

THE LANCET Oncology

Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Mattano LA Jr, Devidas M, Nachman JB, et al, on behalf of the Children's Oncology Group . Effect of alternate-week versus continuous dexamethasone scheduling on the risk of osteonecrosis in paediatric patients with acute lymphoblastic leukaemia: results from the CCG-1961 randomised cohort trial. *Lancet Oncol* 2012; published online Aug 15. [http://dx.doi.org/10.1016/S1470-2045\(12\)70274-7](http://dx.doi.org/10.1016/S1470-2045(12)70274-7).

SUPPLEMENTAL APPENDIX

Effect of alternate-week versus continuous dexamethasone scheduling on the risk of osteonecrosis in paediatric patients with acute lymphoblastic leukaemia: results from the CCG-1961 randomised cohort trial

Supplemental Table 1: Distribution of patients by age, sex, and chemotherapy regimen

Age* (years)	# Patients (%)	RER Regimens				SER Regimens
		Standard Rx Single IM/DI	Standard Rx Double IM/DI	Intensified Rx Single IM/DI	Intensified Rx Double IM/DI	Intensified Rx Double IM/DI
1-21	2056 (100)	325 (16)	325 (16)	327 (16)	324 (16)	450 (22)
Boys	1228 (60)	197 (61)	196 (60)	179 (55)	188 (58)	275 (61)
Girls	828 (40)	128 (39)	129 (40)	148 (45)	136 (42)	175 (39)
10-21	1287 (63)	202 (62)	199 (61)	201 (62)	221 (68)	271 (60)
Boys	762 (59)	117 (58)	115 (58)	114 (57)	127 (58)	160 (59)
Girls	525 (41)	85 (42)	84 (42)	87 (43)	94 (42)	111 (41)
1-9	769 (37)	123 (38)	126 (39)	126 (39)	103 (32)	179 (40)
Boys	466 (61)	80 (65)	81 (64)	65 (52)	61 (59)	115 (64)
Girls	303 (39)	43 (35)	45 (36)	61 (48)	42 (41)	64 (36)
10-15	1025 (50)	165 (51)	160 (49)	159 (49)	176 (54)	216 (48)
Boys	590 (58)	92 (56)	90 (56)	83 (52)	100 (57)	122 (57)
Girls	435 (42)	73 (44)	70 (44)	76 (48)	76 (43)	94 (43)
16-21	262 (13)	37 (11)	39 (12)	42 (13)	45 (14)	55 (12)
Boys	172 (66)	25 (68)	25 (64)	31 (74)	27 (60)	38 (69)
Girls	90 (34)	12 (32)	14 (36)	11 (26)	18 (40)	17 (31)

*Age at ALL diagnosis

Legend

RER = rapid early response, SER = slow early response

DI = delayed intensification, IM = interim maintenance

Rx = treatment

Supplemental Table 2: Standard and Intensified Post-Induction Treatment for Rapid Early Responders

STANDARD POST-INDUCTION TREATMENT Regimens A & B		INTENSIFIED POST-INDUCTION TREATMENT Regimens C & D	
Phase and treatment	Dose	Phase and treatment	Dose
Consolidation (5 wks)		Consolidation (9 wks)	
Cyclophosphamide	1000 mg/m ² /d IV; d 0,14	Cyclophosphamide	1000 mg/m ² /d IV; d 0,28
Cytarabine	75 mg/m ² /d SQ or IV; □ d 1-4,8-11,15-18,22-25	Cytarabine	75mg/m ² /d SQ or IV; □ d 1-4,8-11,29-32,36-39
Mercaptopurine	60 mg/m ² /d PO; d 0-27	Mercaptopurine	60 mg/m ² /d PO; d 0-13,28-41
Methotrexate	IT*; d 0,7,14,21	Methotrexate	IT*; d 0,7,14,21
		Pegaspargase	2500 IU/m ² /d IM; d 14,42
		Vincristine	1.5 mg/m ² /d IV; d 14,21,42,49
Interim Maintenance I□(8 wks)		Interim Maintenance I□(8 wks)	
Mercaptopurine	60 mg/m ² /d PO; d 0-41	Vincristine	1.5 mg/m ² /d IV; □ d 0,10,20,30,40
Methotrexate	15 mg/m ² /d PO; d 7,14,21,35	Methotrexate	100 mg/m ² /d IV; d 0,10,20,30,40 Escalate by 50 mg/m ² /dose as tolerated
Methotrexate	IT*; d 0,28	Pegaspargase	2500 IU/m ² /d IM; d 1,21
		Methotrexate	IT*; d 0,30
Delayed Intensification I□(7 wks)		Delayed Intensification I□(8 wks)	
Dexamethasone	10 mg/m ² /d ÷ BID PO Single DI: d0-20 Double DI: d0-6,14-20	Dexamethasone	10 mg/m ² /d ÷ BID PO Single DI: d0-20 Double DI: d0-6,14-20
Vincristine	1.5 mg/m ² /d IV; d 0,7,14	Vincristine	1.5 mg/m ² /d IV; d 0,7,14
Doxorubicin	25 mg/m ² /d IV; d 0,7,14	Doxorubicin	25 mg/m ² /d IV; d 0,7,14
Asparaginase	6000 IU/m ² /d IM; □ d 3,5,7,10,12,14	Pegaspargase	2500 IU/m ² /d IM; d 3
Methotrexate	IT*; d 0	Methotrexate	IT*; d 0
Cyclophosphamide	1000 mg/m ² /d IV; d 28	Cyclophosphamide	1000 mg/m ² /d IV; d 28
Thioguanine	60 mg/m ² /d PO; d 28-41	Thioguanine	60 mg/m ² /d PO; d 28-41
Cytarabine	75 mg/m ² /d SQ or IV; □ d 29-32,36-39	Cytarabine	75 mg/m ² /d SQ or IV; □ d 29-32,36-39
Methotrexate	IT*; d 28,35	Vincristine	1.5 mg/m ² /d IV; d 42,49
		Pegaspargase	2500 IU/m ² /d IM; d 42
		Methotrexate	IT*; d 28,35
Interim Maintenance II□(8 wks)	Regimen B only Same as Interim Maintenance I	Interim Maintenance II□(8 wks)	Regimen D only Same as Interim Maintenance I
Delayed Intensification II (7 wks)	Regimen B only Same as Delayed Intensification I	Delayed Intensification II (8 wks)	Regimen D only Same as Delayed Intensification I
Maintenance□(12 wks)†		Maintenance□(12 wks) †	
Vincristine	1.5 mg/m ² /d IV; d 0,28,56	Vincristine	1.5 mg/m ² /d IV; d 0,28,56
Prednisone	40 mg/m ² /d ÷ BID PO; □ d 0-4,28-32,56-60	Prednisone	40 mg/m ² /d ÷ BID PO; □ d 0-4,28-32,56-60
Mercaptopurine	75 mg/m ² /d PO; d 0-83	Mercaptopurine	75 mg/m ² /d PO; d 0-83
Methotrexate	20 mg/m ² /d PO d 7,14,21,28,35,42,49,56,63,70,77	Methotrexate	20 mg/m ² /d PO d 7,14,21,28,35,42,49,56,63,70,77
Methotrexate	IT*; d 0 Single DI/IM: also d 28 in cycles 1-4	Methotrexate	IT*; d 0 Single DI/IM: also d 28 in cycles 1-4

* Age-adjusted dose: 1-1.9 years 8 mg; 2-2.9 years 10 mg; ≥3 years 12 mg

† Cycles were repeated until the total duration of therapy, beginning with the first interim maintenance period, reached two years for girls and three years for boys.

Legend

DI = delayed intensification, IM = interim maintenance

IM = intramuscular, IT = intrathecal, IV = intravenous, PO = oral, SQ = subcutaneous

BID = twice daily, d = day(s), wks = weeks, IU = international units

Supplemental Table 3: Distribution of osteonecrosis RER patients by age, sex, and chemotherapy regimen

Age (years)	Reg A (#) ON / Total	Reg B (#) ON / Total	Reg C (#) ON / Total	Reg D (#) ON / Total	RER (#) ON / Total	Standard (#) ON / Total	Intensified (#) ON / Total
1-21	24 / 325	20 / 325	43 / 327	16 / 324	103 / 1301	67 / 652	36 / 649
10-21	23 / 202	20 / 199	41 / 201	14 / 221	98 / 823	64 / 403	34 / 420
Girls	13 / 85	13 / 84	19 / 87	6 / 94	51 / 350	32 / 172	19 / 178
Boys	10 / 117	7 / 115	22 / 114	8 / 127	47 / 473	32 / 231	15 / 242
10-15	11 / 165	14 / 160	26 / 159	11 / 176	62 / 660	37 / 324	25 / 336
Girls	7 / 73	9 / 70	16 / 76	5 / 76	37 / 295	23 / 149	14 / 147
Boys	4 / 92	5 / 90	10 / 83	6 / 100	25 / 365	14 / 174	11 / 190
16-21	12 / 37	6 / 39	15 / 42	3 / 45	36 / 163	27 / 79	9 / 84
Girls	6 / 12	4 / 14	3 / 11	1 / 18	14 / 55	9 / 23	5 / 32
Boys	6 / 25	2 / 25	12 / 31	2 / 27	22 / 108	18 / 56	4 / 53

Legend

RER = rapid early response

Reg = regimen

ON = osteonecrosis