

## **Proposed MA-SPORE-ALL-2003 Study – SR arm only**

### 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 on day 1

##### **I'a (for SR and IR group)**

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

IM L-asparaginase 7,500 U/m<sup>2</sup>/dose 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)

##### **Ib (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 2g (8 weeks)**

##### **Protocol M 2g for SR group**

IV HDMTX 2000mg/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 III Number 1 (4 weeks) – SR and IR**

Dexamethasone p.o. 10mg/m<sup>2</sup>/day in 2 divided doses for 14 days, no tailing of dexamethasone

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

IV doxorubicin 30 mg/m<sup>2</sup>/dose every week on days 1, 8

IM L-Asparaginase 10,000U/m<sup>2</sup>/day every 3 days from day 3 for 4 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 2 weeks

For CNS-2/3, additional IT MTX is given at day 1 of Protocol III.

IV cyclophosphamide 500mg/m<sup>2</sup> on day 15

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

Thioguanine 40mg/m<sup>2</sup>/day ON for 2 weeks from day 15-28

IT MTX on start of every cytarabine block (total of 2 IT)

#### **4. Interim maintenance SR for 10 weeks**

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

Methotrexate 20mg/m<sup>2</sup> weekly ON

Dexamethasone 6mg/m<sup>2</sup>/day in 2 divided doses for 7 days at week 5

IV Vincristine 1.5mg/m<sup>2</sup>/dose on week 5 and 6

IT MTX at week 5 and 6

#### **5. Protocol III Number 2 (4 weeks) – SR and IR**

Dexamethasone p.o. 10mg/m<sup>2</sup>/day in 2 divided doses for 14 days, no tailing of dexamethasone

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

IV doxorubicin 30 mg/m<sup>2</sup>/dose every week on days 1, 8

IM L-Asparaginase 10,000U/m<sup>2</sup>/day every 3 days from day 3 for 4 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 2 weeks

For CNS-2/3, additional IT MTX is given at day 1 of Protocol III.

IV cyclophosphamide 500mg/m<sup>2</sup> on day 15

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

Thioguanine 40mg/m<sup>2</sup>/day ON for 2 weeks from day 15-28

IT MTX on start of every cytarabine block (total of 2 IT)

#### **6. SR and IR maintenance (12 weeks cycles till 2 years from start of therapy)**

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

Methotrexate 20mg/m<sup>2</sup>/dose weekly ON

IV vincristine 1.5 mg/m<sup>2</sup>/dose at week 11 and 12

Dexamethasone 6mg/m<sup>2</sup>/day in 2 divided doses for 7 days at week 11

IT MTX at week 11

#### **7. 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.

#### **Post C-RT, no IT is given.**

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

Patients  $\leq 3$  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.

### 8. Down's syndrome patients.

Patients with Down's 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.

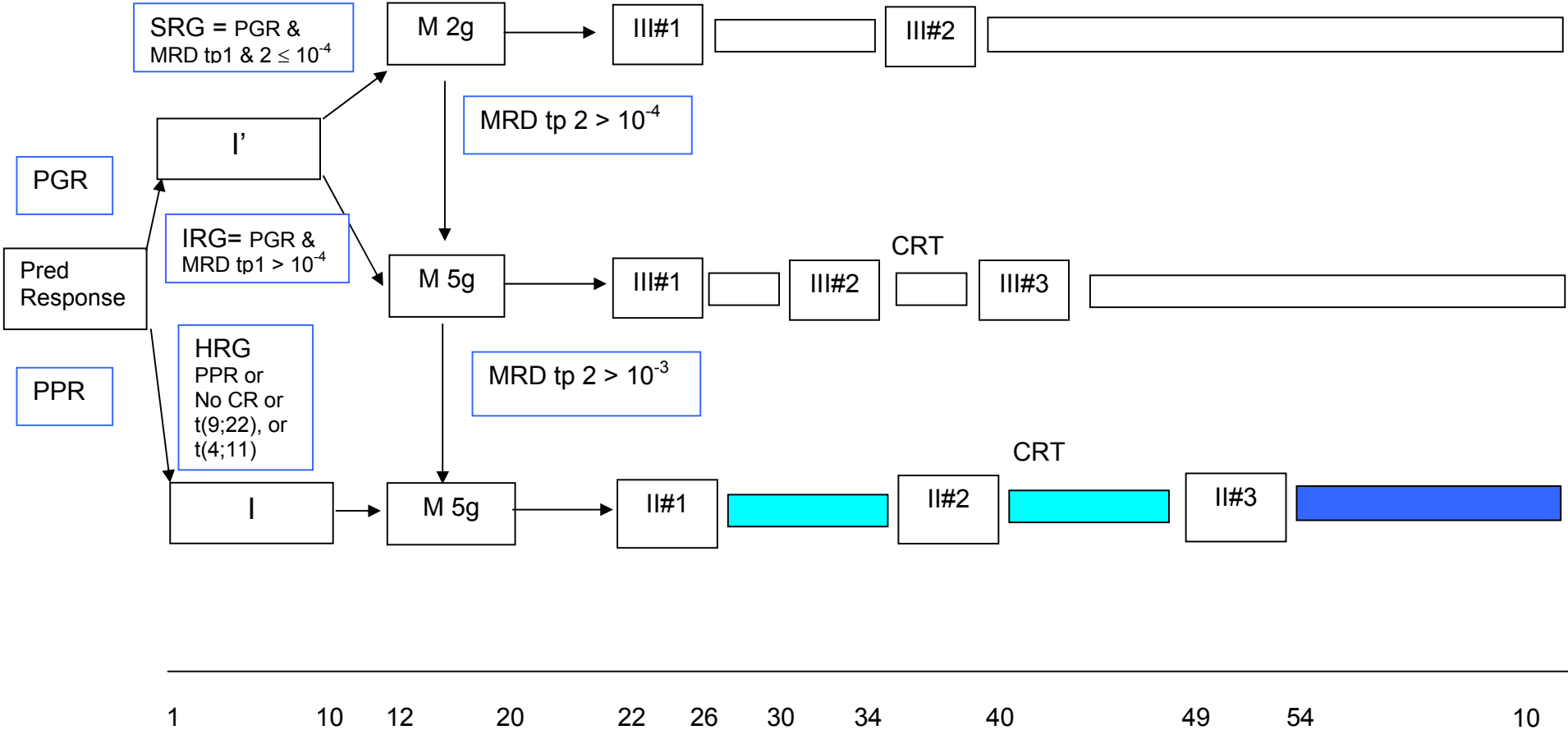
Summary of approximate drug usage in MA-SPORE ALL 2003 SR arm

#### SG-ALL protocol cumulative doses

Dose calculated for 1 m2

SR	Ia	Ib	M	IIIaX2	IIIb X2	Interim M - 10 wk	Maintenance = 5 cycles X 12 wks	Total dose
VCR	4	0	0	4	0	2	10	20
Pred	420	0	0	0	0	0	0	420
Dexa	168	0	0	280	0	0	210	658
L-asp	60000	0	0	80000	0	0	0	140000
IT	3	2	4	0	4	2	5	20
Cycloph	0	2000	0	0	1000	0	0	3000
MP	0	1400	1400	0	0	3500	21000	27300
TG	0	0	0	0	1120	0	0	1120
MTX	0	0	8000	0	0	200	1200	9400
DNR/DOX	0	0	0	120	0	0	0	120
AraC	0	1200	0	0	1200	0	0	2400

### Proposed MA-SPORE-ALL-2002 treatment overview



# MA-SPORE-ALL-2002

## Protocol I'- Pred GR/Prov SR or IR

### Phase I'a

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

**Pred** 60mg/m<sup>2</sup>/dy p.o. in tds = [ ][ ][ ] . [ ] mg tds

**Dexa** 6 mg/m<sup>2</sup>/dy p.o. in bd = [ ][ ][ ] mg bd

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

**ASP** 7,500 u/m<sup>2</sup>/d IM = [ ][ ][ ][ ][ ] u

Or Erwinia 10,000U/dose eod X 4 wks if allergic to Ecoli L-Asp

### Phase Ib

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

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

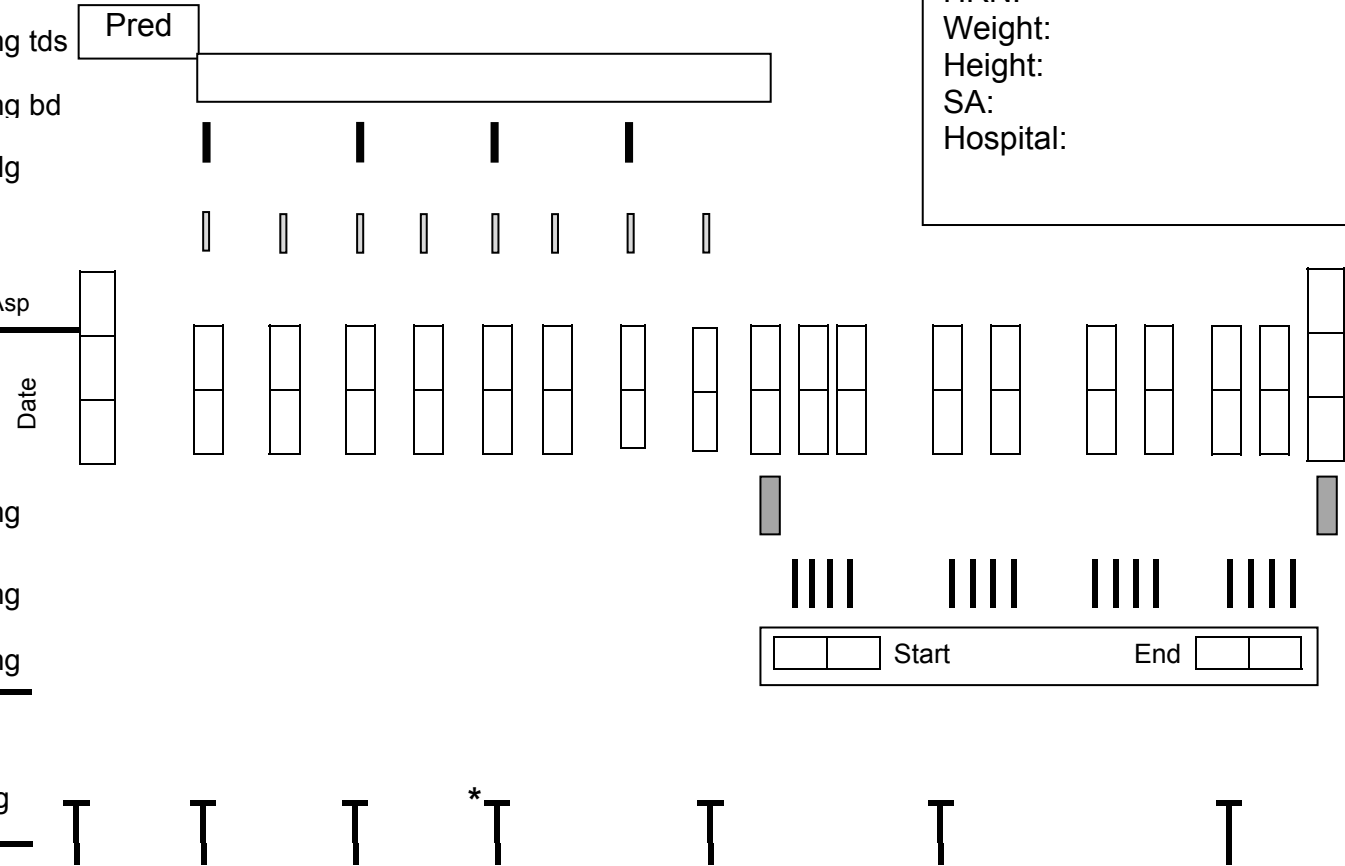
**Ara-C** 75 mg/m<sup>2</sup>/d s/c = [ ][ ][ ] mg

**6MP** 50 mg/m<sup>2</sup>/dy p.o. = [ ][ ][ ] mg

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

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

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



\*CNS leukaemia – CNS 2 and CNS-3

BM Blast % Blast % Blast % Blast %, MRD tp 1

B.M. ○ ○ ○ ○

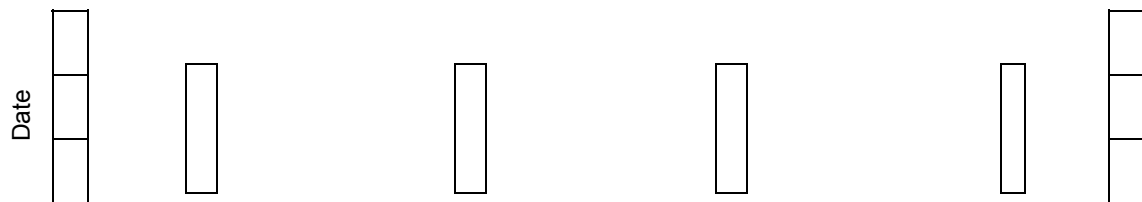


Day 33 : Remission ?  Yes  No

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**MA-SPORE-ALL-2002  
Protocol M 2g - SR**

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



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



HD-MTX 2 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

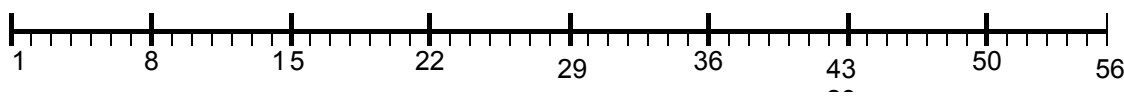


IT : < 1 yr 1-2 yr 2-3 yr > 3 yr

MTX 6 8 10 12   mg

IT IT IT IT

MRD tp2 B.M. ○



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		—		—		—		—

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## MA-SPORE-ALL 2003 Protocol III Number 1 SR/IR

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

### Phase IIIa

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

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

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

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

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

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

### Phase IIIb

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

**CPM** 500 mg/m<sup>2</sup>/d IV (1h) (+ MESNA) = [ ] [ ] [ ] [ ] mg

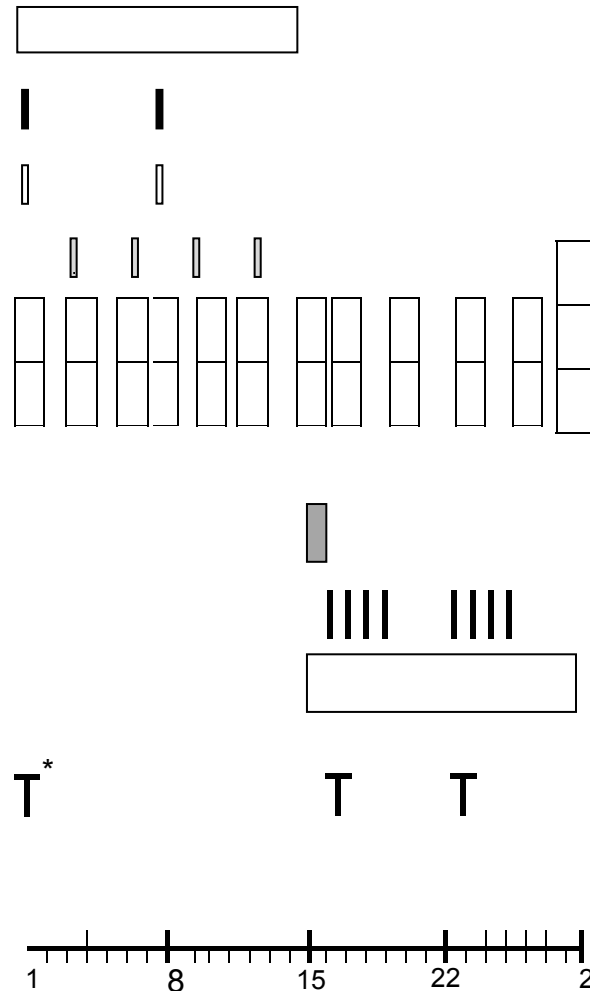
**Ara-C** 75 mg/m<sup>2</sup>/d i.v. = [ ] [ ] [ ] [ ] mg

**TG** 40 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:

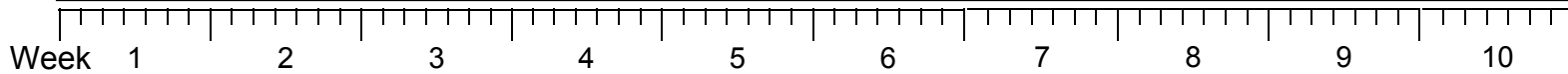
**MA-SPORE- ALL-2002 study  
 Interim Maintenance Phase – SR**

V                      V  
 Dexta  
 IT                      IT

Vincristine 1.5mg/m<sup>2</sup>/dose (max 2mg) at week 5 and 6 = mg  
 Dexamethasone 6mg/m<sup>2</sup>/dose X 7 days at week 5 = mg bd  
 Methotrexate 20mg/m<sup>2</sup>/dose ON once a week = mg  
 Mercaptopurine 50mg/m<sup>2</sup>/dose ON = mg  
 IT MTX at week 5 and 6 = mg  
 Cotrimoxazole 2mg Trimethoprim/kg/dose BD on Mon, Tues = mg bd

M                      M                      M                      M                      M                      M                      M                      M                      M                      M                      M

**MP p.o.** 50 mg/m<sup>2</sup>/d



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

## MA-SPORE-ALL 2003 Protocol III Number 2 SR/IR

### Phase IIIa

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

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

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

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

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

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

### Phase IIIb

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

**CPM** 500 mg/m<sup>2</sup>/d IV = [ ][ ][ ][ ] mg  
(1h) (+ MESNA)

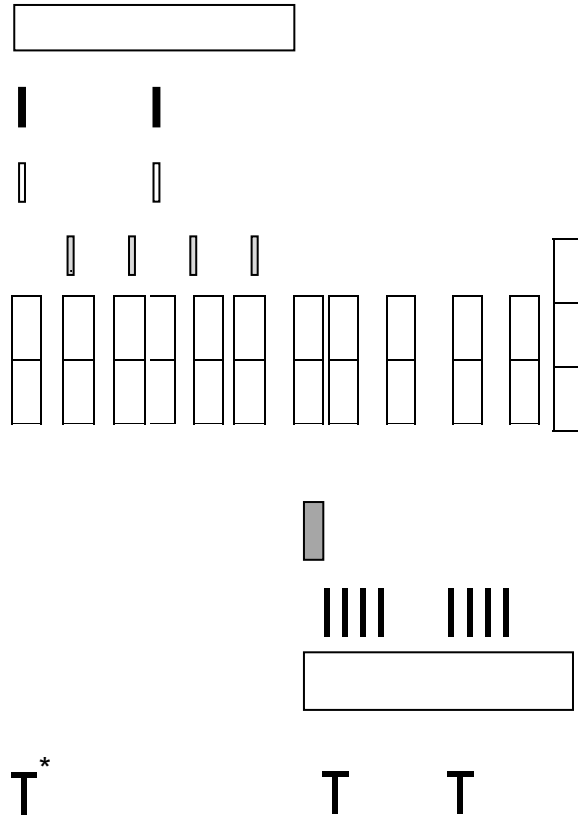
**Ara-C** 75 mg/m<sup>2</sup>/d i.v. = [ ][ ][ ] mg

**TG** 40 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

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



\*CNS leukaemia –  
CNS 2 or CNS 3

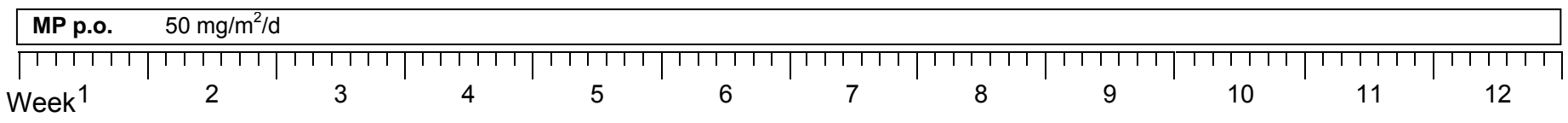


**MA-SPORE ALL 2003  
Maintenance Phase # 2**

Vincristine 1.5mg/m <sup>2</sup> /dose (max 2mg) at week 11 and 12	=	mg
Dexamethasone 6mg/m <sup>2</sup> /dose X 7 days at week 11	=	mg bd
Methotrexate 20mg/m <sup>2</sup> /dose ON once a week	=	mg
Mercaptopurine 50mg/m <sup>2</sup> /dose ON	=	mg
IT MTX at week 11	=	mg
Cotrimoxazole 2mg Trimethoprim/kg/dose BD on Mon, Tues	=	mg bd

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

V                  V  
Dexa  
IT  
M                  M



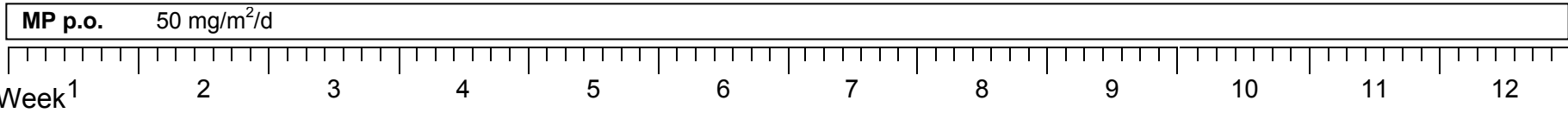
Date												
Week												
6MP/mg												
MTX/mg												
WBC												
ANC												
Hb												
Plt												

**MA-SPORE ALL 2003  
Maintenance Phase # 3**

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

Vincristine 1.5mg/m <sup>2</sup> /dose (max 2mg) at week 11 and 12	=	mg
Dexamethasone 6mg/m <sup>2</sup> /dose X 7 days at week 11	=	mg bd
Methotrexate 20mg/m <sup>2</sup> /dose ON once a week	=	mg
Mercaptopurine 50mg/m <sup>2</sup> /dose ON	=	mg
IT MTX at week 11	=	mg
Cotrimoxazole 2mg Trimethoprim/kg/dose BD on Mon, Tues	=	mg bd

V                      V  
Dexa  
 IT  
 M                      M



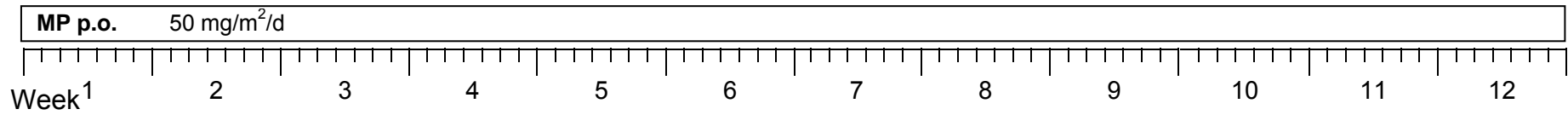
Date												
Week												
6MP/mg												
MTX/mg												
WBC												
ANC												
Hb												
Plt												

**MA-SPORE ALL 2003  
Maintenance Phase # 4**

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

Vincristine 1.5mg/m<sup>2</sup>/dose (max 2mg) at week 11 and 12 = mg  
 Dexamethasone 6mg/m<sup>2</sup>/dose X 7 days at week 11 = mg bd  
 Methotrexate 20mg/m<sup>2</sup>/dose ON once a week = mg  
 Mercaptopurine 50mg/m<sup>2</sup>/dose ON = mg  
 IT MTX at week 11 = mg  
 Cotrimoxazole 2mg Trimethoprim/kg/dose BD on Mon, Tues = mg bd

V V  
 Dexta  
 IT  
 M M



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

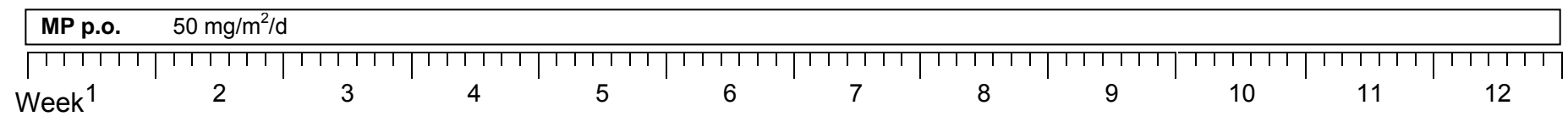


**MA-SPORE ALL 2003  
Maintenance Phase # 6**

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

Vincristine 1.5mg/m <sup>2</sup> /dose (max 2mg) at week 11 and 12	=	mg
Dexamethasone 6mg/m <sup>2</sup> /dose X 7 days at week 11	=	mg bd
Methotrexate 20mg/m <sup>2</sup> /dose ON once a week	=	mg
Mercaptopurine 50mg/m <sup>2</sup> /dose ON	=	mg
IT MTX at week 11	=	mg
Cotrimoxazole 2mg Trimethoprim/kg/dose BD on Mon, Tues	=	mg bd

V                      V  
 Dexta  
 IT  
 M                      M



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