

Malaysia-Singapore AML 2006 treatment protocol

ay/MASPORE AML 2005.doc (modified 16-08-06)

(Not for Down's Syndrome or AML M3/acute promyelocytic leukaemia)

Induction ADE#1

IV Cytarabine 100 mg/m²/dose q12hrly IV bolus for 20 doses (10 days)

IV Daunorubicin 50mg/m²/dose daily at day 1, 3 and 5 to infuse over 20 hours if there is central line, or IV bolus if no central line

IV Etoposide 100 mg/m²/dose daily in 250 mL normal saline over 1 hour infusion for 5 days at day 1-5

TIT

Induction HidAC#2

IV cytarabine 3000mg/m²/dose q12hrly infusion over 3 hours for 6 doses (3 days)

TIT

Consolidation HidAC#3

IV cytarabine 3000mg/m²/dose q12hrly infusion over 3 hours for 6 doses (3 days)

TIT

Consolidation MiDAC#4

IV Mitoxantrone 10 mg/m²/dose in 250mL N/S free flow infusion over 6 hours on days 1-5 (total 5 doses)

IV cytarabine 1000 mg/m²/dose 12 hrly infusion over 2 hours on days 1-3 (total 6 doses)

Consolidation FLAG#5 for high-risk patients without stem cell transplant

NB: In children less than 1 years old or < 10kg, use per kg dosing.

To convert per m² to per kg, divide dose per m² by 30 to obtain dose per kg.

Downs syndrome is treated on reduced dose (see Downs' protocol)

AML M3 t(15;17)/PML-RARA is treated on a separate protocol

TIT

Age (yrs)	MTX	Hydrocortisone	AraC	Volume
< 1	5 mg	5 mg	15mg	3 mL
1-2	7.5mg	7.5 mg	20 mg	4 mL
2-3	10mg	10mg	25mg	5 mL
>3	12.5mg	12.5mg	30mg	6mL

CNS disease

If WBC > 5/uL and blasts seen, patient is CNS III, provided non-traumatic tap.
CNS II disease is traumatic tap with blasts seen.

CNS III disease, to treat with

Weekly TIT until CSF clears or a minimum of 6 weekly doses of TIT

Then TIT with every cycle

Cranial RT is decided individually as there is conflicting evidence of its use.

CNS II disease, to treat with

Weekly TIT until CSF clears or a minimum of 4 weekly doses of TIT

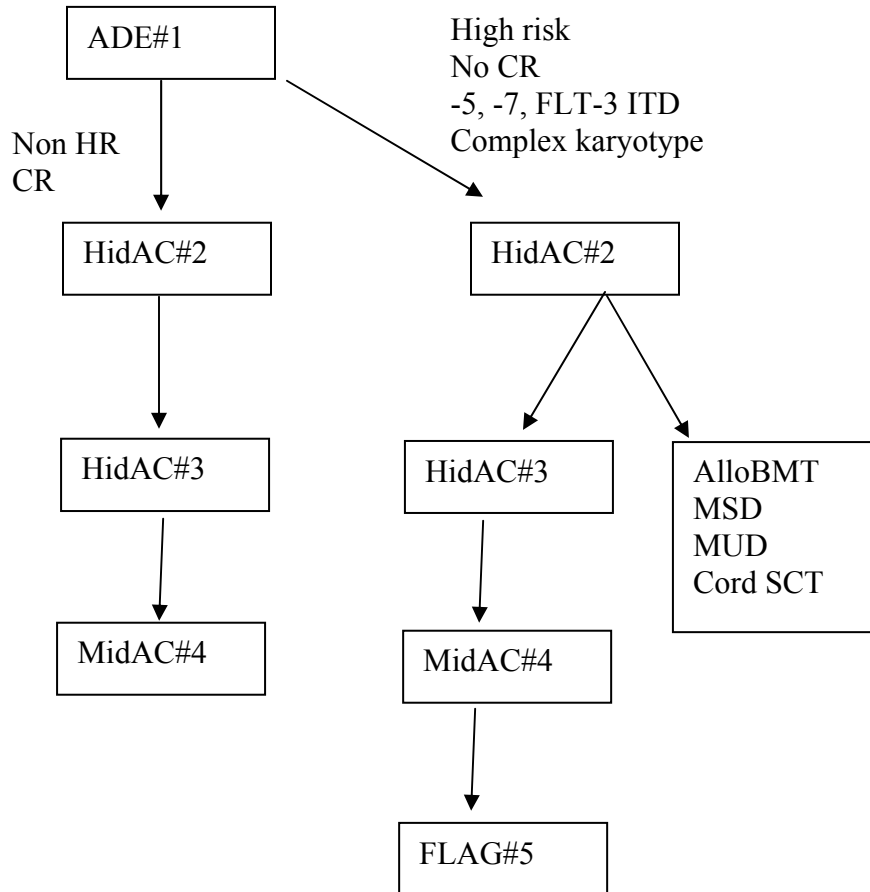
Then TIT with every cycle

Cranial RT is decided individually as there is conflicting evidence of its use.

If CNS negative

TIT with each cycle during the first 3 cycles only.

Roadmap MASPORE AML 2006 for non-Downs and non AML M3 patients:



Protocol details:

At diagnosis.

Investigations needed to be done:

1. FBC with PBF daily
2. RP#2 daily unless tumour lysis syndrome
3. LFT
4. GXM
5. PT/PTT (daily if AML M3 or APL)
6. 2D-echo heart to assess fractional shortening
7. ECG
8. BM aspirate and trephine (important to do trephine for Down's Syndrome to assess for reticulin/marrow fibrosis)
 - a. BMA for morphology and cytochemistry
 - b. BMA for immunophenotyping especially for platelet markers like CD42a and CD61
 - c. BM for karyotyping
 - d. BM for oncogene fusion screening
 - e. BM for cell banking.
 - f. BM trephine to pathology for AML M7.
9. CSF for cytopsin
10. Viral screen including HSV, CMV

Remember management for tumour lysis syndrome, Neutropaenic fever and bleeding.

Arrange for insertion of Hickman's line – prefer double lumen Hickman's

ADE#1

IV hydration D5%/0./45% NaCl at 3L/m²/day with 10mL 8.4% NaHCO₃ per 500mL.
To maintain urine pH 6.5-8 for tumour lysis syndrome
IV frusemide 0.5mg/kg/dose q8-12hlry

IV ondansetron 6mg/m²/dose q6hrly or
IV granisetron 0.05mg/kg/dose q8hrly

Allopurinol 5-10mg/kg/dose q8hrly if at risk of tumour lysis
CaCO₃ 2-3 tablets q6hrly if at risk of tumour lysis

IV Cytarabine 100 mg/m²/dose q12hrly IV bolus for 20 doses (10 days)

IV Daunorubicin 50mg/m²/dose in 500mL N/S daily at day 1, 3, 5 to infuse over 20 hours, if there is central line.
Infuse daunorubicin using a burette in aliquots of 50mL over 2 hours free flow.
If no central line, IV bolus is acceptable. Care to avoid extravasation.

IV Etoposide 100 mg/m²/dose daily in 250 mL normal saline over 1 hour infusion for 5 days at day 1-5. Note that maximum concentration of etoposide is 0.4mg/mL for stability.

TIT

Day	Date	Drug	Drug	
1		AraC + TIT	Dauno	Etoposide
		AraC		
2		AraC		Etoposide
		AraC		
3		AraC	Dauno	Etoposide
		AraC		
4		AraC		Etoposide
		AraC		
5		AraC	Dauno	Etoposide
		AraC		
6		AraC		
		AraC		
7		AraC		
		AraC		
8		AraC		
		AraC		
9		AraC		
		AraC		
10		AraC		
		AraC		

Protocol tests for ADE#1

	Diagnosis	Day 2	D 3	D4	D5	D8	D15
BM	√					√	√
PBld	√	√				√	√
Bld Pro BNP	√	√	√	√	√		
Urine Pro BNP	√	√	√	√	√		
2D echo	√						

HidAC#2

Investigations:

1. FBC – start if ANC > 2,000/uL, and platelets > 80,000/uL.
2. RP#1
3. LFT

IV hydration D5%/0./45% NaCl at 2L/m²/day 10mL 7.45 KCL per 500mL

IV ondansetron 6mg/m²/dose q6hrly or

IV granisetron 0.05mg/kg/dose q8hrly

Methylcellulose or normal saline eyedrops q4hrly to both eyes

IV Cytarabine 3000 mg/m²/dose q12hrly IV over 3 hrs for 6doses (3 days)

TIT

Day	Date	Drug		
1		AraC + TIT		
		AraC		
2		AraC		
		AraC		
3		AraC		
		AraC		

Toxicity from high dose araC (Please see Appendix I for management plan)

1. Cerebellar syndrome
2. Conjunctivitis

Cerebellar syndrome

Observe for nystagmus

1. If nystagmus occurs in conjunction with cerebellar signs, STOP IV cytarabine and abandon HidAC regimen.
2. If nystagmus occurs in isolation, stop IV cytarabine for 24 hrs and then restart.

Conjunctivitis

1. If conjunctivitis occurs despite eyedrops, switch to 0.5% prednisolone eyedrops and stop IV cytarabine for 24 hrs
2. Restart cytarabine at 50% of the dose after 24 hours of rest
3. If blistering noted of the eyes, DO NOT RESTART cytarabine

HidAC#3

Investigations:

1. FBC – start if ANC > 2,000/uL, and platelets > 80,000/uL.
2. RP#1
3. LFT

IV hydration D5%/0./45% NaCl at 2L/m²/day 10mL 7.45 KCL per 500mL

IV ondansetron 6mg/m²/dose q6hrly or

IV granisetron 0.05mg/kg/dose q8hrly

Methylcellulose or normal saline eyedrops q4hrly to both eyes

IV Cytarabine 3000 mg/m²/dose q12hrly IV over 3 hrs for 6doses (3 days)

TIT

Day	Date	Drug		
1		AraC + TIT		
		AraC		
2		AraC		
		AraC		
3		AraC		
		AraC		

Toxicity from high dose araC (Please see Appendix I for management plan)

1. Cerebellar syndrome
2. Conjunctivitis

Cerebellar syndrome

Observe for nystagmus

3. If nystagmus occurs in conjunction with cerebellar signs, STOP IV cytarabine and abandon HidAC regimen.
4. If nystagmus occurs in isolation, stop IV cytarabine for 24 hrs and then restart.

Conjunctivitis

4. If conjunctivitis occurs despite eyedrops, switch to 0.5% prednisolone eyedrops and stop IV cytarabine for 24 hrs
5. Restart cytarabine at 50% of the dose after 24 hours of rest
6. If blistering noted of the eyes, DO NOT RESTART cytarabine

MidAC#4

IV hydration D5%/0./45% NaCl at 2L/m²/day 10mL 7.45 KCL per 500mL

IV ondansetron 6mg/m²/dose q6hrly

IV Mitoxantrone 10 mg/m²/dose in 250mL N/S free flow infusion over 6 hours on days 1-5 (total 5 doses). Do not extravasate.

IV cytarabine 1000 mg/m²/dose 12 hrly infusion over 2 hours on days 1-3 (total 6 doses)

Day	Date	Drug	Drug	
1		AraC	Mitoxantrone	
		AraC		
2		AraC	Mitoxantrone	
		AraC		
3		AraC	Mitoxantrone	
		AraC		
4			Mitoxantrone	
5			Mitoxantrone	

Protocol tests for MidAC#4

	Day 0	Day 2	D 3	D4	D5	D6	
Bld Pro BNP	√	√	√	√	√		
Urine Pro BNP	√	√	√	√	√		
2D echo	√						

FLAG#5 for patients in high risk arm who did not undergo SCT

NOTE: Blood products after FLAG must be irradiated because fludarabine causes severe immunosuppression and there is increased risk of transfusion associated graft-versus-host disease.

IV hydration D5%/0./45% NaCl at 2L/m²/day 10mL 7.45 KCL per 500mL
 IV ondansetron 6mg/m²/dose Q6hrly in 50mL normal saline over 10 min for 6 days Or
 IV granisetron 0.05mg/kg/dose q8 hrly in 50mL N/S over 10 mins for 6 days

S/C GCSF 5ug/kg/day from day 1 until ANC > 1 for 3 consecutive days
 IV Fludarabine 25mg/m²/day in 100 mL 0.9% NaCl over 30 mins for 5 days on Day 1-5

IV Cytarabine 2000 mg/m²/day in 250mL 0.9% NaCl over 4 hours for 5 days to start 4 hours after starting IV fludarabine and to infuse over 4 hours

Methylcellulose or normal saline eyedrops q4hrly to both eyes

Day	1	2	3	4	5	6
GCSF 5ug/kg/day s/c	G	G	G	G	G	G
Fludarabine 25mg/m ² /day x5 days	F	F	F	F	F	
Cytarabine 2g/m ² /day X5 days	A	A	A	A	A	

Day	Date	Drug	Drug	Drug
1		Fludarabine	A	GCSF
2		F	A	G
3		F	A	G
4		F	A	G
5		F	A	G
6				G
7				G
				G
				G
				G

Appendix I. Toxicity from high dose araC

- Cerebellar syndrome
- Conjunctivitis

Cerebellar syndrome

Observe for nystagmus

- If nystagmus occurs in conjunction with cerebellar signs, STOP IV cytarabine and abandon HiDAC regimen.
- If nystagmus occurs in isolation, stop IV cytarabine for 24 hrs and then restart.

Conjunctivitis

- If conjunctivitis occurs despite eyedrops, switch to 0.5% prednisolone eyedrops and stop IV cytarabine for 24 hrs
- Restart cytarabine at 50% of the dose after 24 hours of rest
- If blistering noted of the eyes, DO NOT RESTART cytarabine.

In event of development of cerebellar toxicity (except nystagmus alone) or blistering of the cornea, with high dose cytarabine, do not continue high dose cytarabine. Replace with the following regimen:

- If severe toxicity occurs with HiDAC#2, replace with ADE#2, MACE#3 and AM#4.
- If severe toxicity occurs with HiDAC#3, replace with ADE#3, AM#4.
- If severe toxicity occurs with MiDAC#4, replace with AM#4

ADE replacement 8+3+5

IV Cytarabine 100 mg/m²/dose q12hrly IV bolus for 16 doses (8 days)

IV Daunorubicin 50mg/m²/dose daily at day 1, 3 and 5 to infuse over 20 hours if there is central line, or IV bolus if no central line

IV Etoposide 100 mg/m²/dose daily in 250 mL normal saline over 1 hour infusion for 5 days at day 1-5

TIT

MACE

IV amsacrine 100 mg/m²/day in 100 mL N/S over 1 hr for 5 days

IV cytarabine 200 mg/m²/day in 250 mL N/S over 24 hrs continuous infusion for 5 days

IV Etoposide 100 mg/m²/dose daily in 250 mL normal saline over 1 hour infusion for 5 days at day 1-5

AM replacement – low dose cytarabine and mitoxantrone

IV cytarabine 200 mg/m²/day in 250 mL N/S over 24 hrs continuous infusion for 5 days

IV Mitoxantrone 10 mg/m²/dose in 250mL N/S free flow infusion over 6 hours on days 1-5 (total 5 doses). Do not extravasate.

Appendix II

If urticarial skin reaction to etoposide occurs, stop etoposide. Restart infusion at half the rate.

If anaphylactic allergy to etoposide occurs, replace with

- Oral Thioguanine 100 mg/m²/dose q12hrly for 2 days replacing each day of etoposide.

For example if the patient is allergic and he is scheduled for 3 more days of etoposide in ADE#1, replace with 6 days of oral Thioguanine.