BC Cancer Protocol Summary for Treatment of Lymphoma with DOXOrubicin, Cyclophosphamide, vinCRIStine and predniSONE (CHOP)

Protocol Code	*LYCHOP*
Tumour Group	*Lymphoma*
Contact Physician	*Dr. Laurie Sehn*

ELIGIBILITY:

Special: Patients with previously untreated, advanced stage diffuse large B-cell lymphoma should be treated with LYCHOP-R. This protocol, LYCHOP, is for use for all other patients being treated with CHOP for aggressive histology lymphoma.

Patients must have:

- Diffuse large B-cell,
- Mantle cell,
- Peripheral T-cell, all aggressive varieties or
- Discordant lymphoma with one of the above histologies present

CAUTION:

- Congestive cardiac failure requiring current treatment (LYCHOP may be used but DOXOrubicin should be omitted, see cardiotoxicity below)

TESTS:

- Baseline (required before first treatment): CBC and diff, platelets, bilirubin, ALT
- Baseline (required, but results do not have to be available to proceed with first treatment**;** results must be checked before proceeding with cycle 2): LDH, HBsAg, HBcoreAb
- Before each treatment: CBC and diff, platelets, (and bilirubin if elevated at baseline)
- For all patients planned to receive CHOP x 6-8 cycles, reassess all sites of disease after cycles 4 and 6 to determine duration of treatment

PREMEDICATIONS:

- Antiemetic protocol for highly emetogenic chemotherapy (see protocol SCNAUSEA)

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:

Drug	Dose	BC Cancer Administration Guideline
DOXOrubicin	50 mg/m^2 on day 1	IV push
vinCRIStine	1.4 mg/m^2 * on day 1 (*no cap on dose)	IV in 50 mL NS over 15 mins
cyclophosphamide	750 mg/m^2 on day 1	IV in 100 to 250* mL NS over 20 min to 1 hour (*use 250 mL for doses greater than 1000 mg)
predniSONE	45 mg/m^2 **on days 1 to 5 (**round off dose to nearest 25mg)	PO in am with food

Stage IA or IIA, bulk less than 10 cm, radio-encompassable: Repeat every 21 days or when the neutrophil and platelet counts have recovered sufficiently to allow 100% dosing if that is determined sooner than every 21 days, x 3 cycles then proceed with planned radiation.

All other stages: Repeat every 21 days or when the neutrophil and platelet counts have recovered sufficiently to allow 100% dosing if that is determined sooner than every 21 days, x 6 to 8 cycles (2 cycles post maximum response, minimum 6)

Discontinue if no response after 2 cycles.

DOSE MODIFICATIONS:

1. **Elderly Patients (age greater than 75 years)**:
Cycle 1 doses of cyclophosphamide and DOXOrubicin should be administered at 75% doses. Further treatment should be given at the maximum dose tolerated by the patient, trying to escalate up to full 100% doses, but using the baseline experience with the 75% doses to guide these decisions.

2. **Hematological**: DOXOrubicin, cyclophosphamide and etoposide, if used, see below:

ANC (x10^9/L)	Dose Modification
greater than or equal to 0.8	100%
less than 0.8	100% plus filgrastim* 5 mcg/kg SC daily x 5 days, starting on day 7

The patient should be treated with Filgrastim (G-CSF) in doses sufficient to allow full dose treatment on a 21 day 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 and submit special authority request to Pharmacare for filgrastim coverage)

* *Filgrastim* 300 mcg: up to 75 kg
480 mcg: 76 kg to 110 kg
600 mcg: greater than 110 kg

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.

3. **Neurotoxicity**: vinCRIStine only:

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

4. **Hepatotoxicity**: For DOXOrubicin:

Bilirubin (micromol/L)	Dose Modification
2 to 35	100%
35 to 85	50%
Greater than 85	Omit DOXOrubicin. ***ADD*** cyclophosphamide 350 mg/m^2 to the dose already planned.

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 vinCRIStine:

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

5. **Cardiotoxicity**: DOXOrubicin only:
When DOXOrubicin cannot be used due to proven cardiac dysfunction, it can be replaced by etoposide 50 mg/m^2 IV on day 1, 100 mg/m^2 PO on day 2 and 3. (Use non-DEHP equipment with in-line filter)

PRECAUTIONS:
1. **Neutropenia**: Fever or other evidence of infection must be assessed promptly and treated aggressively.
2. **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.
3. **Extravasation**: DOXOrubicin and vinCRIStine cause pain and tissue necrosis if extravasated. Refer to BC Cancer Extravasation Guidelines.
4. **Hypersensitivity**: If applicable, monitor etoposide infusion for the first 15 minutes for signs of hypotension. Refer to BC Cancer Hypersensitivity Guidelines.
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 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 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 tumour group delegate at (604) 877-6000 or 1-800-663-3333 with any problems or questions regarding this treatment program.

References:

1. Fisher RI, Gaynor ER, Dahlberg S, Oken MM, et al. Comparison of a standard regimen (CHOP) with three intensive chemotherapy regimens for advanced non-Hodgkin's lymphoma. N Engl J Med 1993;328:1002-6.
2. McKelvey EM, Gottlieb JA, Wilson HE, Haut A, et al. Hydroxyldaunomycin (Adriamycin) combination therapy in malignant lymphoma. Cancer 1976;38:484-93.