**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. <u>**CNS prophylaxis**</u>:

☐ **IT treatments # ______ of _______ total**

☐ **LP with IT chemotherapy not required**

<u>**Complete triplicate IT chemotherapy form**</u>

☐ **Methotrexate** 12 mg IT

☐ **Cytarabine** 100mg IT

☐ **Hydrocortisone** 30 mg IT may be given with each IT treatment

6. **Lab:** Methotrexate level <u>**upon completion**</u> **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.)

**<u>Addendum : Dose adjustments</u>**

- **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, <u>reduce to 1gram/$m^2$</u>.
- **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.