

No clear benefit of preventive cranial radiotherapy in childhood Philadelphia-positive acute lymphoblastic leukemia: a retrospective analysis of the EsPhALL2010 study

Authors

Valentino Conter,^{1*} Maria Grazia Valsecchi,^{2,3*} Paola De Lorenzo,^{1,2} Virginie Gandemer,⁴ Mats Heyman,⁵ Vaskar Saha,^{6,7} Paulina Diaz,^{8,9} Chi-Kong Li,¹⁰ Andishe Attarbaschi,^{11,12} Gabriele Escherich,¹³ Jan Stary,¹⁴ Martin Schrappe,¹⁵ Rob Pieters,¹⁶ Gunnar Cario^{15#} and Andrea Biondi^{1,3#}

¹Pediatrics and Tettamanti Center, Fondazione IRCCS San Gerardo dei Tintori, Monza, Italy; ²Biostatistics and Clinical Epidemiology, Fondazione IRCCS San Gerardo dei Tintori, Monza, Italy; ³School of Medicine and Surgery, University of Milano-Bicocca, Milano, Italy; ⁴Department of Pediatric Hemato-Oncology, University Hospital of Rennes, Rennes, France; ⁵Department of Paediatric Oncology, Karolinska University Hospital and Department of Women's and Children's Health, Karolinska Institutet, Stockholm, Sweden; ⁶Division of Cancer Sciences, School of Medical Sciences, Faculty of Biology, Medicine and Health, University of Manchester, Manchester, UK; ⁷Tata Translational Cancer Research Centre, Tata Medical Center, Kolkata, India; ⁸Chilean National Pediatric Oncology Group, Santiago, Chile; ⁹Hospital Dr. Gustavo Fricke, Viña del Mar, Chile; ¹⁰The Chinese

University of Hong Kong, Hong Kong Children's Hospital, Hong Kong SAR, China; ¹¹Department of Pediatric Hematology and Oncology, St. Anna Children's Hospital, Medical University of Vienna, Vienna, Austria; ¹²St. Anna Children's Cancer Research Institute, Vienna, Austria; ¹³University Medical Centre Hamburg-Eppendorf, Clinic of Paediatric Haematology and Oncology, Hamburg, Germany; ¹⁴Department of Pediatric Hematology and Oncology, Second Faculty of Medicine, Charles University and University Hospital Motol, Prague, Czech Republic; ¹⁵University Medical Center Schleswig-Holstein, Pediatrics, Campus Kiel, Kiel, Germany and ¹⁶Princess Máxima Center for Pediatric Oncology, Utrecht, The Netherlands

**VC and MVG contributed equally as first authors.*

#GC and AB contributed equally as senior authors.

Correspondence:

A. BIONDI - andrea.biondi@unimib.it

<https://doi.org/10.3324/haematol.2024.285253>

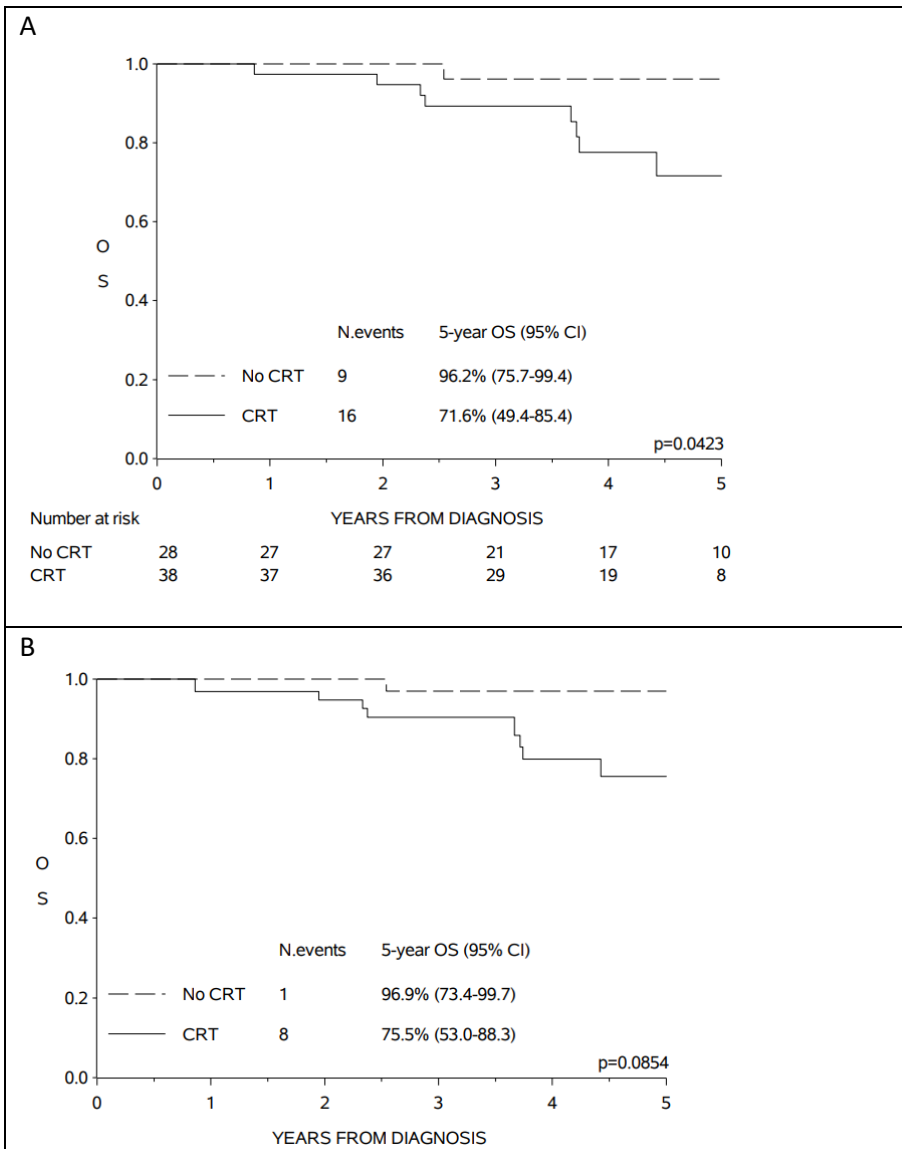
No clear benefit of preventive cranial radiotherapy in childhood Philadelphia-positive acute lymphoblastic leukemia: a retrospective analysis of the EsPhALL2010 study

Valentino Conter et al.

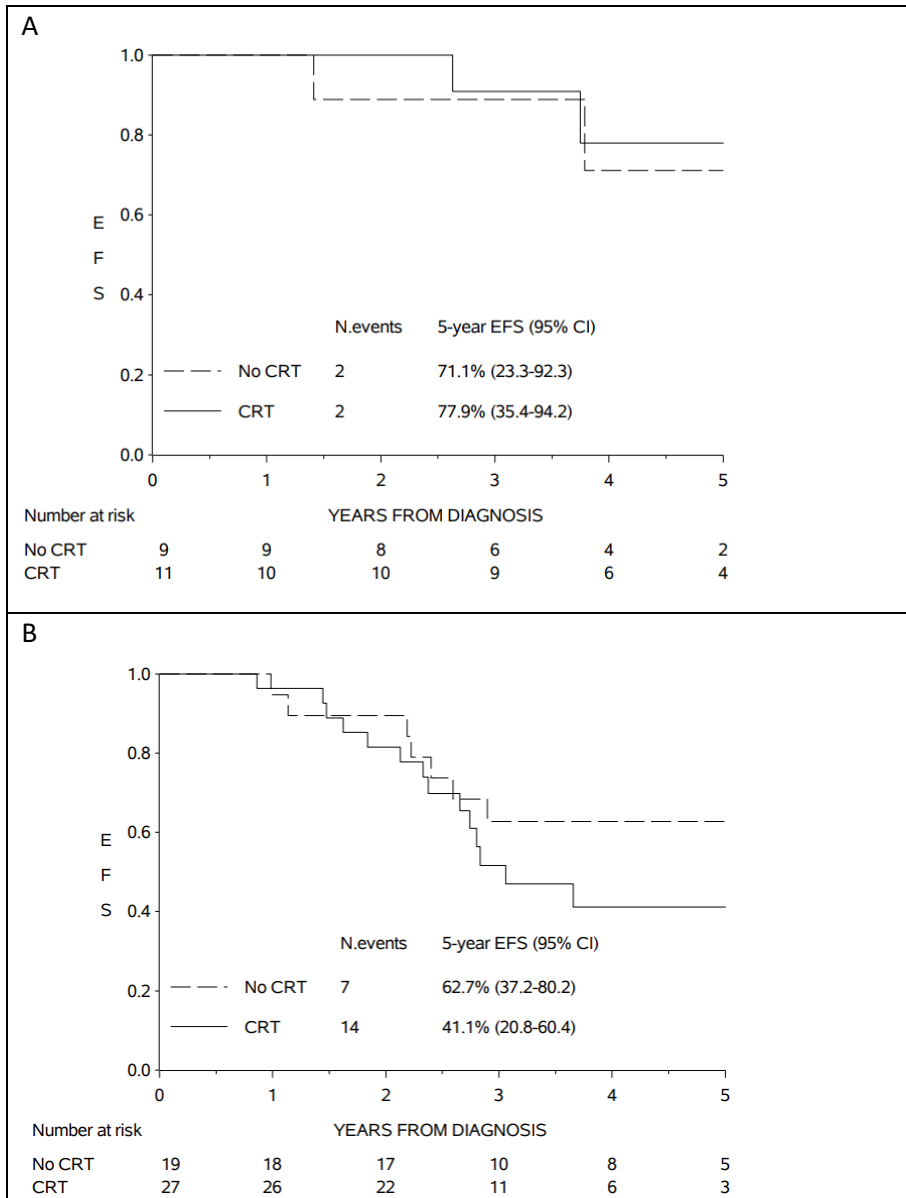
Supplementary material

	N. pts.	N. events	5-year EFS (SE)	95% CI	p-value
Patients analysed	66	25			
ALL consortia					<i>0.8535</i>
AIEOP/BFM	31	11	59.6 (9.8)	38.1 – 75.8	
ALLTogether	35	14	56.5 (9.0)	37.3 – 71.8	
Gender					<i>0.0998</i>
Male	41	13	63.6 (8.4)	44.9 – 77.4	
Female	25	12	48.5 (10.5)	27.1 – 66.9	
Age at diagnosis, years					<i>0.9299</i>
< 4 years	13	6	52.8 (14.1)	23.4 – 75.5	
4 - <10 years	29	10	59.6 (10.5)	36.5 – 76.7	
≥10 years	24	9	59.4 (10.7)	35.8 – 76.8	
WBC at diagnosis, ×10⁹ cells/L					<i>0.0559</i>
< 50	35	9	68.2 (9.1)	46.9 – 82.4	
50 - <100	16	8	48.1 (12.9)	22.4 – 70.0	
≥100	15	8	44.0 (13.3)	18.5 – 67.1	
NCI criteria					<i>0.0408</i>
Standard risk	20	4	74.8 (11.2)	44.9 – 90.0	
High risk	46	21	50.7 (7.9)	34.5 – 64.8	
CNS-Involvement					
Yes	4	2	-	-	-
No	62	23	58.7 (6.8)	44.2 – 70.7	

Supplementary Table 1. 5-year event-free survival (EFS) of 66 patients on chemotherapy at the end of Delayed Intensification I, by baseline covariates. WBC= white blood cell count; NCI criteria: standard risk= patients with WBC<50 ×10⁹/L and age <10 years; high risk= all other patients; CNS= central nervous system. p-value from log-rank test.



Supplementary Figure 1. Estimate of overall survival (OS) according to the standard Kaplan-Meier approach (A) and to the weighted Kaplan-Meier approach based on the inverse probability of treatment (B), by cranial radiotherapy (CRT) administration. The initial plateau in the curves reflects the fact that all 66 patients included in the analysis were still alive in complete remission and on protocol chemotherapy at the planned time of CRT administration (i.e. the end of Delayed Intensification I, about 7 months after diagnosis).



Supplementary Figure 2. Standard Kaplan-Meier estimates of event-free survival (EFS) in NCI standard risk (A) and high risk (B) patients by cranial radiotherapy (CRT) administration. NCI criteria: standard risk= patients with white blood cell count $<50 \times 10^9/L$ and age <10 years; high risk= all other patients. The initial plateau in the EFS curve reflects the fact that all 66 patients included in the analysis were still in complete remission and on protocol chemotherapy at the planned time of CRT administration (i.e. the end of Delayed Intensification I, about 7 months after diagnosis).