Chemotherapy Protocol

ACUTE MYELOID LEUKAEMIA

AMSACRINE-CYTARABINE-ETOPOSIDE

In-Patient Regimen

Regimen

- Acute Myeloid Leukaemia – InP-Amsacrine-Cytarabine-Etoposide (MACE)

Indication

- Consolidation therapy for AML in remission or salvage

Toxicity

<table>
<thead>
<tr>
<th>Drug</th>
<th>Adverse Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amsacrine</td>
<td>Nausea, mucositis, alopecia, hepatotoxicity, cardiac toxicity (as for anthracyclines, the risk of arrhythmias is increased by hypokalaemia)</td>
</tr>
<tr>
<td>Cytarabine</td>
<td>Nausea, vomiting, diarrhoea, fever, rash, itching, anorexia, oral and anal inflammation or ulceration, hepatic dysfunction, ocular pain, foreign body sensation, photophobia and blurred vision, dizziness, headache, confusion, cerebellar toxicity, myalgia and bone pain</td>
</tr>
<tr>
<td>Etoposide</td>
<td>Nausea, mucositis and alopecia, anaphylactic reactions</td>
</tr>
</tbody>
</table>

The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details.

Monitoring

Drugs

- U&Es, LFTs and FBC prior to starting a cycle of treatment

- Prior to starting treatment consider an ECG, ECHO or MUGA scan if there is a cardiac history, the patient is elderly or has a previous history suggestive of potential cardiac disease.

Dose Modifications

The dose modifications listed are for haematological, liver and renal function and drug specific toxicities only. Dose adjustments may be necessary for other toxicities as well.

In principle all dose reductions due to adverse drug reactions should not be re-escalated in subsequent cycles without consultant approval. It is also a general rule for chemotherapy that if a third dose reduction is necessary treatment should be stopped.

Discuss all dose reductions with the relevant consultant.
**Haematological**

In general the treatment can proceed if the neutrophils are greater than $1 \times 10^9/L$ and the platelets are greater than $100 \times 10^9/L$. Always check with the relevant consultant.

Consider blood transfusion if the patient is symptomatic of anaemia or has a haemoglobin of less than 8g/dL (80g/L).

**Hepatic Impairment**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Bilirubin $\mu$mol/L</th>
<th>AST/ALT units/L</th>
<th>Dose (% of original dose)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amsacrine</td>
<td>greater than 34</td>
<td>N/A</td>
<td>60%</td>
</tr>
<tr>
<td>Cytarabine</td>
<td>greater than 34</td>
<td>N/A</td>
<td>50%</td>
</tr>
<tr>
<td>Etoposide</td>
<td>26-51</td>
<td>60-180</td>
<td>50%</td>
</tr>
<tr>
<td></td>
<td>greater than 51</td>
<td>greater than 180</td>
<td>Clinical decision</td>
</tr>
</tbody>
</table>

**Renal Impairment**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Creatinine Clearance (ml/min)</th>
<th>Dose (% of original dose)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amsacrine</td>
<td>less than 60</td>
<td>75%</td>
</tr>
<tr>
<td>Cytarabine</td>
<td>less than 60</td>
<td>60%</td>
</tr>
<tr>
<td></td>
<td>less than 45</td>
<td>50%</td>
</tr>
<tr>
<td></td>
<td>less than 30</td>
<td>Discuss with consultant</td>
</tr>
<tr>
<td>Etoposide</td>
<td>15-50</td>
<td>75%</td>
</tr>
<tr>
<td></td>
<td>less than 15</td>
<td>50%</td>
</tr>
</tbody>
</table>

**Other**

Dose reductions or interruptions in therapy are not necessary for those toxicities that are considered unlikely to be serious or life threatening. For example, alopecia, altered taste or nail changes.
**Regimen**

1 cycle will be set in ARIA

Cycles should proceed when there is neutrophil and platelet recovery.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Days</th>
<th>Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amsacrine</td>
<td>100mg/m²</td>
<td>1, 2, 3, 4, 5</td>
<td>Intravenous infusion in 500ml glucose 5% over 60 minutes</td>
</tr>
<tr>
<td>Cytarabine</td>
<td>200mg/m²</td>
<td>1, 2, 3, 4, 5</td>
<td>Intravenous infusion in 1000ml sodium chloride 0.9% over 22 hours</td>
</tr>
<tr>
<td>Etoposide</td>
<td>100mg/m²</td>
<td>1, 2, 3, 4, 5</td>
<td>Intravenous infusion in 500ml sodium chloride 0.9% over 60 minutes</td>
</tr>
</tbody>
</table>

**Dose Information**

- Amsacrine will be dose banded according to the national dose bands (5mg/ml)
- Cytarabine will be dose banded according to the national dose bands (20mg/ml)
- Etoposide will be dose banded according to the agreed bands

**Administration Information**

**Extravasation**

- Amsacrine - vesicant
- Cytarabine – neutral (irritant in large volumes)
- Etoposide - irritant

**Other**

- Amsacrine must not be infused in sodium chloride 0.9% as precipitation or flocculation occurs. The line should be flushed with glucose 5% before and after administration of amsacrine.

**Additional Therapy**

This is an inpatient regimen please ensure all supportive are prescribed on the inpatient chart or general electronic prescribing system.

- Antiemetics
  
  Starting 15 - 30 minutes prior to chemotherapy
  
  - metoclopramide 10mg three times a day when required oral
  - ondansetron 8mg twice a day on days 1, 2, 3, 4, 5, 6, 7 oral

- Aciclovir 400mg twice a day until neutrophils are greater than 1x10⁹/L
• Antifungal prophylaxis according to consultant choice until neutrophils are greater than 1x10^9/L.

• Mouthwashes according to local or national policy on the treatment of mucositis

• Gastric protection with a proton pump inhibitor or a H₂ antagonist may be considered in patients considered at high risk of GI ulceration or bleed.

Coding

• Procurement – X71.2

• Delivery – X72.1

References

REGIMEN SUMMARY

InP-Amsacrine-Cytarabine-Etoposide (MACE)

Other than those listed below, supportive medication for this regimen will not appear in Aria as prescribed agents. The administration instructions for each warning describes the agents which must be prescribed on the in-patient chart or general electronic prescribing system.

Day 1, 2, 3, 4, 5

1. Warning – Check supportive medicines prescribed
   Administration Instructions
   - ondansetron 8mg twice a day oral or intravenous for 7 days
   - metoclopramide 10mg three times a day when required for nausea oral or intravenous
   - aciclovir 400mg twice a day oral
   - antifungal prophylaxis according to consultant choice

   Always refer to the patient schedule for supportive treatments and fluids.

2. Amsacrine 100mg/m^2 intravenous infusion in 500ml glucose 5% over 60 minutes
   Administration Instructions
   Amsacrine must not be infused in sodium chloride 0.9% as precipitation or flocculation occurs. The line should be flushed with glucose 5% before and after administration of amsacrine.

3. Cytarabine 200mg/m^2 intravenous infusion in 1000ml sodium chloride 0.9% over 22 hours

4. Etoposide 100mg/m^2 intravenous infusion in 500ml sodium chloride 0.9% over 60 minutes
This chemotherapy protocol has been developed as part of the chemotherapy electronic prescribing project. This was and remains a collaborative project that originated from the former CSCCN. These documents have been approved on behalf of the following Trusts:

- Hampshire Hospitals NHS Foundation Trust
- NHS Isle of Wight
- Portsmouth Hospitals NHS Trust
- Salisbury NHS Foundation Trust
- University Hospital Southampton NHS Foundation Trust
- Western Sussex Hospitals NHS Foundation Trust

All actions have been taken to ensure these protocols are correct. However, no responsibility can be taken for errors that occur as a result of following these guidelines.