

THE LANCET Oncology

Supplementary appendix

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Supplement to: Biondi A, Schrappe M, De Lorenzo P, et al. Imatinib after induction for treatment of children and adolescents with Philadelphia-chromosome-positive acute lymphoblastic leukaemia (EsPhALL): a randomised, open-label, intergroup study. *Lancet Oncol* 2012; published online Aug 14. [http://dx.doi.org/10.1016/S1470-2045\(12\)70377-7](http://dx.doi.org/10.1016/S1470-2045(12)70377-7).

Supplementary Table 1. Recruitment overall, by risk group and assigned arm (in Good Risk) and by participating group

Participating Group	Recruitment		Good Risk		Assigned arm		Poor Risk	
			Randomized study		GR-noIM	GR-IM	Observational study	
	N	%	N	%	N	N	N	%
AIEOP	27	15.17	13	14.44	6	7	12	17.14
BFM-G*	41	23.0	20	22.2	9	11	14	20.00
COALL[^]	7	3.93	4	4.44	2	2	3	4.29
CPH	9	5.06	2	2.22	1	1	5	7.14
DCOG	12	6.74	8	8.89	4	4	3	4.29
FRALLE[^]	14	7.87	7	7.78	3	4	3	4.29
MRC[^]	38	21.35	21	23.33	11	10	17	24.29
NOPHO[^]	21	11.80	12	13.33	6	6	7	10.00
Hong-Kong	3	1.69	1	1.11	1	0	2	2.86
PINDA	6	3.37	2	2.22	1	1	4	5.71
Total	178		90		44	46	70	

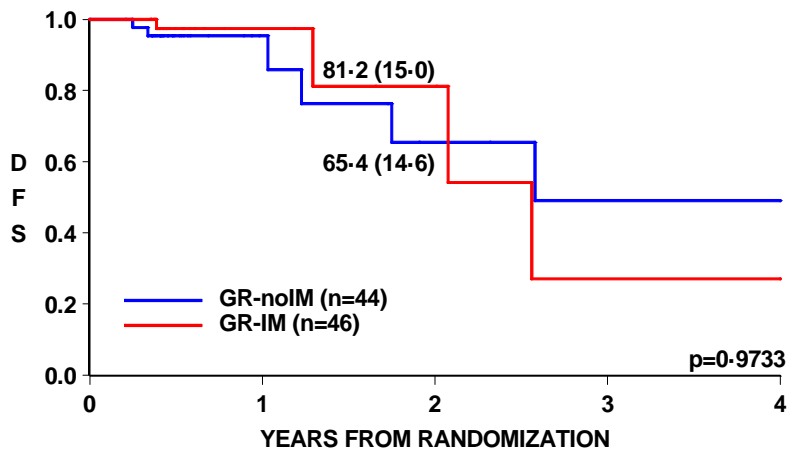
GR-noIM= Good Risk patients randomized not to receive imatinib. GR-IM= Good Risk patients randomized to receive imatinib. N=number of patients. *includes 1 patients enrolled by BFM-Austria. [^]these groups assessed early response in the bone marrow, while the remaining evaluated the peripheral blood.

Supplementary Table 2. Treatment phases of the EsPhALL protocol

Treatment phase	Drug	Single dose	Administration		Total dose per phase	
			Day	Route		
Protocol IB	Cyclophosphamide	1000 mg/m ²	1, 28	iv	2000 mg/m ²	
	6-Mercaptopurine	60 mg/m ²	1-28	oral	1680 mg/m ²	
	Cytosine Arabinoside	75 mg/m ²	3-6, 10-13, 17-20, 24-27	sc	1200 mg/m ²	
	Methotrexate	≥1 year < 2 year = 8 mg ≥2 years <3 years = 10 mg ≥3 years = 12 mg	3, 7	it	age-related	
	Imatinib*	300 mg/m ²	1-28	oral	8400 mg/m ²	
Consolidation block HR1	Dexamethasone	20 mg/m ²	1-5	oral or iv	100 mg/m ²	
	Vincristine	1.5 mg/m ²	1,6	iv	3 mg/m ²	
	Methotrexate	5000 mg/m ²	1	iv	5000 mg/m ²	
	Cytosine Arabinoside	2000 mg/m ²	5	iv	4000 mg/m ²	
	L-Asparaginase	25000 IU/m ²	6	im	25000 IU/m ²	
	Cyclophosphamide	200 mg/m ²	2-4	iv	1000 mg/m ²	
	Methotrexate (MTX)	≥1 year < 2 year = MTX 8 mg	1	it	age-related	
	Cytosine Arabinoside (ARA-C)	ARA-C 20 mg PRED 6 mg ≥2 years <3 years = MTX 10 mg ARA-C 26 mg PRED 8 mg				
	Prednisone (PRED)	≥3 years = MTX 12 mg ARA-C 30 mg PRED 10 mg				
		Imatinib*	300 mg/m ²	6-20	oral	4200 mg/m ²
Consolidation block HR2	Dexamethasone	20 mg/m ²	1-5	oral or iv	100 mg/m ²	
	Vindesine	3 mg/m ²	1,6	iv	6 mg/m ²	
	Methotrexate	5000 mg/m ²	1	iv	5000 mg/m ²	
	Ifosphamide	800 mg/m ²	2-4	iv	4000 mg/m ²	
	L-Asparaginase	25000 IU/m ²	6	im	25000 IU/m ²	
	Daunorubicin	30 mg/m ²	5	iv	30 mg/m ²	
	Methotrexate (MTX)	≥1 year < 2 year = MTX 8 mg	1	it	age-related	
	Cytosine Arabinoside (ARA-C)	ARA-C 20 mg PRED 6 mg ≥2 years <3 years = MTX 10 mg ARA-C 26 mg PRED 8 mg				
	Prednisone (PRED)	≥3 years = MTX 12 mg ARA-C 30 mg PRED 10 mg				
		Imatinib*	300 mg/m ²	6-20	oral	4200 mg/m ²
Consolidation block HR3	Dexamethasone	20 mg/m ²	1-5	oral or iv	100 mg/m ²	
	Cytosine Arabinoside	2000 mg/m ²	1-2	iv	4000 mg/m ²	
	Vepeside	100 mg/m ²	3-5	iv	500 mg/m ²	
	L-Asparaginase	25000 IU/m ²	6	im	25000 IU/m ²	
	Methotrexate (MTX)	≥1 year < 2 year = MTX 8 mg	1	it	age-related	
	Cytosine Arabinoside (ARA-C)	ARA-C 20 mg PRED 6 mg ≥2 years <3 years = MTX 10 mg ARA-C 26 mg PRED 8 mg				
	Prednisone (PRED)	≥3 years = MTX 12 mg ARA-C 30 mg PRED 10 mg				
	Imatinib*	300 mg/m ²	6-20	oral	4200 mg/m ²	
Reinduction Protocol II**	Dexamethasone	10 mg/m ²	1-21 + tapering	oral	235 mg/m ²	
	Vincristine	1.5 mg/m ²	8,15,22,29	iv	6 mg/m ²	
	Doxorubicin	25 mg/m ²	8,15,22,29	iv	100 mg/m ²	
	L-Asparaginase	10000 IU/m ²	8,11,15,18	im	40000 IU/m ²	
	Cyclophosphamide	1000 mg/m ²	36	iv	1000 mg/m ²	
	6-Thioguanine	60 mg/m ²	36-49	oral	840 mg/m ²	
	Cytosine Arabinoside	75 mg/m ²	38-41, 45-48	sc	600 mg/m ²	
	Methotrexate	≥1 year < 2 years = 8 mg ≥2 years <3 years = 10 mg ≥3 years = 12 mg	38, 45	it	age-related	
		Imatinib*	300 mg/m ²	36-63	oral	8400 mg/m ²
	Interim Maintenance	6-Mercaptopurine	50 mg/m ²	1-29	oral	1450 mg/m ²
Methotrexate		20 mg/m ²	8,15,22,29	oral	80 mg/m ²	
Cranial irradiation		1.4-1.7 Gy			Standard: 18 Gy - if < 2 years: 12 Gy - if CNS inv.: 24 Gy	
Continuation therapy Maintenance	6-Mercaptopurine	50 mg/m ²	Daily till day +728 from diagnosis	oral		
	Methotrexate	20 mg/m ²	weekly till day +728 from diagnosis	oral		

iv=intravenous; im=intramuscular; it=intrathecal; sc=subcutaneous. * imatinib was administered to all Poor Risk patients and to Good Risk patients in a randomized fashion. ** Reinduction Protocol II was administered twice, one before and one after Interim Maintenance. During the second administration, intrathecal therapy was omitted due to previous cranial irradiation.

Supplementary Figure 1. Disease-free survival curves with 2-year estimates (standard error) by randomized arm in Good Risk (ITT analysis), censoring at allo-SCT in CR1



Number at risk

GR-noIM	44	19	10	8	5	4	2	2	2
GR-IM	46	16	7	5	4	2	2	2	2

ITT=intention to treat. allo-SCT= allogeneic stem cell transplantation. CR1=First complete remission. GR-noIM= Good Risk patients randomized not to receive imatinib. GR-IM= Good Risk patients randomized to receive imatinib.