

BCCA Protocol Summary for Treatment of Lymphoma with Doxorubicin, Cyclophosphamide, Vincristine and Prednisone (CHOP)

Protocol Code

LYCHOP

Tumour Group

Lymphoma

Contact Physician

Dr. Joseph Connors

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.

Histology:

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

EXCLUSIONS:

- 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
- Baseline (required, but results do not have to be available to proceed with first treatment): 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:

Ondansetron 8 mg PO pre-chemotherapy
Dexamethasone 12 mg PO pre-chemotherapy

TREATMENT:

Drug	Dose	BCCA 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 1-5 (**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 6-8 cycles (2 cycles post maximum response, minimum 6)

Discontinue if no response after 2 cycles.

CNS Prophylaxis:

Patients with initial sinus involvement with large cell lymphoma who have a complete response at the completion of their chemotherapy should receive intrathecal methotrexate 12 mg alternating with intrathecal cytarabine 50 mg twice weekly x 6 doses (3 doses of each over 3 weeks) starting in week 18. (See protocol LYIT for details)

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 300 mcg daily x 5 days, starting 7 days after each IV chemotherapy

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)

Transfuse as needed to keep hemoglobin greater than 90 g/L, platelets greater than 20 x 10⁹/L.

3. Neurotoxicity: vincristine only:

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

4. Hepatotoxicity: doxorubicin only:

Bilirubin (micromol/L)	Dose Modification
2-35	100%
35-85	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.

5. **Cardiotoxicity:** doxorubicin only:

When doxorubicin cannot be used due to proven cardiac dysfunction, it can be replaced by etoposide 50 mg/m² IV on day 1, 100 mg/m² PO on day 2 and 3. (Use non-PVC equipment)

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 lifelong dose of 450 mg/m² to be exceeded. (BCCA Cancer Drug Manual)
3. **Extravasation:** Doxorubicin and vincristine cause pain and tissue necrosis if extravasated. Refer to BCCA Extravasation Guidelines.
4. **Hypersensitivity:** If applicable, monitor etoposide infusion for the first 15 minutes for signs of hypotension. Refer to BCCA 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 100 mg/day orally, for the entire duration of 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.

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

Date activated: 01 Aug 2000

Date revised: 1 June 2011 (Infusion section revised)

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.