**Indication**

- Mantle-cell lymphoma (diffuse, nodular or blastic variants).
- Hyper-CVAD/MA has also been used in adult B-cell Acute Lymphoblastic Leukaemia. The schedule described below does not relate to this indication.

**Pre-treatment Evaluation**

- Document histological sub-type of lymphoproliferative disorder according to WHO Classification.
- Document disease stage clinically, including presence or absence of B symptoms. Investigations should include CT scan of chest, abdomen and pelvis, bone marrow aspirate & trephine biopsy.
- Document FBC (with film), U&E, creatinine, LFTs, calcium, glucose, LDH, immunoglobulin levels, $\beta_2$-microglobulin and a direct antiglobulin test.
- CSF cytology must be obtained for patients with aggressive NHL involving peripheral blood, testis, orbit, paranasal sinus or paraspinal area. If indicated, give CNS-prophylaxis according to local protocols.
- Document height, weight and body surface area.
- Consider ECG ± echocardiogram if clinical suspicion of cardiac dysfunction.
- Give adequate verbal and written information for patients and relatives concerning patient’s disease, treatment strategy and side effects.
- Obtain written consent from patient or guardian.
- If appropriate, discuss the possibility of pregnancy with female patients of child-bearing age and the need for contraception with both male and female patients.
- If appropriate, discuss potential risk of infertility with patient and relatives.
- Consider intravenous hydration in patients with bulk disease and tumour lysis precautions according to local practice.
- Insert a tunneled central venous access line.
# Drug Regimen

## Course 1: Hyper-CVAD (Cycles 1, 3, 5, & 7)

<table>
<thead>
<tr>
<th>Days</th>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-3</td>
<td>Cyclophosphamide</td>
<td>300mg/m²</td>
<td>IV over 2hrs, 12hrly total of 6 doses.</td>
<td>Mesna see below</td>
</tr>
<tr>
<td>4-5</td>
<td>Doxorubicin</td>
<td>50mg/m²</td>
<td>IV continuously over 48hrs</td>
<td></td>
</tr>
<tr>
<td>4 &amp; 11</td>
<td>Vincristine</td>
<td>1.4mg/m²</td>
<td>Intravenous infusion in 50ml sodium chloride 0.9% over 10 minutes, as per national guidance. Nurse to remain with patient throughout infusion</td>
<td>Maximum 2mg</td>
</tr>
<tr>
<td>1-4</td>
<td>Dexamethasone</td>
<td>40mg</td>
<td>Oral, daily</td>
<td></td>
</tr>
</tbody>
</table>

## Course 2: MTX/ARA-C (Cycles 2, 4, 6, & 8)

<table>
<thead>
<tr>
<th>Days</th>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-2</td>
<td>Methotrexate</td>
<td>1g/m²</td>
<td>IV for 24hrs continuously</td>
<td>200mg/m² for 2hrs then 800mg/m² for 22hrs</td>
</tr>
<tr>
<td>2-3</td>
<td>Cytarabine</td>
<td>3g/m²</td>
<td>IV over 2hrs, 12hrly total of 4 doses</td>
<td></td>
</tr>
</tbody>
</table>

## Cycle Frequency

Every 21 days for up to up to 8 cycles (4 cycles if stem cell transplant is considered)

## Dose Modifications

- **Age ≥ 60 years:** reduce Cytarabine to 1g/m²
- **Pleural effusion/ascites:** reduce Methotrexate by 50%
- **Mucositis (grade 3/4):** reduce Methotrexate by 25%
- **Hepatic dysfunction:**
  - Serum Bilirubin (μmol/l) | Modification |
    - 34-50                    | Reduce Vincristine to 1mg    |
    -                        | Reduce Doxorubicin by 25%   |
    - 51-68                   | Reduce Doxorubicin by 50%   |
    - >68 μmol/l              | Reduce Doxorubicin by 75%   |
- **Renal dysfunction:**
  - Serum Creatinine (μmol/l) | Modification |
    - 177 - 265               | Reduce Cytarabine by 1g/m²  |
    -                        | Reduce Methotrexate by 50%  |
    - > 265 μmol/l            | Reduce Methotrexate by 75%  |
• Delay of marrow recovery:

<table>
<thead>
<tr>
<th>Platelets x 10^9/l</th>
<th>Or</th>
<th>Neutrophils x 10^9/l</th>
<th>Dose Given</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;100</td>
<td>&lt;1.0</td>
<td>After 21 days</td>
<td>Postpone next cycle by 7 days</td>
</tr>
</tbody>
</table>
| <100              | <1.0 | After 28 days       | Reduce Cyclophosphamide by 20%  
                      |      |                     | Reduce Doxorubicin by 20%         
                      |      |                     | Reduce Methotrexate by 25%        
                      |      |                     | Reduce ARA-C by 33%               |

Investigations prior to subsequent cycles

- FBC, U&E, Creatinine, Liver function tests, LDH and glucose (if indicated).
- CT after 2 cycles of chemotherapy and at end of therapy
  Bone marrow examination at the end of therapy if involved at diagnosis; during treatment if clinically indicated.

Concurrent Medication

Both cycles:

- Allopurinol 300mg od PO (100mg if creatinine clearance <20mls/min) for first 2 cycles.
- G-CSF 5 ug/kg daily s/c from day 4 (cycle 1) or day 5 (cycle 2) until neutrophils reach >1.0 x 10^9/l.
- PCP prophylaxis is recommended until one month after completion of the regime (stop one day prior to Methotrexate until neutrophil recovery to >1.0 x 10^9/l) - refer to local protocol.
- Systemic oral antifungal prophylaxis is recommended - refer to local protocol.
- Consider Acyclovir antiviral prophylaxis if previous history of VZV or HSV reactivation.

Cycle 1:

Mesna 600mg/m²/day via continuous infusion beginning one hour before first dose of Cyclophosphamide until 12 hours after the final dose.

Cycle 2:

- Dextrose 5%/Sodium Chloride 0.45% + 50mmols Sodium Bicarbonate and 20mmols KCl (per 1 litre of fluid). Start 6 hours before Methotrexate and until Methotrexate excretion to <0.1μmol/l. Infuse at 100mls/h and maintain fluid balance with diuretics. Give additional doses of Sodium Bicarbonate orally to maintain urinary pH at >7.0. Use oral Acetazolamide
ASWCS Haematology Chemotherapy Protocols

(250mg qds PO) to promote excretion if urinary pH drops <7.0.

- Folinic Acid 50mg IV 12 hours after completion of Methotrexate, then 15mg 6 hourly for 8 doses or until Methotrexate level is <0.1µmol/l.
- Stop Co-Tinomazole PCP prophylaxis at least one day prior to Methotrexate and re-start once neutrophils have recovered to >1.0 x 10⁹/l.

Investigations during therapy

- U&Es, Creatinine, Liver function tests, Calcium, Phosphate on alternate days.
- Methotrexate levels at 24h after the completion of Methotrexate infusion and daily until level <0.1µmol/l.

Anti-emetics

According to local protocol.

References


Written by: ASWCS Haematology Site Specific Group

Additional update for vinca alkaloid administration only 30/01/2009
Update written by Becky Bagnall Pharmacist BHOC
Update authorised by Jenny Bird. Head of ASWCS Haematology SSG

Authorised by:

<table>
<thead>
<tr>
<th>Chairman</th>
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<tr>
<td>ASWCS Haematology SSG</td>
<td>ASWCS Drugs &amp; Therapeutics Committee</td>
</tr>
</tbody>
</table>

| Name: Simon Bolam | Name: Steve Falk |
| Signature:       | Signature:       |
| Date:            | Date:            |

Date for review by Haematology SSG: July 2008