CYTARABINE (ARA-C) HIGH DOSE

INDICATION

Consolidation chemotherapy for AML in remission.

Consider dose reduction to 1.5g/m^2 for patient ≥60 years old and for patient under 60 years old with co-morbidities at the discretion of clinician and as discussed at the MDT.

TREATMENT INTENT

Curative

PRE-ASSESSMENT

1. Confirm diagnosis
2. Pregnancy Test - for all women with childbearing potential before each new chemotherapy course.
3. ECG +/- Echo - if clinically indicated.
4. Record performance status (WHO/ECOG).
5. Record height and weight.
6. 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 on the day of treatment.
7. Fertility - it is very important the patient understands the potential risk of infertility, all patients should be offered fertility advice (see fertility guidelines).
8. Hydration and tumour lysis prevention; refer to tumour lysis protocol.
9. Consider dental assessment.
10. Treatment should be agreed in the relevant MDT.
11. Central venous access should be used, e.g. Hickman line or PICC. In urgent cases it may be necessary to start chemotherapy via a peripheral cannula.

DRUG REGIMEN

Days 1, 3 and 5

CYTARABINE 3 g/m^2 * **12 hourly** in 250 mL sodium chloride 0.9% intravenous infusion over 4 hours (6 doses).

*Consider dose reduction to 1.5g/m^2 for patient ≥60 years old and for patient under 60 years old with co-morbidities at the discretion of clinician and as discussed at the MDT.

This course should usually be given once counts have recovered to: Neutrophils > 1 x 10^9/L AND Platelets > 100 x 10^9/L.

DOSE MODIFICATIONS

Cytarabine - discuss with consultant

Renal impairment	Hepatic impairment
High dose 1-3 g/m^2 GFR < 31-59 mL/min: 50% dose GFR < 30 mL/min: omit Haemodialysis: 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

INVESTIGATIONS

- FBC, Coagulation screen, U&E, LFT before every cycle and as clinically indicated

CONCURRENT MEDICATION

Drug	Dose and duration
Aciclovir	200 mg three times a day for duration of treatment and for 3 months after completion
Proton pump inhibitor	As per local formulary
Fungal prophylaxis	As per local policy
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
G-CSF	As per local policy.

(No allopurinol as this is consolidation.)

EMETIC RISK

Days 1-5: Moderate

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

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.

EXTRAVASATION RISK

Cytarabine: neutral

TREATMENT RELATED MORTALITY

1-2%

REFERENCES

1. Mayer RJ, Davis RB, Schiffer CA, Berg DT, Powell BL, Schulman P, Omura GA, Moore JO, McIntyre OR, Frei E 3rd. Intensive postremission chemotherapy in adults with acute myeloid leukemia. Cancer and Leukemia Group B. N Engl J Med. 1994 Oct 6;331(14):896-903.
2. Medical Research Council AML15 Protocol. MRC Working Parties on leukaemia in adults and children. (2002).
3. Pfizer Ltd. Cytarabine 100mg/ml. Updated 29/11/2017. Accessed via http://www.medicines.org.uk/emc
4. 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
H Eagleton	Review of pre-assessment, concurrent medications and mortality	Feb 2016	4.0	
Cheuk-kie Cheung	Indication updated, general formatting	Apr 2017	4.1	
Cheuk-kie Jackie Cheung, Haematology Pharmacist. NSSG Myeloid Group	Annual protocol meeting	Oct 2019	4.2	Oct 2021
Yen Lim, Haematology Pharmacist. NSSG Myeloid Group	Annual protocol meeting. Renal/hepatic dosing updated.	Nov 2021	4.3	Nov 2023