HD Ara-C + Amsacrine

INDICATION
Salvage therapy in relapsed or refractory High Risk AML

TREATMENT INTENT
Curative

PRE-ASSESSMENT
1. Check all appropriate investigations have been performed.
2. Pregnancy Test - for all women with childbearing potential before each new chemotherapy course.
3. Record performance status (WHO/ECOG).
4. Record height and weight.
5. Consent - ensure patient has received adequate verbal and written information regarding their disease, treatment and potential side effects. Document in medical notes all information that has been given. Obtain written consent prior to treatment.
6. Fertility - all relevant patients should be offered fertility advice.
7. Hydration - fluid intake should be at least 3 litres per day. This does not necessarily need to be intravenous.
9. Treatment should be agreed in the relevant MDT.
10. Central venous access should be used, e.g. Hickman line. In urgent cases it may be necessary to start chemotherapy via a peripheral cannula.

DRUG REGIMEN

Days 1 to 5 CYTARABINE 3 g/m² daily* in 250 mL sodium chloride 0.9% intravenous infusion over 3 hours.

*For patients aged 60 years and over the cytarabine dose should be reduced to 2g/m² daily.

Days 1 to 3 AMSACRINE 200 mg/m² daily in 500 mL glucose 5% intravenous infusion over 1 hour.

NB: Amsacrine is incompatible with sodium chloride 0.9%, the giving set must be flushed with 50 mL glucose 5% before and after infusion.
CYCLE FREQUENCY

Patients will have at least one course. Consideration to use further courses requires a consultant decision and this should also ideally be discussed at the Myeloid MDT.

Consolidation
If a patient enters CR, CRi or PR, subsequent consolidation will be discussed at the MDT.

DOSE MODIFICATIONS
For the first course there is no dose modification for blood counts.
For subsequent courses, dose modifications for blood counts need to be discussed with a consultant.

Amsacrine

<table>
<thead>
<tr>
<th>Renal impairment</th>
<th>Hepatic impairment</th>
</tr>
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<tbody>
<tr>
<td>CrCl &lt; 60 mL/min: give 75% dose reduction</td>
<td>Bilirubin &gt; 34 micromol/L: give 60% dose</td>
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Cytarabine

<table>
<thead>
<tr>
<th>Renal impairment</th>
<th>Hepatic impairment</th>
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</thead>
<tbody>
<tr>
<td>GFR &lt; 60 mL/min: give 60% dose</td>
<td>Bilirubin &gt; 34 micromol/L: give 50% dose</td>
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<tr>
<td>GFR &lt; 45 mL/min: give 50% dose</td>
<td>Escalate doses in subsequent cycles in the absence of toxicity</td>
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<tr>
<td>GFR &lt; 30 mL/min: omit</td>
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INVESTIGATIONS

- Bone marrow to confirm diagnosis of AML.
- FBC, U&Es, LFT, Coagulation screen

CONCURRENT MEDICATION

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose and duration</th>
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<tr>
<td>Allopurinol</td>
<td>300 mg daily for first 14 days of initial induction chemotherapy. (If a remission is attained, the subsequent use of allopurinol is not required)</td>
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<tr>
<td>Aciclovir</td>
<td>200 mg three times a day for duration of treatment and for 3 months after completion</td>
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<tr>
<td>Fungal prophylaxis</td>
<td>As per local protocol</td>
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<tr>
<td>Proton pump inhibitor</td>
<td>Daily if clinically indicated</td>
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<tr>
<td>Prednisolone 0.5-1% eye drops or Dexamethasone 0.1% eye drops (depending on local formulary)</td>
<td>One drop into each eye QDS. Continue for 5 days after cytarabine (due to risk of cytarabine-induced conjunctivitis). In the event of conjunctivitis, consider increasing the frequency to 2-hourly until resolution of symptoms. Liaison with local ophthalmologists may be necessary in this situation</td>
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EMETIC RISK

Days 1-3: High
Days 4-5: Moderate

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

Amsacrine  Nausea, mucositis, alopecia. Cardiac toxicity (as for anthracyclines): the risk of arrhythmias is increased by hypokalaemia. Hepatotoxicity is uncommon (elevated serum bilirubin, alkaline phosphatases).

Cytarabine  Nausea, diarrhoea, oral ulceration, hepatic dysfunction. A cytarabine syndrome is also recognised in which patients suffer from fever, myalgia, bone pain, occasional chest pains, maculopapular rash, conjunctivitis and malaise. It usually occurs 6 to 12 hours following administration.

Other  Neutropenia, infections, pyrexia

EXTRAVASATION RISK

Amsacrine: vesicant
Cytarabine: neutral

TREATMENT RELATED MORTALITY

5-10%

REFERENCES


### Review

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<thead>
<tr>
<th>Name</th>
<th>Revision</th>
<th>Date</th>
<th>Version</th>
<th>Review date</th>
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<tbody>
<tr>
<td>Prof Vyas</td>
<td>New document</td>
<td>Feb 2016</td>
<td>1.0</td>
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<tr>
<td>Manuela Sultanova Service coordinator</td>
<td>Review section added, general formatting</td>
<td>Jul 2016</td>
<td>1.1</td>
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