET positive site if feasible
  - If PET positive after 6 cycles and without evidence of progression, but radiation is not feasible → consider close observation or biopsy to direct further treatment on proof of persistent lymphoma

DOSE MODIFICATIONS:
1. Hematological:

<table>
<thead>
<tr>
<th>ANC (x 10^9/L)</th>
<th>Dose Modification</th>
</tr>
</thead>
<tbody>
<tr>
<td>greater than or equal to 0.6</td>
<td>100 %</td>
</tr>
<tr>
<td>less than 0.6</td>
<td>100 % plus filgrastim 300 mcg daily x 5 days, starting 6 days after each IV chemotherapy</td>
</tr>
</tbody>
</table>

The patient should be treated with Filgrastim (G-CSF) in doses sufficient to allow full dose treatment on schedule using the above dose modifications. Note: this guideline applies only if the treatment is potentially curative and after experience with one or more cycles of treatment indicate Filgrastim (G-CSF) is required. (See Pharmacare guidelines)

Transfuse as needed to keep hemoglobin greater than 90 g/L, platelets greater than 20 x 10^9/L

2. Neurotoxicity: vinBLASTine only

<table>
<thead>
<tr>
<th>Toxicity</th>
<th>Dose Modification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dysesthesias, areflexia only</td>
<td>100%</td>
</tr>
<tr>
<td>Abnormal buttoning, writing</td>
<td>67%</td>
</tr>
<tr>
<td>Motor neuropathy, moderate</td>
<td>50%</td>
</tr>
<tr>
<td>Motor neuropathy, severe</td>
<td>Omit</td>
</tr>
</tbody>
</table>
3. **Hepatotoxicity**: DOXOrubicin only

<table>
<thead>
<tr>
<th>Bilirubin (mmol/L)</th>
<th>Dose Modification</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 to 35</td>
<td>100%</td>
</tr>
<tr>
<td>35 to 85</td>
<td>50%</td>
</tr>
<tr>
<td>greater than 85</td>
<td>Omit DOXOrubicin. Substitute cyclophosphamide 375 mg/m²</td>
</tr>
</tbody>
</table>

Note: This adjustment is only necessary for the initial treatment. After the hyperbilirubinemia has resolved adjustment is only necessary if overt jaundice re-occurs. Serum bilirubin does not need to be requested before each treatment.

4. **Cardiotoxicity**: DOXOrubicin only

When DOXOrubicin cannot be used due to proven cardiac dysfunction, each dose of DOXOrubicin can be replaced by etoposide 25 mg/m² IV on the first day (Use non-DEHP equipment with in-line filter), 50 mg/m² PO on the second and third days.

5. **Dacarbazine unavailability**: Occasionally dacarbazine becomes unavailable due to manufacturing or other problems. If this occurs, and only if dacarbazine is completely unavailable, the Lymphoma Tumour Group recommends that Compassionate Access Program (CAP) approval be sought for cyclophosphamide 375 mg/m² to be substituted for each dose of the dacarbazine until the supply is renewed. There are no direct data that this substitution is equally effective, however, cyclophosphamide is an effective drug for Hodgkin’s lymphoma, works via the same class of mechanisms (alkylation), causes the same minimal level of myelosuppression at this dose and is not sterilizing for men or women at this dose. When used at this dose no adjustment for myelosuppression is required.

6. **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.

**PRECAUTIONS:**

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

1. **Cardiac Toxicity**: DOXOrubicin is cardiotoxic and must be used with caution, if at all, in patients with severe hypertension or cardiac dysfunction. Cardiac assessment is recommended if patient has received greater than or equal to 300 mg/m² of DOXOrubicin. (BC Cancer Drug Manual). Work-up may include an assessment of cardiac ejection fraction, and cardiac oncology referral if necessary.

2. **Extravasation**: DOXOrubicin and vinBLAStine cause pain and tissue necrosis if extravasated. Refer to BC Cancer Extravasation Guidelines.

3. **Infusion-Related Reactions**: If applicable, monitor etoposide infusion for the first 15 minutes for signs of hypotension. Refer to BC Cancer Infusion-Related Reactions Guidelines.

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