

Hyper-CVAD regimen for NHL and ALL:

Part A: Cyclophosphamide, Vincristine, Doxorubicin, Dexamethasone

Contact Physician: _____ **Pager:** _____

Diagnosis: _____

Cycle: 1 3 5 7 (circle one) Day 1= _____ Cycle 1: Consent form done

Weight: _____ **Height:** _____ **BSA:** _____

Adjusted IBW: _____ **Adjusted BSA:** _____

Allergies: _____

Cyclophosphamide 300mg/m² IV every 12 hours times 6 doses, days 1-3

Mesna 600mg/m²/day CIVI over 24 hours, days 1-3 (optional)

Doxorubicin 50mg/m² CIVI over 24 hours, day 4 (for EF <50%, optional total dose over 48 hours)

Vincristine 2 mg IV days 4 and 11

Dexamethasone 40 mg PO days 1-4 and 11-14

CNS prophylaxis:

- Patients with ALL, Burkitt's, Lymphoblastic lymphoma, and other aggressive NHL patients per MD discretion are to receive IT chemotherapy with each cycle.
- If CNS is positive at diagnosis, then twice weekly lumbar punctures with intrathecal chemotherapy until negative times two, then per protocol.

Mathotrexate 12 mg IT with each cycle

Cytarabine 100 mg IT with each cycle

Hydrocortisone 30 mg IT may be given with each IT treatment

For Philadelphia positive chromosome:

Imatinib mesylate 400mg PO daily on days 1-14 of each chemotherapy cycle.

1. Hydration:

- Start Sodium Chloride 0.9% 100mL/hour IV prior to starting chemotherapy. Continue hydration throughout cyclophosphamide administration and for 12 hours after the last dose of cyclophosphamide.

Optional hydration for Cycle #1 only: Start IV hydration 6 hours prior to starting chemotherapy with:

- Dextrose 5% in Water with sodium bicarbonate 100 mEq/liter at _____ mL/hour. Continue hydration until further changes made.

*Note: consider rasburicase substitution for allopurinol if very high risk for tumor lysis at presentation due to high white count or bulky disease (WBC > 50,000; LDH >5 times ULN)

- Notify MD if urine output is < 400 ml/ 4 hours.**

2. Prophylactic medications: (check the appropriate medications)

- Allopurinol: 300mg PO daily for _____ days, cycle 1
- Acyclovir: 400mg PO twice daily
- TMP/Sulfa: 160/800mg 1 tablet PO twice daily every Sat/Sun
- Antifungal:
- GI prophylaxis:
- Senokot-S 50mg/8.6mg 2 tablets PO daily for constipation.

3. Anti-emetics: (Moderate anti-emetic protocol)

- Ondansetron 12mg PO every 12 hours, Days 1-5, first dose prior to start of chemotherapy. If doxorubicin is given over 48 hours, give Days 1-6.
- Ondansetron 12mg IV every 12 hours, Days 1-5, if unable to tolerate PO. If Doxorubicin is given over 48hours, give Days 1-6.
- Dexamethasone: see below, administer first dose prior to IV chemotherapy.
- Lorazepam: 0.5mg - 1 mg PO or IV every 4 hours prn nausea
- Prochlorperazine 10mg PO every 6 hours prn nausea

4. Chemotherapy:

- **Cyclophosphamide** (300mg/m²) _____ mg in Sodium Chloride 0.9% 250mL IV over 3 hours every 12 hours for total of six doses, Days 1-3. (Total dose 1800mg/m²)
 - Mesna** (600mg/m²/day) _____ mg in Sodium Chloride 0.9% 500mL continuous IV infusion over 24 hours daily times 3 days. Begin one hour prior to start of cyclophosphamide. (Mesna is optional. Total dose 1800mg/m² over 72 hours)

- **Doxorubicin** (50mg/m²/day) _____ mg in Sodium Chloride 0.9% 500mL continuous IV infusion over 24 hours starting 2 hours after last dose of cyclophosphamide.
 - If EF<50% then give **Doxorubicin** (25mg/m²/day) _____ mg in Sodium Chloride 500mL continuous IV infusion over 24 hours for 2 days. Start 2 hours after last dose of cyclophosphamide (Total dose 50mg/m² over 48 hours).

- **VinCRISTine** 2 mg slow IV push Day 4 _____ and Day 11_____. (Day 11 may be given as an outpatient.)

- **Dexamethasone** 40 mg PO daily, Days 1-4 and Days 11-14. Days 1-4= _____, Days 11-14 = _____. Administer first dose 30-60 minutes prior to IV chemotherapy.

- Imatinib mesylate** 400mg PO daily days 1-14 for Philadelphia positive chromosome patients. When patient receiving first cycle check with pharmacy and start prescription insurance authorization for outpatient coverage.

5. CNS prophylaxis:

- IT treatment # _____ of _____ total**
- LP with IT chemotherapy not required**

Complete triplicate IT chemotherapy form.

- Methotrexate** 12 mg IT on Day _____
- Cytarabine** 100 mg IT on Day _____
- Hydrocortisone** 30 mg IT may be given with each IT treatment.

6. **Filgrastim** (Wt. \leq 70kg=300mcg; $>$ 70kg=480mcg) _____ mcg subcutaneous daily, beginning 24 hours after completion of chemotherapy. Start on Day _____. Discontinue when neutrophils count is greater than 1000 after nadir.

Or

Pegfilgrastim (Neulasta) 6mg subcutaneous on _____. Give 24 hours after completion of chemotherapy. May only receive as outpatient, give day after discharge or first clinic day after discharge (days 5-7). If discharge delayed, use daily filgrastim.

7 Discharge:

CBC, diff, platelet to be done every Monday and Thursday starting _____. If done at outside clinic, fax to (608) 266-6020.

Antibiotic prophylaxis during nadir: _____

Imatinib mesylate 400mg PO daily days 1-14 for Philadelphia positive chromosome. When patient receiving first cycle check with pharmacy and start prescription insurance authorization for outpatient coverage.

- Hyper-CVAD part B to be given in 21 days from start of cycle A or when ANC $>$ 1,000 and platelet count $>$ 50,000. Total 8 cycles (4 rounds A&B).

Signed: _____ Pager: _____

Reference: JCO 18(3) 2000: 547-561 (ALL regimen). Blood 103(12) 2004: 4396-4407 (Ph+ ALL). Blood 104(6) 2004: 1624-1630 (LL protocol).

Treatment: Four cycles of Hyper-CVAD alternating with four cycles of methotrexate and cytarabine.

- No maintenance for patients with mature B-cell ALL.
- Patients with Ph-positive ALL recommend allogeneic transplant.
- Consider radiation therapy for lymphoblastic lymphoma patients prior to maintenance therapy.
- All other patients (non mature B-cell) to receive 2 years of maintenance with POMP chemotherapy (6-mercaptopurine 50 mg PO 3 times daily, methotrexate 20 mg/m² PO weekly, vincristine 2 mg IV monthly, prednisone 200 mg PO daily for five days every monthly with vincristine.)

Addendum: Dose Adjustment Guidelines

Mesna: May be omitted. However, encourage IV hydration per orders and monitor urine output: 400ml/4 hours. MD to be notified if signs of hematuria.

Vincristine: Total bilirubin more than 2mg/dL, reduce to 1mg. Eliminate for total bilirubin greater than 3mg/dL or for grades 3-4 peripheral neuropathy or ileus. Dose reduction for neurotoxicity.

Doxorubicin: Bilirubin 2-3mg/dL reduce by 50%; if bilirubin 3-4mg/dL reduce by 75%, for bilirubin > 5mg/dL eliminate.

Imatinib mesylate, reduce to 300mg for grades 3-4 hepatotoxicity.

