FLAG

For treatment of relapsed, refractory AML and ALL, and for high risk AML
For patients with previous anthracycline exposure or not considered suitable for an anthracycline

Drugs/Dosage/Administration:

Day	Drug	Dose	Route	Frequency
1 – 7, then according to clinical situation and Consultant decision	G-CSF (see Comments)	Lenograstim 263mcg **or** Filgrastim 300mcg	s/c bolus	Once daily
2 – 6 (5 doses)	Fludarabine	30mg/m^2 diluted in 0.9% sodium chloride	IV in 100 – 250ml 0.9% sodium chloride over 30 minutes	Once daily
2 – 6 (5 doses)	Cytarabine	2000mg/m^2 in 500ml 0.9% sodium chloride (If age > 60, give 1000mg/m^2)	IV over 4 hours, starting exactly 4 hours after start of Fludarabine infusion	Once daily
2 – 8	Corticosteroid eye drops e.g. Maxidex	One drop	To each eye	Every 4 hours, increasing to 2 hourly if eyes become sore

Other drugs: For patients with potential for tumour lysis syndrome, ensure initiation of prophylactic measures according to Alliance guidelines for management of TLS.
PCP prophylaxis - prescribe according to unit practice/protocol (generally until 6 months after completion of treatment, or according to CD_4 counts)
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.

Frequency: 1 - 2 cycles as specified above, with the second cycle given only if the following criteria are met: ≤ 15% blasts in bone marrow after Cycle 1
not considered to have adverse genetic abnormalities
neutrophils > 1.0 x 10^9/L and platelets > 100 x 10^9/L

Main Toxicities: myelosuppression; alopecia; mucositis; conjunctivitis (cytarabine); prolonged T cell immunosuppression (fludarabine); encephalopathy (fludarabine); ovarian failure; infertility

Anti-emetics: highly emetogenic on Days 2 - 6

Extravasation: non-vesicants

Reason for Update: posaconazole tablets available; suspension dose removed	Approved by Chair of Alliance TSSG: Dr A Laurie
Version: 7	Date: 16.3.15
Supersedes: Version 6	Review date: April 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	Day 1, then three times weekly
	LFTs	Day 1, then once weekly
	Mg^{2+} & Ca^{2+}	Day 1
	Uric acid	baseline
	Cr^{51}-EDTA/24 hour urine	if serum creatinine > 150µmol/L

Comments: Sperm banking if appropriate and time allows.

It is important that patient receives G-CSF one day before starting chemotherapy.

All patients must receive irradiated blood products for all future transfusions - inform patient and blood bank.

Dose Modifications

Haematological Toxicity:
Cycle 1: There are no modifications for myelosuppression
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 marrow infiltration, discuss with Consultant.

Renal Impairment:

CrCl (ml/min)	Fludarabine Dose
> 70	Give 100% dose
30 – 70	Give 50% dose
< 30	Contra-indicated

Hepatic Impairment:

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

Patient Information: Macmillan leaflets for Cytarabine and Fludarabine

References:
Estey, E at al; JCO (1994); 671 – 678
AML 15 trial, MRC 2004
AML 17 trial, V5 May 2010