CYTARABINE (Ara-C) High Dose + 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.
8. Consider dental assessment.
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/m^2 daily* in 250 mL sodium chloride 0.9% intravenous infusion over 4 hours.

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

Days 1 to 3 **AMSACRINE** 200 mg/m^2 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

Renal impairment	Hepatic impairment
GFR < 60 mL/min: 75% dose	Mild/moderate impairment: 75% dose Severe impairment: Not recommended

Cytarabine

Renal impairment	Hepatic impairment
High dose 1-3 g/m^2 GFR < 31-59 mL/min: 50% dose GFR < 30 mL/min: omit Haemodialysis: give 50% dose, start HD 4-5 hours after administration	Mild/moderate impairment: no dose adjustment necessary Severe impairment: 25-50% dose and increase as tolerated

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INVESTIGATIONS

- FBC, U&Es, LFT, Coagulation screen

CONCURRENT MEDICATION

Drug	Dose and duration
Allopurinol	300 mg daily for first 14 days of initial induction chemotherapy. (If a remission is attained, the subsequent use of allopurinol is not required)
Aciclovir	200 mg three times a day for duration of treatment and for 3 months after completion
Fungal prophylaxis	As per local protocol
Proton pump inhibitor	Daily if clinically indicated, as per local formulary
Prednisolone 0.5-1% eye drops or Dexamethasone 0.1% eye drops (depending on local formulary)	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

EMETIC RISK

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

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

Amsacrine	Nausea, mucositis, alopecia, pain/phlebitis on infusion, thrombocytopenia, seizures, urticaria. Cardiac toxicity (as for anthracyclines): the risk of arrhythmias is increased by hypokalaemia. Hepatotoxicity is uncommon (elevated serum bilirubin, alkaline phosphatases).
Cytarabine	Nausea, diarrhoea, abdominal pain, oral ulceration, hepatic dysfunction, CNS, GI and pulmonary toxicity, reversible corneal toxicity, somnolence, convulsion, pulmonary oedema. 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

1. S Tauro, P Shankaranarayana, IC Nitu-Whalley, N Duncan, G Begum, JIO Craig, RE Marcus, CF Craddock and P Mahendra. Stem Cell transplantation after salvage therapy with high-dose Cytarabine and amsacrine in adults with high risk leukaemia. Bone Marrow Transplantation (2003) 32, 273-278.
2. Krens S D et al (2019). Dose recommendations for anticancer drugs in patients with renal or hepatic impairment. *Lancet Oncol*; **20:** e201–08

REVIEW

Name	Revision	Date	Version	Review date
Prof Vyas	New document	Feb 2016	1.0	
Manuela Sultanova Service coordinator	Review section added, general formatting	Jul 2016	1.1	
Cheuk-kie Jackie Cheung, Haematology Pharmacist. NSSG Myeloid Group	Annual protocol meeting. Cytarabine diluent changed.	Oct 2019	1.2	Oct 2021
Yen Lim, Haematology Pharmacist. NSSG Myeloid Group	Annual protocol meeting. Renal/hepatic dosing and regimen specific complications updated.	Nov 2021	1.3	Nov 2023