1 Acute Leukaemia

1.01 Cytoreduction – hydroxycarbamide

Indication

- ALL and AML - initial cytoreduction

Pre-treatment Evaluation

- Morphology of blood and bone marrow aspirate. Trial patients: send 6 unstained slides to Leeds General Infirmary.
- Trephine biopsy and ‘roll preparations’ should be made if the aspirate is difficult.
- Immunophenotyping (including TdT, B & T markers, myeloid markers, cytoplasmic μ, surface Ig) preferable on bone marrow (BM) or peripheral blood (PB) blasts. For trial patients immunophenotyping is performed in the Haematology Department at the Royal Marsden Hospital. Samples should be sent by courier.
- Cytochemistry: myeloperoxidase, PAS, acid phosphatase (if T-cell suspected) – note this may not be done routinely in some labs where immunochrometry is readily available.
- Cytogenetic analysis, usually on bone marrow. FISH analysis for common translocations and mono/trisomies may be useful.
- Molecular analysis for relevant chimaeric genes, especially PML/RARA, BCR-ABL and (AML/ETO if available). Trial patients should have 4ml of bone marrow in culture medium, and 30ml heparinised blood sent to UCH.
- Lumbar puncture (glucose, protein, microbiological culture, cytospin, gene rearrangement studies). This is not performed in MRC UKALL XII patients unless clinical suspicion of CNS disease (the first LP is at D21 with IT methotrexate).
- Serological tests for: Hepatitis B & C, CMV, and HIV (with consent).
- ECHO especially if cardiac history, elderly or previous history suggestive of potential cardiac disease (inc diabetes and hypertension)
- CT chest, abdomen, pelvis (MRI if CNS disease) as indicated
- Clotting screen.
- FBC and blood film.
- Renal/liver/bone panel, LDH, CRP, uric acid, serum glucose.
- Central venous catheter insertion.
- HLA typing (including siblings) if patient appropriate for allogenic transplant, -pre phase 2.
- Document height, weight and body surface area.
- 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 childbearing age and the need for contraception with both male and female patients.
- If appropriate, discuss potential risk of infertility with patient and relatives.
Drug Regimen (OPCS code X70.1)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydroxycarbamide (Hydroxurea)</td>
<td>2grams (4x500mg capsules) every 6-8 hours as clinically indicated</td>
<td>oral</td>
</tr>
</tbody>
</table>

**Cycle Frequency**

Continuous

**Dose Modifications**

In patients with impaired renal and/or liver function the experience is limited. Therefore special care should be taken in the treatment of these patients, especially at the beginning of therapy.

There is lack of information about dose adjustment in hepatic failure and probably no dose reduction necessary (a clinical decision should be made).

In **renal impairment** these dose adjustments should be considered.

<table>
<thead>
<tr>
<th>Creatinine clearance</th>
<th>Hydroxycarbamide Dose</th>
<th>Allopurinol Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>45-60ml/min</td>
<td>85%</td>
<td>100 to 200mg daily</td>
</tr>
<tr>
<td>30-45ml/min</td>
<td>80%</td>
<td>100 daily or alternate days</td>
</tr>
<tr>
<td>10-30 ml/min</td>
<td>75%</td>
<td>100 to 200mg daily</td>
</tr>
<tr>
<td>&lt;10 ml/min</td>
<td>50%</td>
<td>100 daily or alternate days</td>
</tr>
</tbody>
</table>

**Investigations prior to subsequent cycles**

During therapy with Hydroxycarbamide frequent monitoring of blood counts should be conducted as well as monitoring of hepatic and renal function.

**Treatment Duration**

Until blood counts returned to normal range.
Concurrent Medication

- Adequate hydration, if tumour lysis is expected, add 50mmol Sodium Bicarbonate per litre hydration fluid. Adjust the sodium bicarbonate concentration to maintain the urinary pH between 7 and 8 (i.e. alkaline).
- Allopurinol should be given as soon as possible at a daily oral dose of 300 mg daily (adjusted as above for renal failure). Patients with high counts at diagnosis can be considered for treatment with Rasburicase to reduce the effect of tumour lysis. Forced diuresis may be necessary.
- Anti-ulcer drug as per local policy
- Administer CMV negative blood products until the patient’s CMV status is known. Red cell transfusions should be avoided if there is any risk of leukostasis
- Antimicrobial prophylaxis as per local policy.

Anti-emetics

Low emetic potential, regular antiemetics may not be needed - follow local protocol

Adverse effects

- Hydroxycarbamide should be administered with caution to patients who receive concomitant or have received previous therapy with other antineoplastic drugs or irradiation, since adverse reactions can occur more frequently and more severe than those reported with the use of hydroxycarbamide, other antineoplastic drugs or irradiation alone. These effects primarily include bone marrow depression, gastric irritation, and mucositis
- An exacerbation of erythema caused by previous or simultaneous irradiation may occur.
- Hydroxycarbamide (Medac) should not be administered to patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption.

References

- emc.medicines.org.uk
Patient information

- Leukaemia Research Fund - Adult Acute Myeloid Leukaemia booklet
- CancerBACUP - Acute myeloid leukaemia booklet
- Cancer BACUP fact file – patient drug information leaflets

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