

**MA-SPORE ALL 2003 Enrolment Form. Provisional HR risk.**

Plse fax to 65-67797486 Dr A Yeoh or email to paeyej@nus.edu.sg

**PERSONAL PARTICULARS****Patient #:**

Name : \_\_\_\_\_  
 HRN : \_\_\_\_\_  
 Date of Birth : \_\_\_\_\_  
 Age/Sex : \_\_\_\_\_  
 Date of Dx : \_\_\_\_\_  
 Institution\* : NUH/KKH/UMMC/ SJMC  
 Doctor i/c : \_\_\_\_\_

Anthropometric Data

Height : \_\_\_\_\_ cm \_\_\_\_\_ centile OFC : \_\_\_\_\_ cm \_\_\_\_\_ centile  
 Weight : \_\_\_\_\_ kg \_\_\_\_\_ centile Surface Area: \_\_\_\_\_ m<sup>2</sup>

**PRESENTATING FEATURES**

Symptoms (Duration)  
 Fever : No / Yes (\_\_\_\_\_)  
 Pallor : No/ Yes (\_\_\_\_\_)  
 Bruising : No/ Yes (\_\_\_\_\_)  
 Bone pain : No/ Yes (\_\_\_\_\_)  
 Wt Loss : No/ Yes (\_\_\_\_\_)  
 Others : (\_\_\_\_\_)  
 (specify) \_\_\_\_\_

Signs  
 Liver : \_\_\_\_\_ cm  
 Spleen : \_\_\_\_\_ cm  
 Lymph Nodes : \_\_\_\_\_  
 Testicular Enlargement: \_\_\_\_\_

**INVESTIGATIONS/CSF**

TWC : \_\_\_\_\_ x 10<sup>9</sup>/L  
 Hb : \_\_\_\_\_ g/dl  
 Plt : \_\_\_\_\_ 10<sup>9</sup>/L  
 Polys : \_\_\_\_\_ % Lymph : \_\_\_\_\_ %  
 Monos : \_\_\_\_\_ % Eosin : \_\_\_\_\_ %  
 Blast : \_\_\_\_\_ % ABC: \_\_\_\_\_ 10<sup>9</sup>/L  
 ALT : \_\_\_\_\_ U/L AST : \_\_\_\_\_ U/L  
 LDH : \_\_\_\_\_ U/L Creatine: \_\_\_\_\_ umol/L  
 TPMT Activity:  
 TPMT genotype\*: Normal/\*3A/\*3C/\*6  
 CSF : WBC \_\_\_\_\_ /uL; RBC \_\_\_\_\_ /uL  
 Blasts Seen/Not seen  
 CNS\* I/ II/ III  
**Day 8 Absolute blast count:**  
 Day 8 BM blast %:  
 Day 15 BM blast %:  
 Day 33 BM blast %:  
 MRD tp#1:  
 MRD tp#2  
 CXR\* : \_\_\_ Mediastinal mass Pres/Abs  
 2D echo: FS \_\_\_\_\_ LVEF \_\_\_\_\_  
 ECG: Qtc \_\_\_\_\_

**BMA / TREPHINE**

Morphology and Cytochemistry\*\*:  
 FAB L1/L2/L3  
 (Plse append morphology report)  
 Immunophenotyping\*\*:  
 T-lineage / B-lineage\*  
 CALLa\* +ve/-ve  
 If B-lineage\* : early preB/preB  
 DNA Index = \_\_\_\_\_  
 Cytogenetics\*:  
 Hypodiploid/Normodip/Pseudodip/  
 Hyperdip 47-50/Hyperdip  
 TEL-AML1/t(12;21) : Present/Absent  
 BCR-ABL/t(9;22) : Present/Absent  
 E2A-PBX1/t(1;19) : Present/Absent  
 MLL-AF4/t(4;11) : Present/Absent  
 Other fusions:

Biopsy:

\_\_\_\_\_

\* Circle the appropriate  
 \*\*Plse submit morphology, immunophenotype,  
 karyotype reports.

**Final Risk Group\*: SR/IR/HR**

**Proposed MA-SPORE-ALL-2003 Study – HR arm**  
Treatment overview

**1. Induction (Protocol I) – 10 weeks**

Prednisolone 60 mg/m<sup>2</sup>/day p.o. in 3 divided doses from day 1 -7  
IT MTX

**1a (for HR group – prednisolone poor responders only)**

Dexamethasone 6mg/m<sup>2</sup>/day in 2 divided doses from day 8 to 36 (total 28 days), no tailing of dexamethasone.

IV Vincristine 1.5mg/m<sup>2</sup>/dose weekly for week 2,3,4,5

IV Daunorubicin 25 mg/m<sup>2</sup>/dose weekly for week 2,3,4,5

IM L-asparaginase 7,500 U/m<sup>2</sup> from day 8 twice a week for 8 doses (4 weeks)

If allergic to E coli L-asp, switch to Erwinia L-asp 20,000U/m<sup>2</sup>/dose M,W,F X 4 weeks

IT MTX at day 8, d15, d33 (CNS2/3 additional IT at day 22)

**1b (all groups)**

IV cyclophosphamide 1000mg/m<sup>2</sup> day 36 and 64

Mercaptopurine p.o. 50mg/m<sup>2</sup>/day ON

IV or S/C cytarabine 75mg/m<sup>2</sup> for 4 days block X 4 blocks

IT MTX at day 45, 59 (beginning of the 2<sup>nd</sup> and 4<sup>th</sup> block of cytarabine)

**2. Protocol M 5g (8 weeks)**

**Protocol M 5g for IR/HR groups**

IV HDMTX 5000mg/m<sup>2</sup> every 2 weeks with folinic rescue X 4 courses

IV folinic acid 15mg/m<sup>2</sup>/dose at 42, 48, 54 hours from start of IV MTX

Mercaptopurine p.o. 25mg/m<sup>2</sup>/day ON

IT MTX with each HDMTX given on day 1

**3. Protocol II # 1 (5 weeks) - HR**

Dexamethasone 10mg/m<sup>2</sup>/day p.o. in 2 divided doses for 21 days, no tailing of dexamethasone

IV Vincristine 1.5mg/m<sup>2</sup> on days 1, 8, 15

IV doxorubicin 30mg/m<sup>2</sup> on days 1, 8, 15

IM L-asparaginase 10,000U/m<sup>2</sup>/dose every 3 days from day 3 for 6 doses

If allergic to E coli L-asp, switch to IM Erwinia L-asp 20,000U/m<sup>2</sup>/dose M,W,F X 3 weeks

For CNS 2/3, additional IT MTX is given at day 1 and day 8.

IV Cyclophosphamide 1000mg/m<sup>2</sup> on day 22  
Thioguanine p.o. 50mg/m<sup>2</sup> ON for 2 weeks from day 22-36  
IV or S/C cytarabine 75mg/m<sup>2</sup>/dose for 4 days block X 2 blocks  
IT MTX on start of every cytarabine block (total of 2 IT)

#### 4. Interim maintenance HR #1 (8 weeks)

IV vincristine 1.5 mg/m<sup>2</sup> every 10 days for 8 doses  
IV methotrexate 100mg/m<sup>2</sup>/dose every 10 days with IV VCR for 8 doses  
24 hours after giving IV MTX, administer IM L-asparaginase 15,000U/m<sup>2</sup> every week for 8 weeks  
If allergic to E coli L-asp, switch to Erwinia L-asp 30,000U/m<sup>2</sup>/dose twice a week for 8 weeks  
IT MTX every 20 days X 4 doses

#### 5. Protocol II # 2 (5 weeks) - HR

Dexamethasone 10mg/m<sup>2</sup>/day p.o. in 2 divided doses for 21 days, no tailing of dexamethasone  
IV Vincristine 1.5mg/m<sup>2</sup> on days 1, 8, 15  
IV doxorubicin 30mg/m<sup>2</sup> on days 1, 8, 15  
IM L-asparaginase 10,000U/m<sup>2</sup>/dose every 3 days from day 3 for 6 doses  
If allergic to E coli L-asp, switch to IM Erwinia L-asp 20,000U/m<sup>2</sup>/dose M,W,F X 3 weeks  
For CNS 2/3, additional IT MTX is given at day 1 and day 8.

IV Cyclophosphamide 1000mg/m<sup>2</sup> on day 22  
Thioguanine p.o. 50mg/m<sup>2</sup> ON for 2 weeks from day 22-36  
IV or S/C cytarabine 75mg/m<sup>2</sup>/dose for 4 days block X 2 blocks  
IT MTX on start of every cytarabine block (total of 2 IT)

#### 6. Interim maintenance HR #2 (8 weeks)

IV vincristine 1.5 mg/m<sup>2</sup> every 10 days for 8 doses  
IV methotrexate 100mg/m<sup>2</sup>/dose every 10 days with IV VCR for 8 doses  
24 hours after giving IV MTX, administer IM L-asparaginase 15,000U/m<sup>2</sup> every week for 8 weeks  
If allergic to E coli L-asp, switch to Erwinia L-asp 30,000U/m<sup>2</sup>/dose twice a week for 8 weeks  
IT MTX every 20 days X 4 doses

## **7. Protocol II # 3 (5 weeks) - HR**

Dexamethasone 10mg/m<sup>2</sup>/day p.o. in 2 divided doses for 21 days, no tailing of dexa  
IV Vincristine 1.5mg/m<sup>2</sup> on days 1, 8, 15  
IV doxorubicin 30mg/m<sup>2</sup> on days 1, 8, 15  
IM L-asparaginase 10,000U/m<sup>2</sup>/dose every 3 days from day 3 for 6 doses  
If allergic to E coli L-asp, switch to IM Erwinia L-asp 20,000U/m<sup>2</sup>/dose M,W,F X 3 weeks  
For CNS 2/3, additional IT MTX is given at day 1 and day 8.

IV Cyclophosphamide 1000mg/m<sup>2</sup> on day 22  
Thioguanine p.o. 50mg/m<sup>2</sup> ON for 2 weeks from day 22-36  
IV or S/C cytarabine 75mg/m<sup>2</sup>/dose for 4 days block X 2 blocks  
IT MTX on start of every cytarabine block (total of 2 IT)

## **8. HR maintenance (12 weeks cycles till 2 years)**

IV vincristine 1.5 mg/m<sup>2</sup> every 4 wks  
Dexamethasone p.o. 10mg/m<sup>2</sup>/day for 7 days every 4 weeks  
Mercaptopurine p.o. 75mg/m<sup>2</sup>/day ON  
Methotrexate p.o. 20mg/m<sup>2</sup>/dose weekly ON  
IT MTX on week 1 of cycle

## **9. Cranial radiotherapy**

Cranial radiotherapy 18 Gy only for patients with CNS leukaemia (CNS-3 disease) and if age > 3 at time of scheduled C-RT

For T-ALL and WBC > 100,000/uL at presentation in the IR arm, C-RT 12 Gy is given during the interim maintenance phase between the second and third Protocol III blocks.

For all high risk patients (HR arm), C-RT 12 Gy is given during interim maintenance phase between the second and third Protocol II' blocks.

After C-RT, no IT in maintenance phase only.

C-RT is given in 1.5 Gy per fraction per day from Mon-Fridays.

Patients ≤ 3 years old at the time of the scheduled C-RT do not receive C-RT. They continue to receive IT every monthly during maintenance phase for year 1 and 2 monthly on year 2.

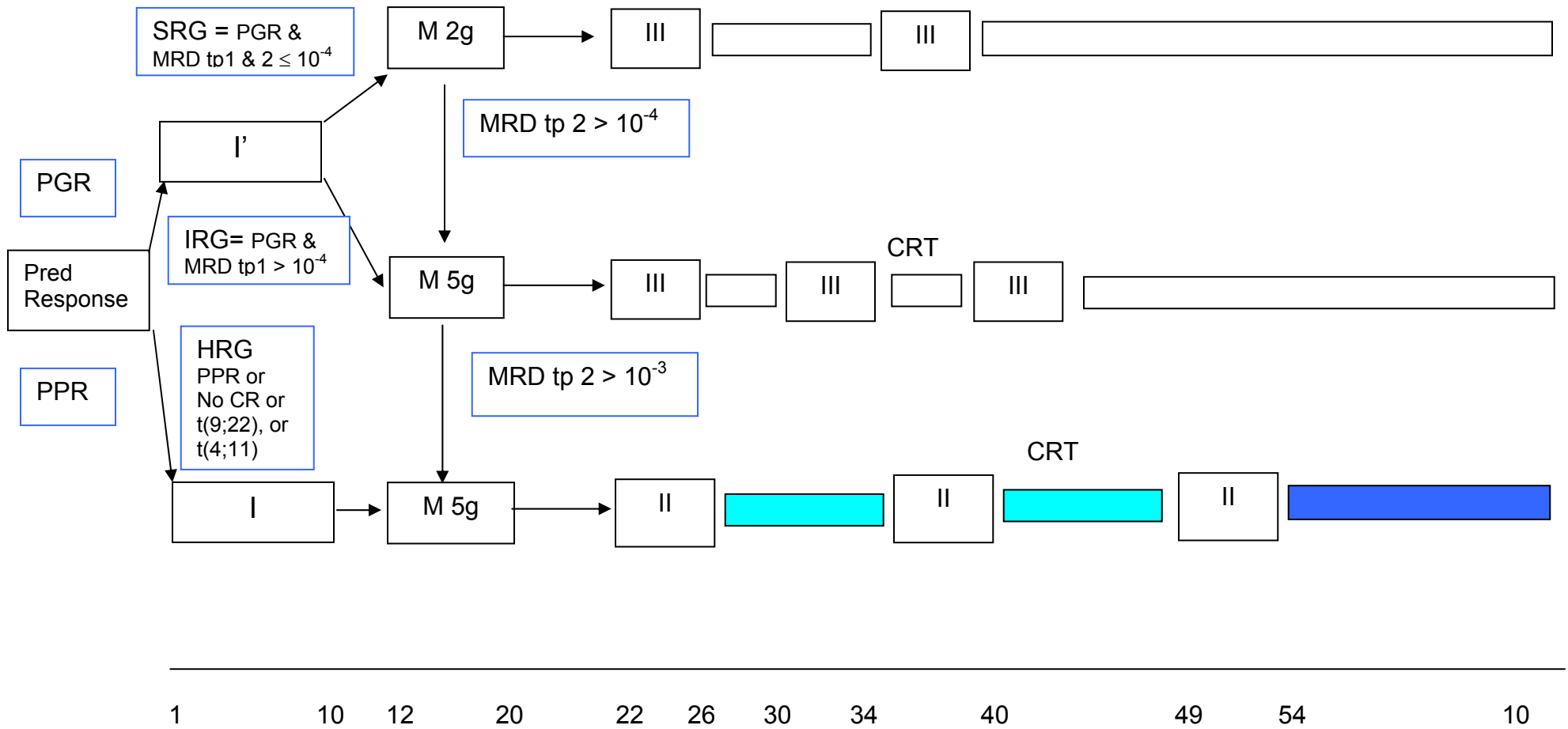
CNS-2 patients receive IT schedule like CNS-3 patients except without C-RT unless they satisfy other criteria for C-RT i.e., T-ALL and WBC > 100,000/uL or HR arm.

10. Downs syndrome patients.

Patients with Downs syndrome are treated on the Standard Risk arm only and the dose of HDMTX is limited to 1000mg/m<sup>2</sup>. They do not routinely receive cranial irradiation. For CNS-3 disease, if they do not clear the CSF blast after 2 doses of IT MTX, they qualify for cranial irradiation.

HR	la	lb	M	IlaX3	IlbX3	Interim M 8wk X 2	Maintenance = 4cycles X 12 wks	Total dose	
VCR	4	0	0	9	0	16	12	41	
Pred	420	0	0	0	0	0	0	420	
Dexa	168	0	0	630	0	0	840	1638	
L-asparaginase	60000	0	0	180000	0	240000	0	480000	
IT	3	2	4	6	0	8	4	27	Omit IT after CRT
Cyclophosphamide	0	2000	0	0	3000	0	0	5000	
MP	0	1400	1400	0	0	0	25200	28000	
TG	0	0	0	0	1680	0	0	1680	
MTX	0	0	20000	0	0	1600	960	22560	
DNR/DOX	100	0	0	270	0	0	0	370	
AraC	0	1200	0	0	1800	0	0	3000	

# Proposed MA-SPORE-ALL-2003 treatment overview



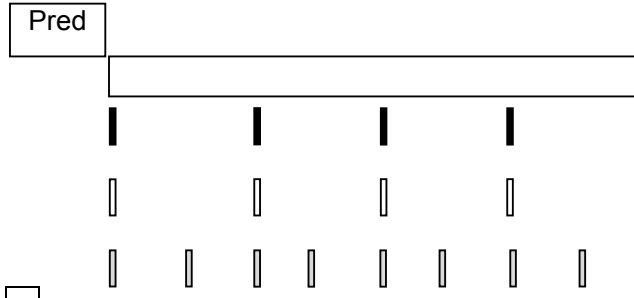
**Phase Ia**

BW= \_\_\_\_\_ kg Ht= \_\_\_\_\_ cm  
 SA= \_\_\_\_\_ m<sup>2</sup>

**MA-SPORE-ALL-2003  
 Protocol I- Pred PR/Prov HR**

Name: \_\_\_\_\_  
 HRN: \_\_\_\_\_  
 Weight: \_\_\_\_\_  
 Height: \_\_\_\_\_  
 SA: \_\_\_\_\_  
 Hospital: \_\_\_\_\_

**PRED** 60 mg/m<sup>2</sup>/day p.o.in tds x 1wk = [ ] [ ] [ ] . [ ] mg tds  
**Dexa** 6mg/m<sup>2</sup>/day p.o. in bd [ ] [ ] [ ] mg bd  
**VCR** 1.5 mg/m<sup>2</sup>/d i.v. = [ ] . [ ] mg  
**DNR** 25 mg/m<sup>2</sup>/d i.v. = [ ] [ ] . [ ] mg  
**ASP** 7500 u/m<sup>2</sup>/d IM = [ ] [ ] [ ] [ ] [ ] u



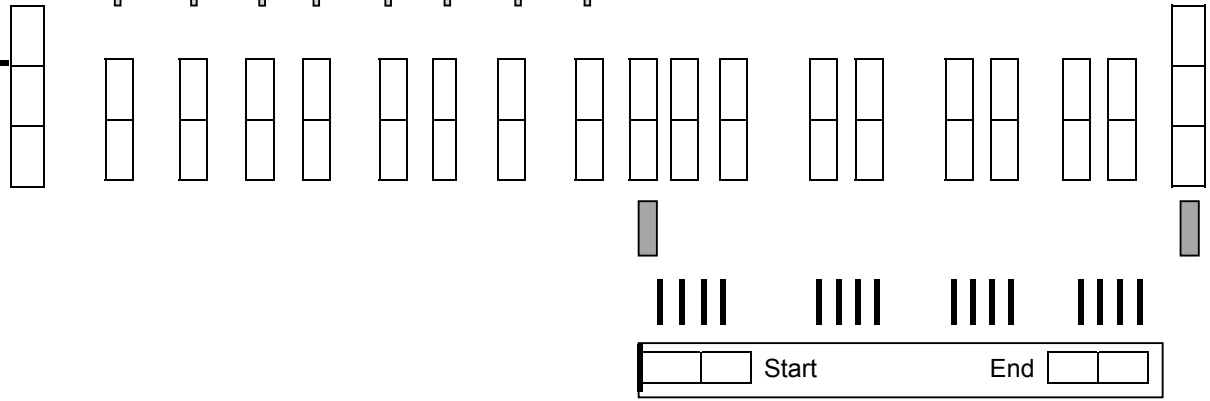
Or Erwinia 20,000U/dose eod X 4 wks if allergic to Ecoli L-Asp

**Phase Ib**

BW= \_\_\_\_\_ kg Ht= \_\_\_\_\_ cm  
 SA= \_\_\_\_\_ m<sup>2</sup>

Date

**CPM** 1 000 mg/m<sup>2</sup>/d(1h) (+ MESNA) = [ ] [ ] [ ] [ ] mg  
**Ara-C** 75 mg/m<sup>2</sup>/d i.v. = [ ] [ ] [ ] mg  
**6MP** 50 mg/m<sup>2</sup>/day p.o. = [ ] [ ] [ ] mg



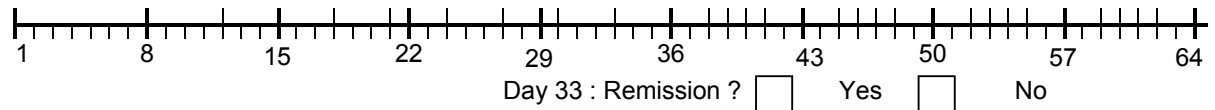
IT : < 1 yr 1-2 yr 2-3 yr > 3 yr

MTX 6 8 10 12 [ ] [ ] mg



BM Blast % Blast % Blast % Blast %  
 B.M. ○ ○ ○ ○

\*CNS leukaemia –  
 CNS 2 or CNS 3



**MA-SPORE-ALL-2003  
Protocol M 5g – IR/HR**

Name:  
HRN:  
Weight:  
Height:  
SA:  
Hospital:

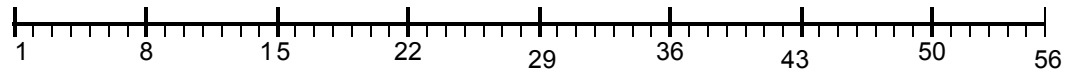
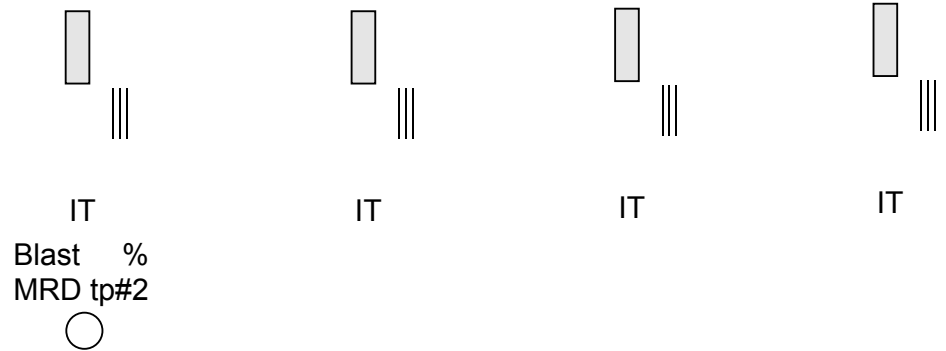
Date


6MP 25 mg/m<sup>2</sup>/d p.o. =  •  mg

HD-MTX 5 g/m<sup>2</sup> IV (24h) 10% in 0.5h =  •  g  
90% in 23.5h =  •  g

Folinic acid 15 mg/m<sup>2</sup>, 42, 48, 54 hour =  mg

IT: < 1 yr 1-2 yr 2-3 yr > 3 yr  
MTX 6 8 10 12  mg



MTX-level / Folinic acid Rescue  
MTX [μmol/l] / Folinic acid [mg]

	MTX 1 [μmol/l]	FA [mg]	MTX 1 [μmol/l]	FA [mg]	MTX 1 [μmol/l]	FA [mg]	MTX 1 [μmol/l]	FA [mg]
24h	—		—		—		—	
42h		—		—		—		—
48h	—	—	—	—	—	—	—	—
54 h		—		—		—		—

**MA-SPORE-ALL-2003  
Protocol II Number 1  
HR only**

Name: \_\_\_\_\_  
 HRN: \_\_\_\_\_  
 Weight: \_\_\_\_\_  
 Height: \_\_\_\_\_  
 SA: \_\_\_\_\_  
 Hospital: \_\_\_\_\_

**Phase IIa**

BW= \_\_\_\_\_ kg    Ht= \_\_\_\_\_ cm  
 SA= \_\_\_\_\_ m<sup>2</sup>

**DEXA** 10 mg/m<sup>2</sup>/d po in bd = [ ] [ ] [ ] . [ ] mg bd

**VCR** 1.5 mg/m<sup>2</sup>/d i.v. = [ ] . [ ] mg

**ADR** 30 mg/m<sup>2</sup>/d iv(6h) = [ ] [ ] . [ ] mg

**ASP** 10 000 u/m<sup>2</sup>/d IM every 3 days = [ ] [ ] [ ] [ ] [ ] u

If allergic, replace with Erwinia 20,000U/m<sup>2</sup> eod X 3 wks

**Phase IIb**

BW= \_\_\_\_\_ kg    Ht= \_\_\_\_\_ cm  
 SA= \_\_\_\_\_ m<sup>2</sup>

**CPM** 1 000 mg/m<sup>2</sup>/d IV (1h) (+ MESNA) = [ ] [ ] [ ] [ ] mg

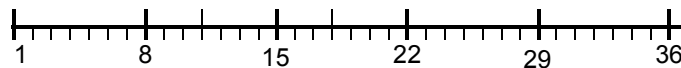
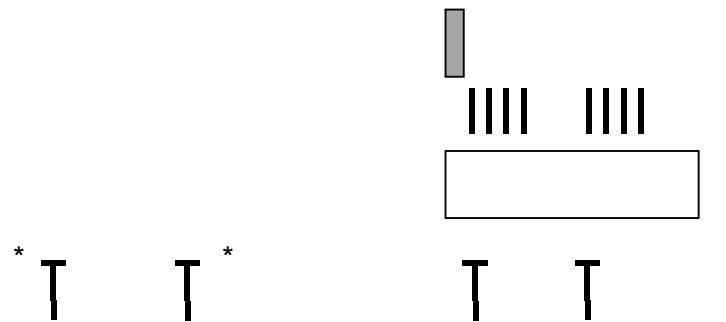
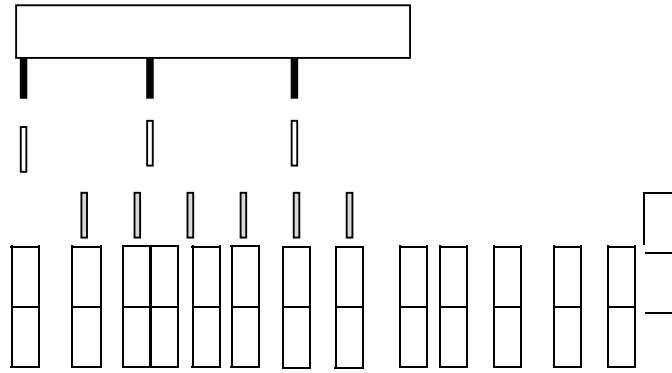
**Ara-C** 75 mg/m<sup>2</sup>/d i.v. = [ ] [ ] [ ] [ ] mg

**TG** 50 mg/m<sup>2</sup>/d p.o. = [ ] [ ] [ ] [ ] mg

**IT :** < 1 yr   1-2 yr   2-3 yr   > 3 yr

**MTX**    6        8        10       12    [ ] [ ] [ ] mg  
                  |        |        |        |        |

\*CNS leukaemia –  
 CNS 2 or CNS 3

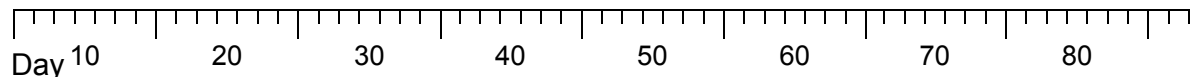


Name:  
 HRN:  
 Weight:  
 Height:  
 SA:  
 Hospital:

### Interim Maintenance HR #1

Vincristine 1.5mg/m<sup>2</sup>/dose (max 2mg) every 10 days for 8 cycles = mg  
 IV Methotrexate 100mg/m<sup>2</sup>/dose once every 10 days for 8 cycles = mg  
 24 hours after IV MTX, give IM L-asparaginase 15,000U/m<sup>2</sup>/dose  
 every 10 days for 8 cycles = U  
 (If allergic to E coli L-asp, switch to Erwinia 30,000U/m<sup>2</sup>/dose, twice a week)  
 IT MTX at every 20 days starting from day 20 X 4 doses = mg

	IT		IT		IT		IT
V	V	V	V	V	V	V	V
M	M	M	M	M	M	M	M
L	L	L	L	L	L	L	L



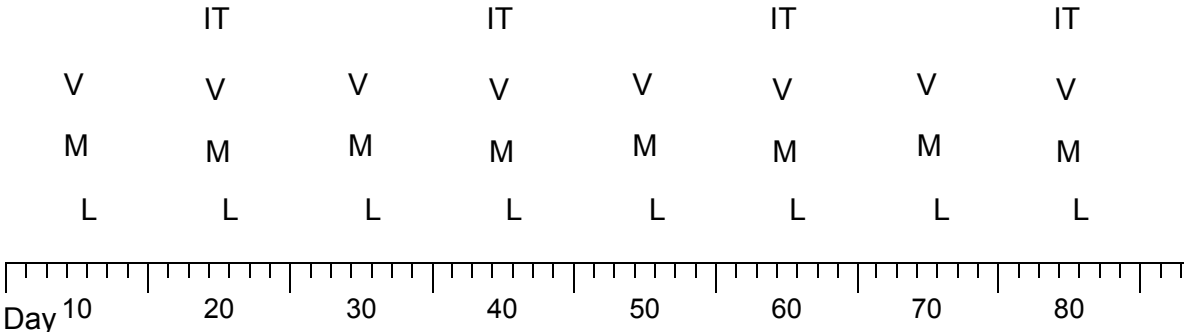
Date								
Week								
VCR/mg								
MTX/mg								
L-asp/U								
WBC								
ANC								
Hb								
Plt								



Name:  
 HRN:  
 Weight:  
 Height:  
 SA:  
 Hospital:

**Interim Maintenance HR #2**

Vincristine 1.5mg/m<sup>2</sup>/dose (max 2mg) every 10 days for 8 cycles = mg  
 IV Methotrexate 100mg/m<sup>2</sup>/dose once every 10 days for 8 cycles = mg  
 24 hours after IV MTX, give IM L-asparaginase 15,000U/m<sup>2</sup>/dose  
 every 10 days for 8 cycles = U  
 (If allergic to E coli L-asp, switch to Erwinia 30,000U/m<sup>2</sup>/dose, twice a week)  
 IT MTX at every 20 days starting from day 20 X 4 doses = mg



Date								
Week								
VCR/mg								
MTX/mg								
L-asp/U								
WBC								
ANC								
Hb								
Plt								



Name:  
 HRN:  
 Weight:  
 Height:  
 SA:  
 Hospital:

MA-SPORE ALL 2003 HR maintenance phase #1

Vincristine 1.5mg/m<sup>2</sup>/dose (max 2mg) every 4 weeks = mg  
 Dexamethasone 10mg/m<sup>2</sup>/day X 7 days every 4 weeks = mg tds  
 Methotrexate 20mg/m<sup>2</sup>/dose ON once a week = mg  
 Mercaptopurine 75mg/m<sup>2</sup>/dose ON = mg  
 IT MTX at week 1 (omit if Cranial RT given ) = mg

V

V

V

Dexa

Dexa

Dexa

IT

M

M

M

M

M

M

M

M

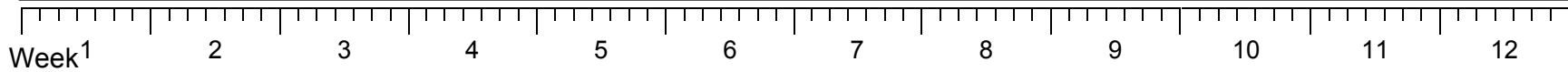
M

M

M

M

MP p.o. 75 mg/m<sup>2</sup>/d ON



Date												
Week												
6MP/mg												
MTX/mg												
WBC												
ANC												
Hb												
Pit												

MA-SPORE ALL 2003 HR maintenance phase # 2

Name:  
 HRN:  
 Weight:  
 Height:  
 SA:  
 Hospital:

Vincristine 1.5mg/m<sup>2</sup>/dose (max 2mg) every 4 weeks = mg  
 Dexamethasone 10mg/m<sup>2</sup>/day X 7 days every 4 weeks = mg tds  
 Methotrexate 20mg/m<sup>2</sup>/dose ON once a week = mg  
 Mercaptopurine 75mg/m<sup>2</sup>/dose ON = mg  
 IT MTX at week 1 (omit if Cranial RT given ) = mg

V

Dexa

IT

M

M

M

M

V

Dexa

M

M

M

M

V

Dexa

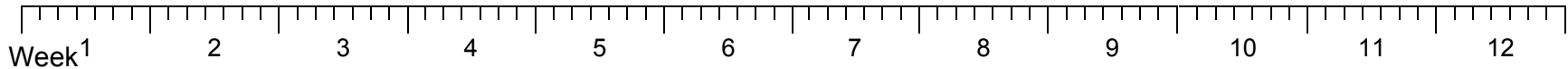
M

M

M

M

**MP p.o. 75 mg/m<sup>2</sup>/d ON**

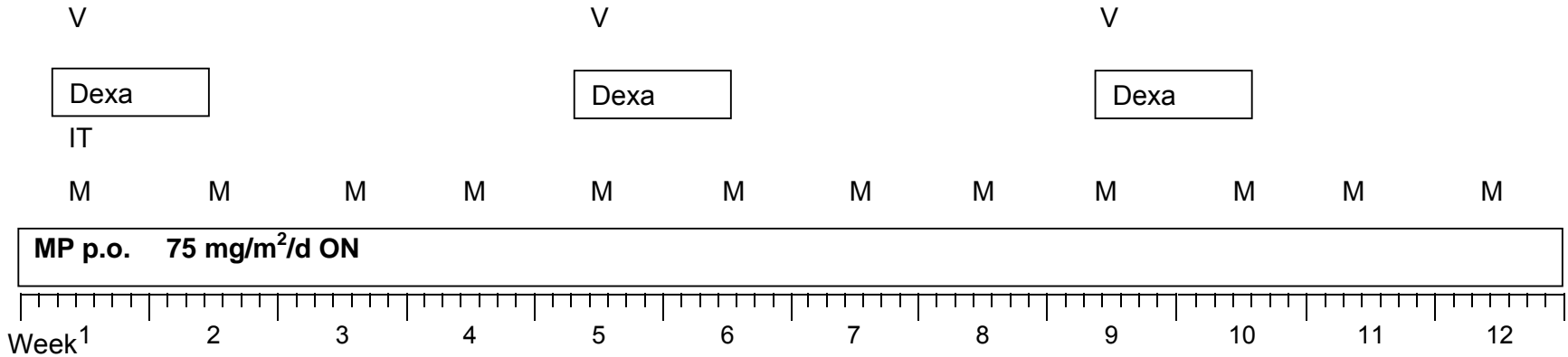


Date												
Week												
6MP/mg												
MTX/mg												
WBC												
ANC												
Hb												
Plt												

MA-SPORE ALL 2003 HR maintenance phase #3

Name:  
 HRN:  
 Weight:  
 Height:  
 SA:  
 Hospital:

Vincristine 1.5mg/m<sup>2</sup>/dose (max 2mg) every 4 weeks = mg  
 Dexamethasone 10mg/m<sup>2</sup>/day X 7 days every 4 weeks = mg tds  
 Methotrexate 20mg/m<sup>2</sup>/dose ON once a week = mg  
 Mercaptopurine 75mg/m<sup>2</sup>/dose ON = mg  
 IT MTX at week 1 (omit if Cranial RT given ) = mg



Date												
Week												
6MP/mg												
MTX/mg												
WBC												
ANC												
Hb												
Plt												

MA-SPORE ALL 2003 HR maintenance phase #4

Name:  
 HRN:  
 Weight:  
 Height:  
 SA:  
 Hospital:

Vincristine 1.5mg/m<sup>2</sup>/dose (max 2mg) every 4 weeks = mg  
 Dexamethasone 10mg/m<sup>2</sup>/day X 7 days every 4 weeks = mg tds  
 Methotrexate 20mg/m<sup>2</sup>/dose ON once a week = mg  
 Mercaptopurine 75mg/m<sup>2</sup>/dose ON = mg  
 IT MTX at week 1 (omit if Cranial RT given ) = mg

V

Dexa

IT

M

M

M

M

V

Dexa

M

M

M

M

V

Dexa

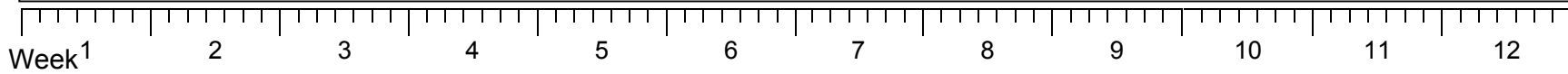
M

M

M

M

**MP p.o. 75 mg/m<sup>2</sup>/d ON**

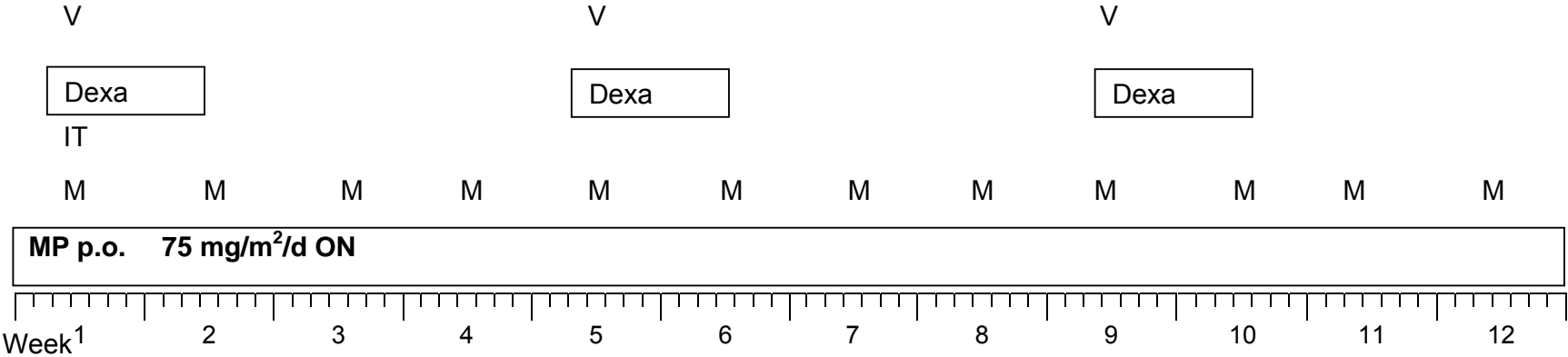


Date													
Week													
6MP/mg													
MTX/mg													
WBC													
ANC													
Hb													
Plt													

MA-SPORE ALL 2003 Maintenance Phase HR #5

Name:  
 HRN:  
 Weight:  
 Height:  
 SA:  
 Hospital:

Vincristine 1.5mg/m<sup>2</sup>/dose (max 2mg) every 4 weeks = mg  
 Dexamethasone 10mg/m<sup>2</sup>/day X 7 days every 4 weeks = mg tds  
 Methotrexate 20mg/m<sup>2</sup>/dose ON once a week = mg  
 Mercaptopurine 75mg/m<sup>2</sup>/dose ON = mg  
 IT MTX at week 1 (omit if Cranial RT given ) = mg



Date												
Week												
6MP/mg												
MTX/mg												
WBC												
ANC												
Hb												
Plt												

Name:  
 HRN:  
 Weight:  
 Height:  
 SA:  
 Hospital:

**MA-SPORE- ALL-2003 Maintenance Phase – HR #6**

Vincristine 1.5mg/m<sup>2</sup>/dose (max 2mg) every 4 weeks = mg  
 Dexamethasone 10mg/m<sup>2</sup>/day X 7 days every 4 weeks = mg tds  
 Methotrexate 20mg/m<sup>2</sup>/dose ON once a week = mg  
 Mercaptopurine 75mg/m<sup>2</sup>/dose ON = mg  
 IT MTX at week 1 (omit if Cranial RT given ) = mg

V

V

V

Dexa

Dexa

Dexa

IT

M

M

M

M

M

M

M

M

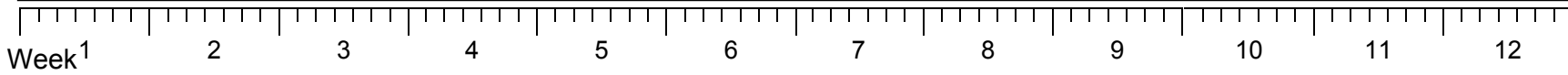
M

M

M

M

**MP p.o. 75 mg/m<sup>2</sup>/d ON**



Date												
Week												
6MP/mg												
MTX/mg												
WBC												
ANC												
Hb												
Plt												