Hyper- CVAD regimen for NHL and ALL:
Part B: Methotrexate, Cytarabine

Contact Physician:_____ Pager: _____

Diagnosis:_____

Cycle: 2 4 6 8 (Circle one) Day 1 = ____ Consent form done □

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

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

Allergies:_____

Methotrexate 200mg/m² IV over 2 hours followed by 800mg/m² CIVI over 22 hours, Day 1
Calcium leucovorin rescue
Cytarabine 3 grams/m² IV over 2 hours every 12 hours times 4 doses, Day 2&3
Optional for patients with ALL: Methylprednisolone 50mg IV twice daily, Day 1-3

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.
  Methotrexate 12 mg IT each cycle
  Cytarabine 100 mg IT each cycle
  Hydrocortisone 30 mg IT may be given with each IT treatment

For Philadelphia positive patients:
Imatinib mesylate 400mg PO days 1-14 each cycle.

1. **Hydration:** Start IV hydration 6 hours prior to methotrexate with Sodium Chloride 0.45% with sodium bicarbonate 50 mEq/liter at 150mL/hour or _____mL/hour. Continue hydration until methotrexate level is undetectable.

2. **Prophylactic medications:** (check the appropriate medications)
   - ☐ Allopurinol: 300mg PO daily for _____ days, cycle 1.
   - ☐ Acyclovir: 400mg PO twice daily
   - ☐ TMP/Sulfa: Hold until methotrexate level is undetectable.
   - ☐ Antifungal:
   - ☐ Prednisolone 1% eye drops, one drop each eye four times daily, days 2&3 while receiving cytarabine administration.
   - ☐ Sodium bicarbonate 50 mEq IV every 8 hours prn urine pH < 7

3. **Anti-emetics:** (moderate anti-emetic protocol)
   - ☐ Ondansetron: 16mg PO every 12 hours times 7 doses, first dose prior to initiating methotrexate.
   - ☐ Ondansetron 16mg IV every 12 hours times 7 doses, if unable to tolerate PO.
   - ☐ Dexamethasone 8 mg PO daily days 1-3, first dose pre-methotrexate. Not required for ALL patients receiving methylprednisolone.
   - ☐ Lorazepam: 0.5mg - 1 mg PO or IV every 4 hours prn nausea
   - ☐ Prochlorperazine: 10mg PO every 6 hours prn nausea

4. **Chemotherapy:**
   - **Methotrexate** (200mg/m²) _____ mg in Dextrose 5% in Water 250mL IV over 2 hours followed by (800mg/m²) _____mg in Dextrose 5% in Water 1000mL CIVI over 22 hours given on day 1. Day 1=_____.

   - **Check urine pH every shift**. For urine pH less than 7, give sodium bicarbonate 50 mEq IV. Discontinue when methotrexate level is undetectable.

   - **Calcium leucovorin** 15 mg PO every 6 hours starting 24 hours after the completion of methotrexate. Continue until methotrexate blood levels are undetectable. **Notify MD if patient unable to tolerate PO.**

NOTE:
If methotrexate level post infusion is more than 20*u*mol/L at the end of the infusion, more than 1 *u*mol/L 24 hours later, or more than 0.1 *u*mol/L 48 hours after the end of MTX infusion, then start calcium leucovorin 50 mg IV every 6 hours. See below for methotrexate lab orders.

- **Cytarabine** (3grams/m²) _____ grams in Sodium Chloride 0.9% 250mL IV over 2 hours every 12 hours for four doses, given on days 2 and 3. (For patients over the age of 60 or if serum creatinine is > 1.5, reduce cytarabine to 1gram/m^2). Day 2=_____.

- **Neuro checks prior to each dose of cytarabine**.

☐ **Methylprednisolone** 50 mg IV twice daily Days 1-3, _____. (To be given to acute lymphoblastic leukemia patients only, optional per physician discretion)

☐ **Imatinib mesylate** 400mg PO daily, Days 1-14 (For Philadelphia positive patients.) When patient receiving first cycle check with pharmacy and start prescription insurance authorization for outpatient coverage.

5. **CNS prophylaxis**:
   ☐ **IT treatments # _____ of _____ total**
   ☐ **LP with IT chemotherapy not required**

   Complete triplicate IT chemotherapy form
   ☐ **Methotrexate** 12 mg IT
   ☐ **Cytarabine** 100mg IT
   ☐ **Hydrocortisone** 30 mg IT may be given with each IT treatment

6. **Lab:** Methotrexate level **upon completion of methotrexate infusion** then every AM _____. Discontinue daily methotrexate levels once level is undetectable. (Methotrexate levels drawn after hours will be processed the following morning)

7. □ **Filgrastim** (Wt. ≤70kg=300mcg, >70kg=480mcg) _____ mcg subcutaneous daily, beginning 24 hours after completion of chemotherapy and methotrexate level is undetectable. Start on day _____. Discontinue when neutrophil count is greater than 1000 after nadir.

OR

□ **Pegfilgrastim** 6mg subcutaneous on_____. Give 24 hours after completion of chemotherapy and methotrexate level is undectectable. May only receive as outpatient, give day after discharge or first clinic day after discharge(days 5-7). If discharge delayed, use daily filgrastim.

8. **Discharge:**

WBC, diff, Hgb, platelet counts every Monday and Thursday starting _____. If done at outside clinic, fax to (608) 266-6020 attention Dr. _____.

□ Antibiotic prophylaxis during nadir: _____.

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

Next cycle Hyper-CVAD to be given in 21 days from start of part B or when ANC>1000 and platelet count >50,000. Total 8 cycles (4 rounds A&B).

Signed: _____ Pager: _____

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

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

- No maintenance for patients with mature B-cell ALL.
- Consider Radiation therapy for lymphoblastic lymphoma patients prior to maintenance therapy.
- Patients with Philadelphia positive ALL, recommend allogeneic transplant.
- 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 X5 monthly with vincristine.)

Addendum : Dose adjustments

- **Methotrexate:** For creatinine levels 1.5-2mg/dL reduce by 25%, for creatinine >2mg/dL reduce by 50%. For previous delayed excretion, nephrotoxicity, or grade 3 or greater mucositis, decrease by 25-50%
- **Cytarabine:** For patients >60 years or older, a creatinine level greater than 2mg/dL, or if the methotrexate level at the end of the methotrexate infusion (hour 0) is 20 *u*mol/L or more, reduce to 1gram/m^2.
- **For grade 3-4 myelosuppression associated complications other than neutropenia or thrombocytopenia** consider dose reductions for future cycles of MTX/Ara- C of 25-33%. The MTX dose to 750mg/m^2 then to 500mg/m^2 then to 250mg/m^2; and the Ara-C to 2gram/m^2, then 1.5gram/m^2 then 1gram/m^2.
- **Imatinib mesylate** reduce to 300mg for grade 3-4 hepatotoxicity during intensive chemotherapy courses.