

MA-SPORE ALL 2003 Enrolment Form. Provisional IR risk.

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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: _____ m²

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 10⁹/L
 Hb : _____ g/dl
 Plt : _____ 10⁹/L
 Polys : _____% Lymph : _____%
 Monos : _____% Eosin : _____%
 Blast : _____% ABC: _____ 10⁹/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 / TREPINE

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 – IR arm only

Treatment overview

1. Induction (Protocol I) – 10 weeks

Prednisolone 60 mg/m²/day p.o. in 3 divided doses from day 1 -7
IT MTX on day 1

I'a- for IR group

Dexamethasone 6mg/m²/day in 2 divided doses from day 8 to 36 (total 28 days), no tailing of dexamethasone.

IV Vincristine 1.5mg/m²/dose weekly for week 2,3,4,5

IM L-asparaginase 7,500 U/m²/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/m²/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/m² day 36 and 64

Mercaptopurine p.o. 50mg/m²/day ON

IV or S/C cytarabine 75mg/m² for 4 days block X 4 blocks

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

2. Protocol M 5g for IR group

IV HDMTX 5000mg/m² every 2 weeks with folinic rescue X 4 courses

IV folinic acid 15mg/m²/dose at 42, 48, 54 hours from start of IV MTX

Mercaptopurine p.o. 25mg/m²/day ON

IT MTX with each HDMTX given on day 1

3. Protocol III Number 1 (4 weeks) –IR

Dexamethasone p.o. 10mg/m²/day in 2 divided doses for 14 days, no tailing of dexamethasone

IV Vincristine 1.5 mg/m²/dose week on days 1, 8

IV doxorubicin 30 mg/m²/dose every week on days 1, 8

IM L-Asparaginase 10,000U/m²/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/m²/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/m² on day 15

IV or S/C cytarabine 75 mg/m²/dose for 4 days blocks X 2 blocks

Thioguanine 40mg/m²/day ON for 2 weeks from day 15-28

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

4. Interim maintenance IR Number 1 (4 weeks)

Mercaptopurine p.o. 50 mg/m²/day ON

Methotrexate 20mg/m² weekly ON

Dexamethasone 6mg/m²/day in 2 divided doses for 7 days at week 3

IV Vincristine 1.5mg/m²/dose on week 3

IT MTX at week 3

5. Protocol III Number 2 (4 weeks) –IR

Dexamethasone p.o. 10mg/m²/day in 2 divided doses for 14 days, no tailing of dexamethasone

IV Vincristine 1.5 mg/m²/dose week on days 1, 8

IV doxorubicin 30 mg/m²/dose every week on days 1, 8

IM L-Asparaginase 10,000U/m²/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/m²/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/m² on day 15

IV or S/C cytarabine 75 mg/m²/dose for 4 days blocks X 2 blocks

Thioguanine 40mg/m²/day ON for 2 weeks from day 15-28

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

6. Interim maintenance IR Number 2 (4 weeks)

Mercaptopurine p.o. 50 mg/m²/day ON

Methotrexate 20mg/m² weekly ON

Dexamethasone 6mg/m²/day in 2 divided doses for 7 days at week 3

IV Vincristine 1.5mg/m²/dose on week 3

IT MTX at week 3

7. Protocol III Number 3 (4 weeks) –IR

Dexamethasone p.o. 10mg/m²/day in 2 divided doses for 14 days, no tailing of dexamethasone

IV Vincristine 1.5 mg/m²/dose week on days 1, 8

IV doxorubicin 30 mg/m²/dose every week on days 1, 8

IM L-Asparaginase 10,000U/m²/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/m²/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/m² on day 15

IV or S/C cytarabine 75 mg/m²/dose for 4 days blocks X 2 blocks

Thioguanine 40mg/m²/day ON for 2 weeks from day 15-28

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

8. IR maintenance (12 weeks cycles till 2 years from start of therapy)

Mercaptopurine p.o. 50mg/m²/day ON

Methotrexate 20mg/m²/dose weekly ON

IV vincristine 1.5 mg/m²/dose at week 11 and 12

Dexamethasone 6mg/m²/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 ≤ 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.

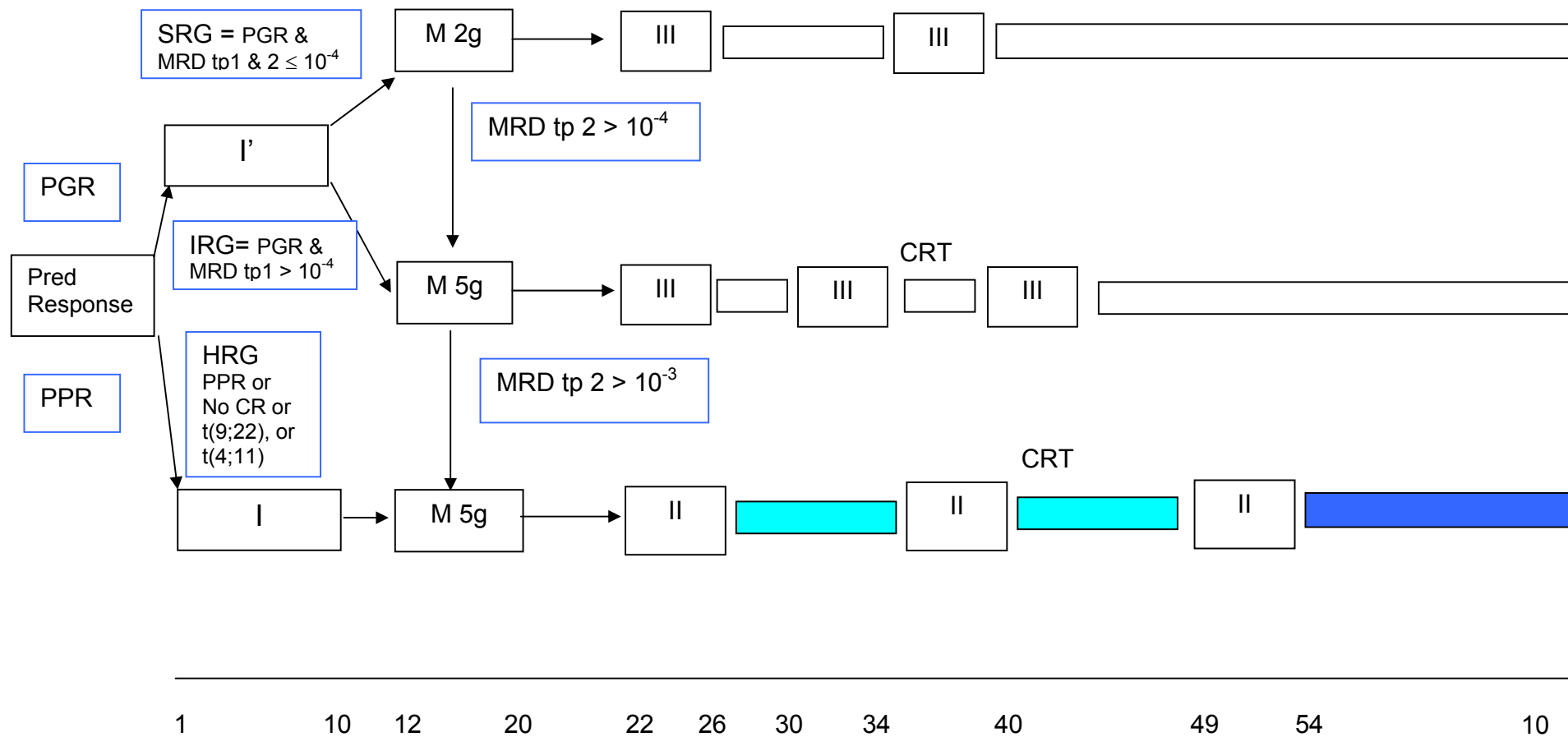
8. Downs syndrome patients.

Patients with Downs syndrome are treated on the *Standard Risk arm only* and the dose of HDMTX is limited to 1000mg/m². 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 IR arm

| IR | la | lb | M | IIIaX3 | IIIbX3 | Interim M 4wk X 2 | Maintenance = 5 cycles X 12 wks | Total dose | |
|------------------|-------|------|-------|--------|--------|----------------------|---------------------------------------|------------|----------------------|
| VCR | 4 | 0 | 0 | 6 | 0 | 2 | 10 | 22 | |
| Pred | 420 | 0 | 0 | 0 | 0 | 0 | 0 | 420 | |
| Dexa | 168 | 0 | 0 | 420 | 0 | 84 | 210 | 882 | |
| L-asparaginase | 60000 | 0 | 0 | 120000 | 0 | 0 | 0 | 180000 | |
| IT | 3 | 2 | 4 | 0 | 6 | 2 | 5 | 22 | Omit after CRT |
| Cyclophosphamide | 0 | 2000 | 0 | 0 | 1500 | 0 | 0 | 3500 | |
| MP | 0 | 1400 | 1400 | 0 | 0 | 2800 | 21000 | 26600 | |
| TG | 0 | 0 | 0 | 0 | 1680 | 0 | 0 | 1680 | |
| MTX | 0 | 0 | 20000 | 0 | 0 | 160 | 1200 | 21360 | |
| DNR/DOX | 0 | 0 | 0 | 180 | 0 | 0 | 0 | 180 | |
| AraC | 0 | 1200 | 0 | 0 | 1800 | 0 | 0 | 3000 | |

Proposed MA-SPORE-ALL-2002 treatment overview



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

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

Date

| | | | | | |
|--|--|--|--|--|--|
| | | | | | |
| | | | | | |
| | | | | | |

6MP 25 mg/m²/d p.o. = • mg

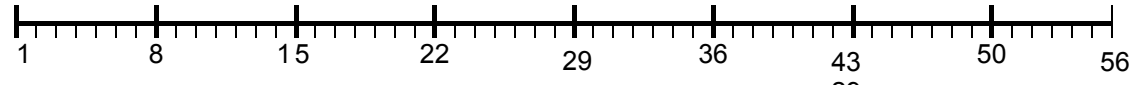
HD-MTX 5 g/m² IV (24h) 10% in 0.5h = • g
90% in 23.5h = • g

Folinic acid 15 mg/m², 42, 48, 54 hour = mg

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



IT
Blast %
MRD tp#2
○



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 III Number 1 SR/IR

Phase IIIa

| | |
|--------------------------|--------------|
| BW= _____ kg | Ht= _____ cm |
| SA= _____ m ² | |

DEXA 10 mg/m²/d po = [][][] . [] mg bd

VCR 1.5 mg/m²/d iv = [] . [] mg

ADR 30 mg/m²/d iv(6h) = [][] . [] mg

ASP 10 000 u/m²/d IM = [][][][][] u

If allergic, replace with Erwinia 20,000U/m² eod X 2 wks

Phase IIIb

| | |
|--------------------------|--------------|
| BW= _____ kg | Ht= _____ cm |
| SA= _____ m ² | |

CPM 500 mg/m²/d IV (1h) (+ MESNA) = [][][][] mg

Ara-C 75 mg/m²/d i.v. = [][][] mg

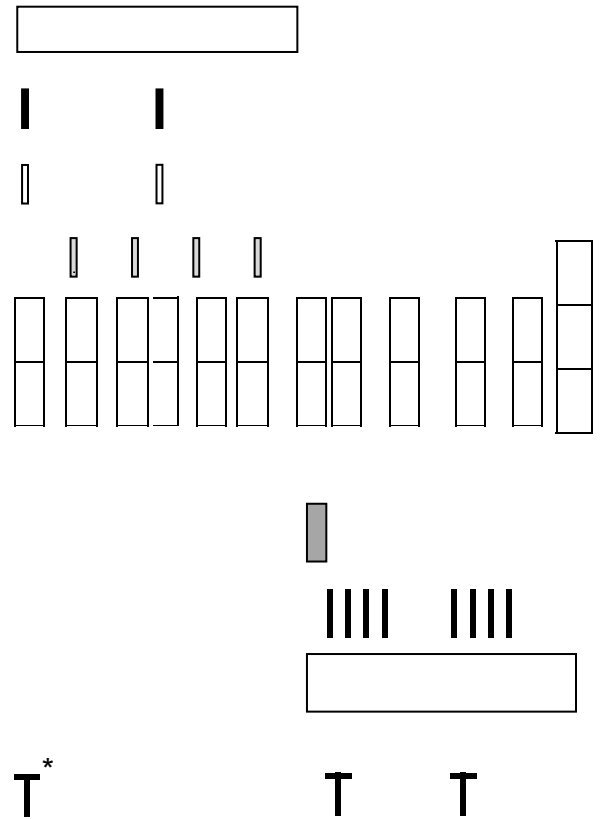
TG 40 mg/m²/d p.o. = [][][] mg

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: _____



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

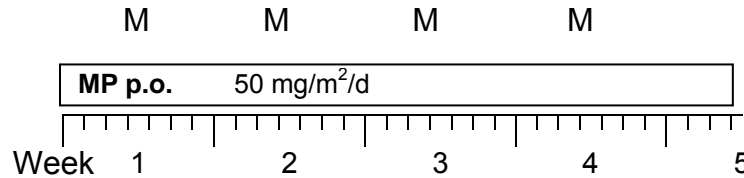
**MA-SPORE- ALL-2002 study
 Interim Maintenance Phase Number 1 – IR**

V

Dexa

IT

Vincristine 1.5mg/m²/dose (max 2mg) at week 3 = mg
 Dexamethasone 6mg/m²/dose X 7 days at week 3 = mg bd
 Methotrexate 20mg/m²/dose ON once a week = mg
 Mercaptopurine 50mg/m²/dose ON = mg
 IT MTX at week 3 = mg
 Cotrimoxazole 2mg Trimethoprim/kg/dose BD on Mon, Tues = mg bd



| | | | | |
|--------|--|--|--|--|
| 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 ² | |

DEXA 10 mg/m²/d po = . mg bd

VCR 1.5 mg/m²/d iv = . mg

ADR 30 mg/m²/d iv(6h) = . mg

ASP 10 000 u/m²/d IM = u

If allergic, replace with Erwinia 20,000U/m² eod X 2 wks

Phase IIIb

| | |
|--------------------------|--------------|
| BW= _____ kg | Ht= _____ cm |
| SA= _____ m ² | |

CPM 500 mg/m²/d IV (1h) (+ MESNA) = mg

Ara-C 75 mg/m²/d i.v. = mg

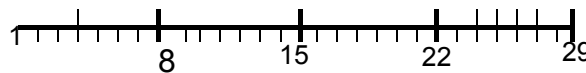
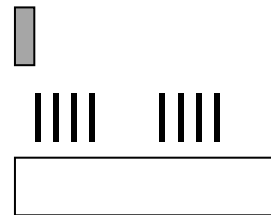
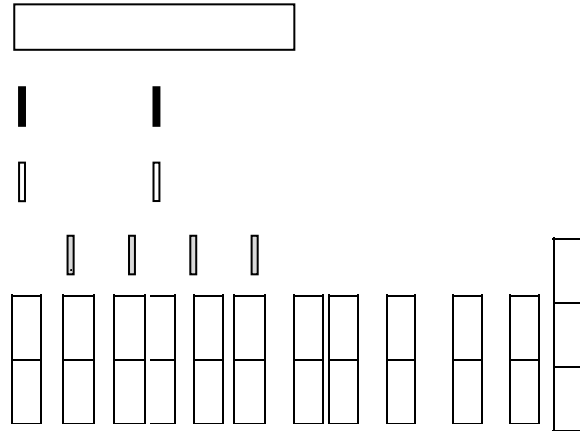
TG 40 mg/m²/d p.o. = mg

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: _____



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

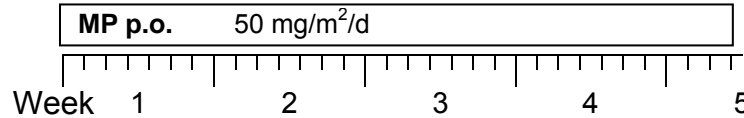
**MA-SPORE- ALL-2002 study
 Interim Maintenance Phase Number 2 – IR**

V

Dexa

IT

Vincristine 1.5mg/m²/dose (max 2mg) at week 3 = mg
 Dexamethasone 6mg/m²/dose X 7 days at week 3 = mg bd
 Methotrexate 20mg/m²/dose ON once a week = mg
 Mercaptopurine 50mg/m²/dose ON = mg
 IT MTX at week 3 = mg
 Cotrimoxazole 2mg Trimethoprim/kg/dose BD on Mon, Tues = mg bd



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

MA-SPORE-ALL 2003 Protocol III Number 3

SR/IR

Phase IIIa

| | |
|--------------------------|--------------|
| BW= _____ kg | Ht= _____ cm |
| SA= _____ m ² | |

DEXA 10 mg/m²/d po = . mg bd

VCR 1.5 mg/m²/d iv = . mg

ADR 30 mg/m²/d iv(6h) = . mg

ASP 10 000 u/m²/d IM = u

If allergic, replace with Erwinia 20,000U/m² eod X 2 wks

Phase IIIb

| | |
|--------------------------|--------------|
| BW= _____ kg | Ht= _____ cm |
| SA= _____ m ² | |

CPM 500 mg/m²/d IV (1h) (+ MESNA) = mg

Ara-C 75 mg/m²/d i.v. = mg

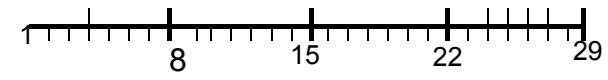
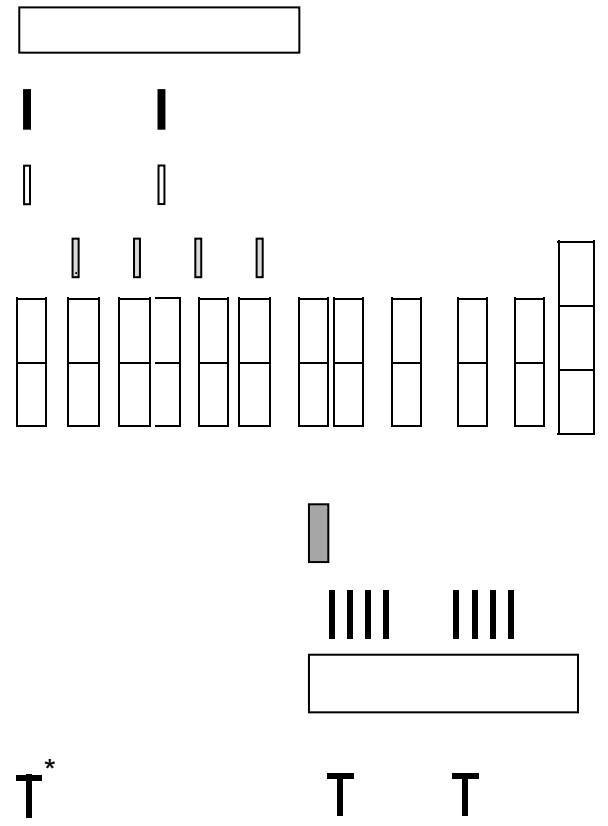
TG 40 mg/m²/d p.o. = mg

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 2003
Maintenance Phase # 2**

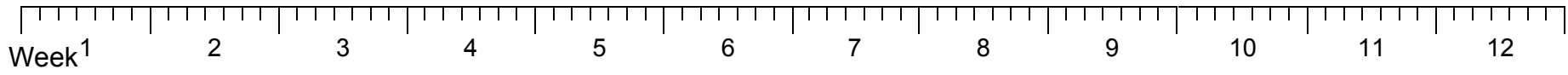
Name:
 HRN:
 Weight:
 Height:
 SA:
 Hospital:

Vincristine 1.5mg/m²/dose (max 2mg) at week 11 and 12 = mg
 Dexamethasone 6mg/m²/dose X 7 days at week 11 = mg bd
 Methotrexate 20mg/m²/dose ON once a week = mg
 Mercaptopurine 50mg/m²/dose ON = mg
 IT MTX at week 11 = mg
 Cotrimoxazole 2mg Trimethoprim/kg/dose BD on Mon, Tues = mg bd

V V
 Dexamethasone
 IT
 M M

M M M M M M M M M M M M

MP p.o. 50 mg/m²/d



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

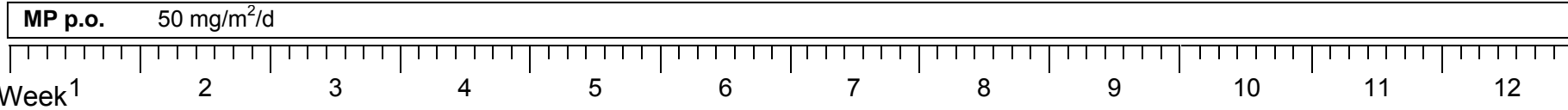
**MA-SPORE ALL 2003
Maintenance Phase # 2**

| | | |
|--|---|-------|
| Vincristine 1.5mg/m ² /dose (max 2mg) at week 11 and 12 | = | mg |
| Dexamethasone 6mg/m ² /dose X 7 days at week 11 | = | mg bd |
| Methotrexate 20mg/m ² /dose ON once a week | = | mg |
| Mercaptopurine 50mg/m ² /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

M M M M M M M M M M M M



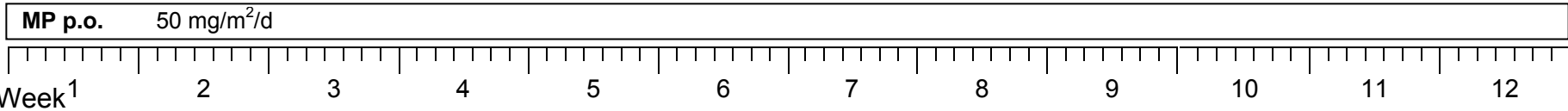
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|--------|--|--|--|--|--|--|--|--|--|--|--|--|--|
| Date | | | | | | | | | | | | | |
| Week | | | | | | | | | | | | | |
| 6MP/mg | | | | | | | | | | | | | |
| MTX/mg | | | | | | | | | | | | | |
| WBC | | | | | | | | | | | | | |
| ANC | | | | | | |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

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

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

Vincristine 1.5mg/m²/dose (max 2mg) at week 11 and 12 = mg
 Dexamethasone 6mg/m²/dose X 7 days at week 11 = mg bd
 Methotrexate 20mg/m²/dose ON once a week = mg
 Mercaptopurine 50mg/m²/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 # 4**

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

Vincristine 1.5mg/m²/dose (max 2mg) at week 11 and 12 = mg
 Dexamethasone 6mg/m²/dose X 7 days at week 11 = mg bd
 Methotrexate 20mg/m²/dose ON once a week = mg
 Mercaptopurine 50mg/m²/dose ON = mg
 IT MTX at week 11 = mg
 Cotrimoxazole 2mg Trimethoprim/kg/dose BD on Mon, Tues = mg bd

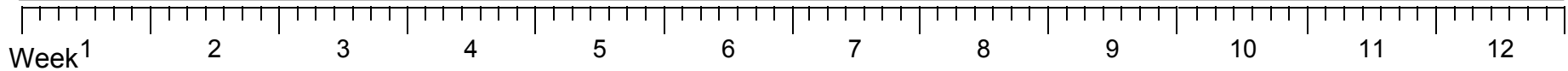
V V

Dexa

IT

M M M M M M M M M M M M M

MP p.o. 50 mg/m²/d



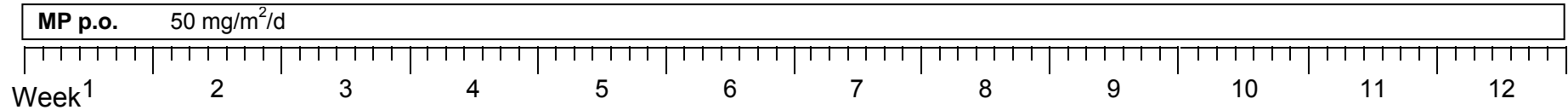
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|--------|--|--|--|--|--|--|--|--|--|--|--|--|--|
| Date | | | | | | | | | | | | | |
| Week | | | | | | | | | | | | | |
| 6MP/mg | | | | | | | | | | | | | |
| MTX/mg | | | | | | | | | | | | | |
| WBC | | | | | | | | | | | | | |
| ANC | | | | | | |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

**MA-SPORE ALL 2003
Maintenance Phase # 5**

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

| | | |
|--|---|-------|
| Vincristine 1.5mg/m ² /dose (max 2mg) at week 11 and 12 | = | mg |
| Dexamethasone 6mg/m ² /dose X 7 days at week 11 | = | mg bd |
| Methotrexate 20mg/m ² /dose ON once a week | = | mg |
| Mercaptopurine 50mg/m ² /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



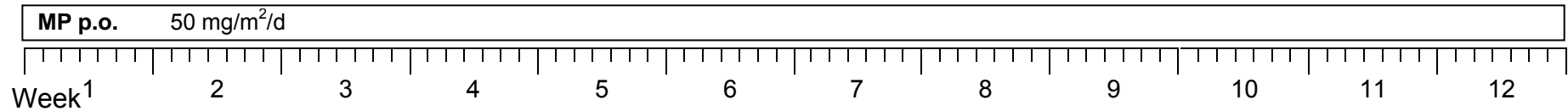
| | | | | | | | | | | | | | |
|--------|--|--|--|--|--|--|--|--|--|--|--|--|--|
| Date | | | | | | | | | | | | | |
| Week | | | | | | | | | | | | | |
| 6MP/mg | | | | | | | | | | | | | |
| MTX/mg | | | | | | | | | | | | | |
| WBC | | | | | | | | | | | | | |
| ANC | | | | | | | | | | | | | |
| Hb | |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

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

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

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

V V
 Dexamethasone
 IT
 M M



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