DA

Induction chemotherapy for AML for patients aged < 60,
and for patients aged ≥ 60 for whom intensive therapy is considered appropriate

Drugs/Dosage/Administration: Usually 2 cycles are given, as follows:

Cycle 1 (DA 3 + 10):

Day	Drug	Dose	Route	Frequency
1 – 10* (20 doses)	Cytarabine	100mg/m^2	Slow IV bolus **or** in 100ml sodium chloride 0.9% over 15 minutes	Every 12 hours
1, 3 and 5 (3 doses)	Daunorubicin	Age < 60 yrs: **60** mg/m^2 Age ≥ 60 yrs: **50** mg/m^2	Slow bolus via fast-running infusion of sodium chloride 0.9%	Alternate days

*Often one dose only given on Day 1 (pm), with last dose on the morning of Day 11

Cycle 2 (DA 3 + 8):

Day	Drug	Dose	Route	Frequency
1 – 8* (16 doses)	Cytarabine	100mg/m^2	Slow IV bolus **or** in 100ml sodium chloride 0.9% over 15 minutes	Every 12 hours
1, 3 and 5 (3 doses)	Daunorubicin	50 mg/m^2	Slow bolus via fast-running infusion of sodium chloride 0.9%	Alternate days

*Often one dose only given on Day 1 (pm), with last dose on the morning of Day 9

Other Drugs: For patients with potential for tumour lysis syndrome, ensure initiation of prophylactic measures according to Alliance guidelines for management of TLS.
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.
#In the first cycle of treatment, give prophylaxis from the start of the cycle regardless of the initial neutrophil count.
Consider aciclovir prophylaxis (400mg bd), especially if history of VZV or HSV reactivation

Frequency: 2 cycles as above, with the second cycle 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; ovarian failure; infertility

Anti- emetics: Days 1 - 5: highly emetogenic; Day 6 onwards: mildly emetogenic

Extravasation: Daunorubicin is a vesicant

Reason for Update: posaconazole tablets available, so suspension dose removed; dose of daunorubicin reviewed and indication exanded	Approved by Chair of Alliance TSSG: Dr A Laurie
Version: 7	Date: 8.5.15
Supersedes: Version 6	Review date: June 2017
Prepared by: S Taylor	Checked by: C Tucker

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

Comments: Sperm banking if appropriate and time allows.

Check any previous anthracycline exposure, particularly if AML is 2nd malignancy. Maximum cumulative dose of daunorubicin = 600mg/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. MUGA/echo should be repeated if there is suspicion of cardiac toxicity at any point during treatment, or if cumulative dose of daunorubicin and any previous anthracyclines approaches maximum.

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

Dose Modifications

Haematological Toxicity:	Cycle 1:	There are no modifications for low blood counts.
	Cycle 2:	Proceed once neutrophils > 1.0 x 10^9/L and platelets > 100 x 10^9/L. If low counts are thought to be due to disease, discuss with Consultant. Delay in count recovery after treatment should be managed according to local protocols/practice.

Renal Impairment: The SPC states that the dose of daunorubicin should be reduced in patients with impaired renal function. However, there is no dosing advice according to creatinine clearance. The advice is as follows:

Serum Creatinine (µmol/L)	Daunorubicin Dose
105 – 265	Give 75% dose
> 265	Give 50% dose

NB. A serum creatinine > 105µmol/L may not correspond to renal impairment, particularly in younger patients. However, if there *is* evidence of impaired renal function eg reduced creatinine clearance, Cr^{51}-EDTA, or according to Cockcroft and Gault, then it is reasonable to use the serum creatinine to guide the dose reduction.

Hepatic Impairment:

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

Bilirubin (µmol/l)	Daunorubicin Dose
20 – 50	Give 75% dose
50 - 85	Give 50% dose
> 85	Omit

Patient Information: Macmillan leaflets for Daunorubicin and Cytarabine

References: MRC AML trials 16 & 17

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