MACE (AMSACRINE + CYTARABINE + ETOPOSIDE)

INDICATION

Consolidation chemotherapy for AML in remission
Induction therapy for relapsed / refractory AML

TREATMENT INTENT

Curative.
Due to the potential toxicity of this protocol (especially mucositis) it is recommended that patients remain inpatients until count recovery

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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. 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. **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 to 5	**AMSACRINE** 100 mg/m^2 daily in 500 mL glucose 5% intravenous infusion over 1 hour (5 doses)
Days 1 to 5	**CYTARABINE** 200 mg/m^2 daily in 250 mL sodium chloride 0.9% intravenous infusion over 22 hours (5 doses)
Days 1 to 5	**ETOPOSIDE** 100 mg/m^2 daily in 500-1000 mL sodium chloride 0.9% intravenous infusion over 1 hour (5 doses)

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

MACE is usually given as just a single cycle.

DOSE MODIFICATION - discuss with 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
No dose reduction necessary normally as doses not considered high dose	Mild/moderate impairment: no dose adjustment necessary Severe impairment: 25-50% dose and increase as tolerated

Etoposide

Renal impairment	Hepatic impairment
GFR (mL/min) GFR >50 mL/min: 100% GFR 15-50 mL/min: 75% GFR <15ml/min: 50% HD: Not dialysed, consider 75% Subsequent doses should be based on clinical response.	Bilirubin ≤50micromol/L with normal albumin and renal function: 100% dose Bilirubin >50 micromol/L or decreased albumin levels: Consider 50% dose, increase if tolerated

INVESTIGATIONS

- FBC, U&E, LFT.

CONCURRENT MEDICATION

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

(No allopurinol as this is consolidation.)

EMETIC RISK

Days 1 to 5: Moderate

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

Amsacrine	Nausea, mucositis, alopecia, pain/phlebitis on infusion, thrombocytopenia, seizures, urticaria, fever. 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.
Etoposide	Nausea, mucositis, alopecia, hypertension, transient systolic hypotension following rapid IV administration. Anaphylactic reactions have been reported rarely and have responded to stopping the infusion and the administration of an antihistamine and hydrocortisone. High risk for gram negative sepsis, recommend inpatient care until regeneration

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EXTRAVASATION RISK

Amsacrine: vesicant
Cytarabine: neutral
Etoposide: irritant

TREATMENT RELATED MORTALITY

2-10% depending on patient factors

REFERENCES

1. Hann IM, Stevens RF, Goldstone AH, Rees JK, Wheatley K, Gray RG, Burnett AK. Randomized comparison of DAT versus ADE as induction chemotherapy in children and younger adults with acute myeloid leukemia. Results of the Medical Research Council's 10th AML trial (MRC AML10). Adult and Childhood Leukaemia Working Parties of the Medical Research Council. Blood. 1997 Apr 1;89(7):2311-8.
2. Medical Research Council AML15 Protocol. MRC Working Parties on leukaemia in adults and children. (2002).
3. 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	Review pre-assessment, concurrent medications, adding treatment intent and mortality, formatting	Feb 2016	4.0	
Cheuk-kie Jackie Cheung, Haematology Pharmacist. NSSG Myeloid Group	Annual protocol meeting. Cytarabine diluent changed.	Oct 2019	4.1	Oct 2021
Yen Lim, Haematology Pharmacist. NSSG Myeloid Group	Annual protocol meeting. Renal/hepatic dosing updated.	Nov 2022	4.2	Nov 2024