BC Cancer Protocol Summary for Treatment of Hodgkin Lymphoma with Cyclophosphamide, vinBLAStine, Procarbazine, predniSONE, DOXOrubicin, vinCRIStine and Bleomycin

Protocol Code	*LYCVPPABO*
Tumour Group	*Lymphoma*
Contact Physician	*Dr. Kerry Savage*

ELIGIBILITY:
- Histology: Hodgkin lymphoma, all stages
- Only for patients who cannot be treated with (LY)ABVD due to a specific drug contraindication

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 each treatment: CBC & diff, platelets, (and bilirubin if elevated at baseline)

PREMEDICATIONS:

ondansetron 8 mg PO pre-chemotherapy
dexamethasone 12 mg PO pre-chemotherapy
hydrocortisone 100 mg IV in 50 to 100 mL NS over 15 to 30 minutes prior to bleomycin on day 8

SUPPORTIVE MEDICATIONS:

If HBsAg or HBcoreAb positive, start lamiVUDine 100 mg PO daily for the duration of chemotherapy and continue for one year from treatment completion for patients who are HBsAg positive and for six months for patients who are HBcoreAb positive.

TREATMENT:

Day 1:

Drug	Dose	BC Cancer Administration Guideline
vinBLAStine	6 mg/m^2 on day 1	IV in 50 mL NS over 15 minutes
cyclophosphamide	600 mg/m^2 on day 1	IV in 100 to 250* mL NS over 20 minutes to 1 hour (*use 250 mL for doses greater than 1000 mg)
procarbazine	100 mg/m^2 on days 1 to 7	PO
predniSONE	45 mg/m^2 days 1 to 14	PO in am with food

Day 8:

Drug	Dose	BC Cancer Administration Guideline
DOXOrubicin	35 mg/m^2 on day 8	IV push
vinCRIStine (* no cap on dose)	1.4 mg/m^2 on day 8	in 50 mL NS over 15 mins
bleomycin	10 unit/m^2 on day 8	IV in 50 mL NS over 15 min

Repeat each treatment cycle every 28 days.

Limited stage: CVPPABO x 2 cycles then PET scan
If PET negative -> CVPPABO x 2 more cycles
If PET positive or indeterminate -> involved field radiation
Advanced stage: CVPPABO x 6 then CT scan (and marrow biopsy if positive prior to ABVD)
If CR, no further treatment
If otherwise in CR but residual mass greater than 2 cm do PET scan
If PET negative, no further treatment
If PET positive and encompassable in a reasonable radiation field -> residual disease radiation
If PET positive and not encompassable in a reasonable radiation field -> close observation or biopsy to direct further treatment on proof of persistent lymphoma.

DOSE MODIFICATIONS:
1. **Hematological**:

Standard dose reduction for day 1

ANC (x 10^9/L)	Dose Modification
greater than or equal to 0.8	100 %
less than 0.8	100 % plus Filgrastim 300 mcg daily x 5 days, starting day 9 of each cycle

Standard dose reduction for day 8

ANC (x 10^9/L)	Dose Modification
greater than or equal to 0.8	100 %
less than 0.8	Omit DOXOrubicin from this cycle

* *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)*

Consider RBC transfusion support in individuals that have an expected hemoglobin nadir below 70 to 80 g/L and platelet transfusions to keep platelets greater than 20 x 10^9/L.

2. **Neurotoxicity**: vinBLAStine and vinCRIStine only

Toxicity	Dose Modification
Dysesthesias, areflexia only	100%
Abnormal buttoning, writing	67%
Motor neuropathy, moderate	50%
Motor neuropathy, severe	Omit

2. **Hepatotoxicity**: For DOXOrubicin:

Bilirubin (mmol/L)	Dose Modification
2 to 35	100%
35 to 85	50%
greater than 85	Omit DOXOrubicin. Substitute Cyclophosphamide 525 mg/m^2 on day 8

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.

Hepatotoxicity: For vinBLAStine:

Bilirubin (micromol/L)	Dose Modification
Less than 25	100%
25 to 50	50%
Greater than 50	25%.

Hepatotoxicity: For vinCRIStine:

Bilirubin (micromol/L)	Dose Modification
Less than or equal to 25	100%
26 to 50	50%
Greater than 50	25%.

4. **Cardiotoxicity**: DOXOrubicin only:
When DOXOrubicin cannot be used due to proven cardiac dysfunction, each dose of DOXOrubicin can be replaced by etoposide 35 mg/m^2 IV on day 8 (Use non-DEHP equipment with 0.2 micron in-line filter), 70 mg/m^2 PO on days 9 and 10.

PRECAUTIONS:
1. **Bleomycin**: may cause severe and life threatening pulmonary toxicity. Limiting the total dose to 270 units should decrease the risk but clinical assessment before each cycle must include a careful survey of respiratory symptoms, chest auscultation, and chest radiograph for pulmonary toxicity. Pulmonary function tests should be repeated in suspect cases. Febrile reaction can be prevented by hydrocortisone premedication. Oxygen may precipitate or aggravate bleomycin pulmonary toxicity. The FI O_2 must not exceed 30-40% unless absolutely necessary. The anesthesiologist must be aware of the bleomycin history before any surgery: an alert bracelet is recommended.
2. **Neutropenia**: fever or other evidence of infection must be assessed promptly and treated aggressively.

3. **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/m^2 of doxorubicin. (BC Cancer Cancer Drug Manual). Work-up may include an assessment of cardiac ejection fraction, and cardiac oncology referral if necessary.
4. **Extravasation**: DOXOrubicin, vinCRIStine and vinBLAStine cause pain and tissue necrosis if extravasated. Refer to BC Cancer Extravasation Guidelines.
5. **Hypersensitivity:** If applicable, monitor etoposide infusion for the first 15 minutes for signs of hypotension. Refer to BC Cancer Hypersensitivity Guidelines.
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 continue for one year from treatment completion for patients who are HBsAg positive and for six months for patients who are HBcoreAb positive.. 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. Kerry Savage or tumour group delegate at (604) 877-6000 or 1-800-663-3333 with any problems or questions regarding this treatment program.

Reference

Klimo PK, Connors JM. The MOPP/ABV Hybrid program: Combination chemotherapy based upon early introduction of seven effective drugs for advanced Hodgkin's disease. J Clin Oncol 1985;3:1174-82.