MIDAC

Consolidation chemotherapy for AML

Drugs/Dosage/Administration:

Day	Drug	Dose	Route	Frequency
1 – 5 (5 doses)	Mitoxantrone	**Age < 60 yrs:** 10mg/m^2 in sodium chloride 0.9% **Age ≥ 60 yrs:** 8mg/m^2 in sodium chloride 0.9%	Slow IV bolus via fast-running infusion of sodium chloride 0.9%	Once daily
1 - 3 (6 doses)	Cytarabine	**Age < 60 yrs:** 1000mg/m^2 in 500ml 0.9% sodium chloride **Age ≥ 60 yrs:** 500mg/m^2 in 500ml 0.9% sodium chloride	IV infusion over 2 hours	Twice daily

Other Drugs: Corticosteroid eye drops e.g. Maxidex: one drop into each eye every 4 hours during high-dose cytarabine, and continuing for 5 days after cytarabine completed (8 days total)
Posaconazole to be taken during each cycle of chemotherapy, only when neutrophils drop to < 0.5x10^9/L and until they are > 0.5x10^9/L.
Consider aciclovir prophylaxis (400mg bd), especially if history of VZV or HSV reactivation

Frequency: usually a single cycle, to be given only if neutrophils ≥ 1.0 x 10^9/L and platelets ≥ 100 x 10^9/L

Main Toxicities: prolonged (> 7 days) myelosuppression, with risk of infections and haemorrhage (see Comments); alopecia; mucositis; cardiomyopathy; cytarabine syndrome; ovarian failure; infertility

Anti- emetics: highly emetogenic on days 1 - 5

Extravasation: non-vesicants

Regular Investigations:

FBC	alternate days until neutropenia or thrombocytopenia occur, then daily until recovery
U&Es	Day 1, then 3 x weekly
LFTs	Day 1, then 3 x weekly
Mg^{2+} and Ca^{2+}	Day 1, then weekly
Echo/MUGA	see Comments

Comments: Check any previous anthracycline exposure, particularly if AML is 2nd malignancy.
Maximum cumulative dose of mitoxantrone = 160mg/m^2
A baseline MUGA scan/echo should be performed where the patient is considered at risk of having impaired cardiac function e.g. significant cardiac history, hypertension, obese, smoker, elderly, previous exposure to anthracyclines, previous thoracic radiotherapy. Echo/MUGA should be repeated if there is suspicion of cardiac toxicity at any point during treatment, or if cumulative dose of mitoxantrone and any previous anthracyclines approaches maximum.

Reason for Update: posaconazole tablets available; suspension dose removed	Approved by Chair of Alliance TSSG: Dr A Laurie
Version: 6	Date: 16.3.15
Supersedes: Version 5	Review date: April 2017
Prepared by: S Taylor	Checked by: C Tucker

This regimen causes prolonged myelosuppression, which should be supported according to local policies, including those for neutropenic sepsis, the use of blood products and isolation.

Dose Modifications

Haematological Toxicity: Proceed with treatment only once neutrophils ≥ 1.0 x 10^9/L and platelets ≥ 100 x 10^9/L
Delay in count recovery after treatment should be managed according to local protocols / practice.

Renal Impairment: No dose reductions required

Hepatic Impairment:

Bilirubin(µmol/L)	Cytarabine Dose
> 34	Give 50% dose

Bilirubin(µmol/L)	Mitoxantrone Dose
> 60	Give maximum of 8mg/m^2

Patient Information: Macmillan leaflets for Mitoxantrone and Cytarabine

References: AML 15 trial, MRC 2005
AML 14 trial, MRC 2004