Chemotherapy Protocol

ACUTE MYELOID LEUKAEMIA

CYTARABINE (1000)-FLUDARABINE-IDARUBICIN (FLA-IDA)

In-Patient Regimen

Regimen

- Acute Myeloid Leukaemia – InP-Cytarabine (1000)-Fludarabine-Idarubicin (FLA-Ida)

Indication

- Induction chemotherapy for patients with acute myeloid leukaemia (AML). Its use is particularly for patients under 60 years of age but it can be applied to older patients according to clinician's assessment. Its use is often particularly in patients with relapsed or resistant AML or ALL.

- The standard dose of cytarabine is 2000mg/m². The dose may be decreased to 1000mg/m² in those who are over the age of sixty or those younger and less fit.

Toxicity

<table>
<thead>
<tr>
<th>Drug</th>
<th>Adverse Effect</th>
</tr>
</thead>
<tbody>
<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>Fludarabine</td>
<td>Transfusion related GVHD, neurotoxicity, opportunistic infections, GI disturbances</td>
</tr>
<tr>
<td>Idarubicin</td>
<td>Myelosuppression, cardiac toxicity (cardiac failure, arrhythmias or cardiomyopathies), red discoloration of the urine, alopecia, nausea or vomiting, oral mucositis, elevation of liver enzymes and bilirubin</td>
</tr>
</tbody>
</table>

Patients treated with fludarabine carry a lifelong risk of transfusion associated graft versus host disease (TA-GVHD). Where blood products are required these patients must receive only irradiated blood products for life. Local blood transfusion departments must be notified as soon as the decision to treat is made and the patient must be issued with an alert card to carry with them at all times.

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.

**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 symptomatic of anaemia or has a haemoglobin of less than $8g/dL$ ($80g/L$).

**Hepatic Impairment**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Bilirubin µmol/L</th>
<th>AST/ALT units/L</th>
<th>Dose (% of original dose)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cytarabine</td>
<td>greater than 34</td>
<td>N/A</td>
<td>50%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Escalate doses in subsequent cycles in the absence of toxicity</td>
</tr>
<tr>
<td>Fludarabine</td>
<td>N/A</td>
<td>N/A</td>
<td>No dose adjustment required</td>
</tr>
<tr>
<td>Idarubicin</td>
<td>40-85</td>
<td>N/A</td>
<td>50%</td>
</tr>
<tr>
<td></td>
<td>Greater than 85</td>
<td>N/A</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>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>Fludarabine</td>
<td>greater than 70</td>
<td>100%</td>
</tr>
<tr>
<td></td>
<td>30-70</td>
<td>50%</td>
</tr>
<tr>
<td></td>
<td>less than 30</td>
<td>Discuss with consultant</td>
</tr>
<tr>
<td>Idarubicin</td>
<td>20-50</td>
<td>75%</td>
</tr>
<tr>
<td></td>
<td>10-20</td>
<td>75% with caution</td>
</tr>
<tr>
<td></td>
<td>Less than 10</td>
<td>50% with caution</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

3 cycles (1 cycle will be set in ARIA)

Cycles two and three 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>Cytarabine</td>
<td>1000mg/m²</td>
<td>1, 2, 3, 4, 5</td>
<td>Intravenous infusion in 1000ml sodium chloride 0.9% over 240 minutes</td>
</tr>
<tr>
<td>Fludarabine</td>
<td>30mg/m²</td>
<td>1, 2, 3, 4, 5</td>
<td>Intravenous infusion in 100ml sodium chloride 0.9% over 30 minutes</td>
</tr>
<tr>
<td>Idarubicin</td>
<td>8mg/m²</td>
<td>3, 4, 5</td>
<td>Intravenous bolus over 5-10 minutes</td>
</tr>
</tbody>
</table>

Dose Information

- Cytarabine will be dose banded according to the national dose bands (100mg/ml)
- The standard dose of cytarabine is 2000mg/m². The dose may be decreased to 1000mg/m² in those who are elderly
- Fludarabine will be dose banded according to the national dose band (25mg/ml)
- Idarubicin will be dose banded according to the national dose band (1mg/ml)
- The maximum safe cumulative dose of idarubicin is not known, although 150mg/m² would be considered problematic. Always consider previous anthracycline exposure.

Administration Information

Extravasation

- Cytarabine – neutral (irritant in large volumes)
- Fludarabine – neutral
- Idarubicin - vesicant

Other

- The administration of fludarabine must precede that of cytarabine by four hours

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 1x10^9/L

• Pentamidine 300mg nebu le every 28 days until the neutrophils are greater than 1x10^9/L

• Discuss the need and choice of antifungal with a consultant

• Prednisolone eye drops 0.5% into each eye four times a day. Continue for 5 days after cytarabine administration

• Allopurinol 300mg daily for first 7 days of initial induction chemotherapy.

• 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 – X71.5

• Delivery – NA

References
REGIMEN SUMMARY

InP-Cytarabine (1000)-Fludarabine-Idarubicin (FLA-Ida)

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

1. Warning – Check blood transfusion status
   Administration Instructions
   Patients treated with fludarabine carry a lifelong risk of transfusion associated graft versus host disease. Where blood products are required these patients must receive ONLY IRRADIATED BLOOD PRODUCTS for life. Ensure transfusion departments are notified and the patient has been issued with an alert card.

2. 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
   - consider pentamidine 300mg once every 28 days nebul
   - discuss the need and choice of antifungal with a consultant
   - consider allopurinol 300mg once a day for 7 days oral (review cycle 2 or if consolidation treatment)
   - prednisolone 0.5% eye drops, 1 drop each eye four times a day. Continue for 5 days after cytarabine administration is complete
   
   Always refer to the patient schedule for supportive treatments and fluids.

3. Fludarabine 30mg/m$^2$ intravenous infusion in 100ml sodium chloride 0.9% over 30 minutes
   Administration Instructions
   The fludarabine must precede the administration of the cytarabine by four hours.

4. Warning – Administration times
   Administration Instructions
   The cytarabine should be given four hours after the fludarabine.

5. Cytarabine 1000mg/m$^2$ in 1000ml sodium chloride 0.9% intravenous infusion over 240 minutes
   Administration Instructions
   The cytarabine should be given four hours after the fludarabine.

Days 3, 4, 5

5. 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
   - consider pentamidine 300mg once every 28 days nebul
   - discuss the need and choice of antifungal with a consultant
   - consider allopurinol 300mg once a day for 7 days oral (review cycle 2 or if consolidation treatment)
   - prednisolone 0.5% eye drops, 1 drop each eye four times a day. Continue for 5 days after cytarabine administration is complete
   
   Always refer to the patient schedule for supportive treatments and fluids.

6. Idarubicin 8mg/m$^2$ intravenous bolus over 5-10 minutes
7. **Fludarabine** 30mg/m² intravenous infusion in 100ml sodium chloride 0.9% over 30 minutes  
   Administration Instruction  
   The fludarabine must precede the administration of the cytarabine by four hours

8. **Warning – Administration times**  
   Administration Instructions  
   The cytarabine should be given four hours after the fludarabine

9. **Cytarabine** 1000mg/m² in 1000ml sodium chloride 0.9% intravenous infusion over 240 minutes  
   Administration Instructions  
   The cytarabine should be given four hours after the fludarabine
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.