

Combination therapy with crizotinib and vinblastine for relapsed or refractory pediatric ALK-positive anaplastic large cell lymphoma

Fabian Knörr,^{1,2*} Kim PJ Schellekens,^{3,4*} Reineke A Schoot,³ Judith Landman-Parker,⁵ Heiko-Manuel Teltschik,⁶ Jan Förster,¹ Amambay Riquelme,¹ Alwin DR Huitema,^{3,7,8} Natasha KA van Eijkelenburg,³ Auke Beishuizen,^{3,4} C Michel Zwaan,^{3,4} Wilhelm Woessmann^{1#} and Jasper van der Lugt^{3#}

¹Pediatric Hematology and Oncology, University Medical Center Hospital Hamburg-Eppendorf, Hamburg, Germany; ²Mildred Scheel Cancer Career Center HaTriCS4, University Medical Center Hamburg-Eppendorf, Hamburg, Germany; ³Princess Máxima Center for Pediatric Oncology, Utrecht, The Netherlands; ⁴Erasmus Medical Center, Sophia Children's Hospital, Rotterdam, The Netherlands; ⁵Pediatric Hematology, Immunology, Oncology, Sorbonne Université, Hôpital Armand Trousseau, APHP, Paris, France; ⁶Pediatrics 5 – Oncology, Hematology, and Immunology, Olgahospital, Stuttgart, Germany; ⁷Department of Pharmacy and Pharmacology, Netherlands Cancer Institute, Amsterdam, The Netherlands and ⁸Department of Clinical Pharmacy, University Medical Center Utrecht, Utrecht University, Utrecht, The Netherlands

**FK and KPJS contributed equally as co-first authors*

#WW and JvdL contributed equally as senior authors

Correspondence:

F. KNÖRR - f.knoerr@uke.de

<https://doi.org/10.3324/haematol.2022.281896>

Supplementary appendix

Combination therapy with crizotinib and vinblastine for relapsed or refractory pediatric ALK-positive anaplastic large cell lymphoma

Author list

Fabian Knörr^{1-2*}, Kim Schellekens^{3,4*}, Reineke Schoot³, Judith Landman-Parker⁵, Heiko-Manuel Teltschik⁶, Jan Förster¹, Amambay Riquelme¹, Alwin Huitema^{3,7,8}, Natasha van Eijkelenburg³, Auke Beishuizen^{3,4}, C. Michel Zwaan^{3,4}, Wilhelm Woessmann^{1**}, Jasper van der Lugt^{3**}

Author affiliations

- 1 Pediatric Hematology and Oncology, University Medical Center Hospital Hamburg-Eppendorf, Hamburg, Germany
 - 2 Mildred Scheel Cancer Career Center HaTriCS4, University Medical Center Hamburg-Eppendorf, Hamburg, Germany
 - 3 Princess Máxima Center for Pediatric Oncology, Utrecht, The Netherlands
 - 4 Erasmus Medical Center, Sophia Children's Hospital, Rotterdam, The Netherlands
 - 5 Pediatric Hematology, Immunology, Oncology, Sorbonne université, Hôpital Armand Trousseau, APHP, Paris, France
 - 6 Pediatrics 5 (Oncology, Hematology, and Immunology), Olgahospital, Stuttgart, Germany
 - 7 Dept. Pharmacy & Pharmacology, Netherlands Cancer Institute, Amsterdam, The Netherlands
 - 8 Dept. Clinical Pharmacy, University Medical Center Utrecht, Utrecht University, Utrecht, The Netherlands
- * These authors contributed equally
** These authors contributed equally

List of supplementary material

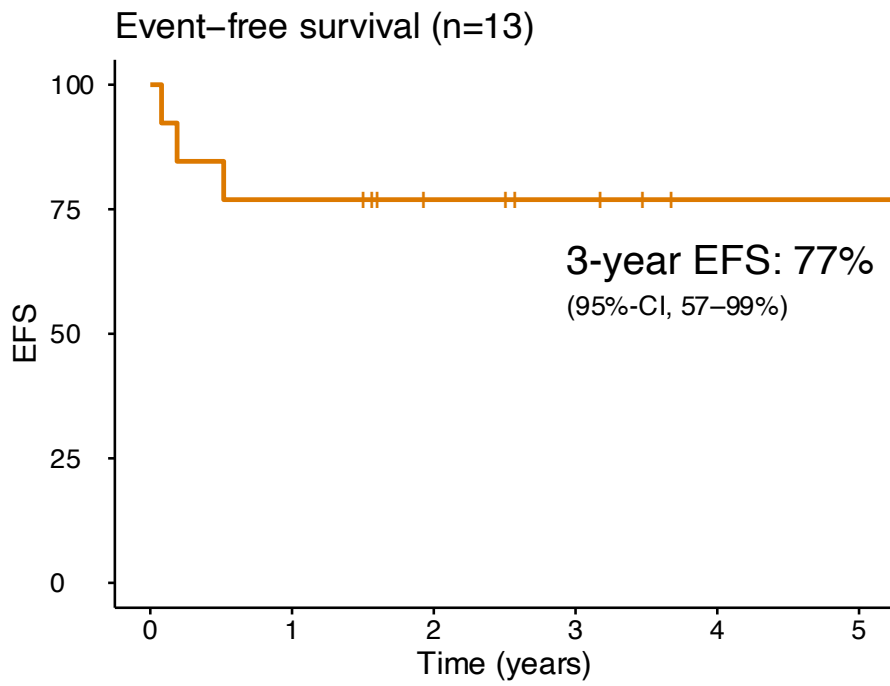
Supplementary Table 1: Additional patient characteristics	2
Supplementary Figure 1: Event-free survival	3
Supplementary Figure 2: Overall survival	3

Supplementary Table 1: Additional patient characteristics

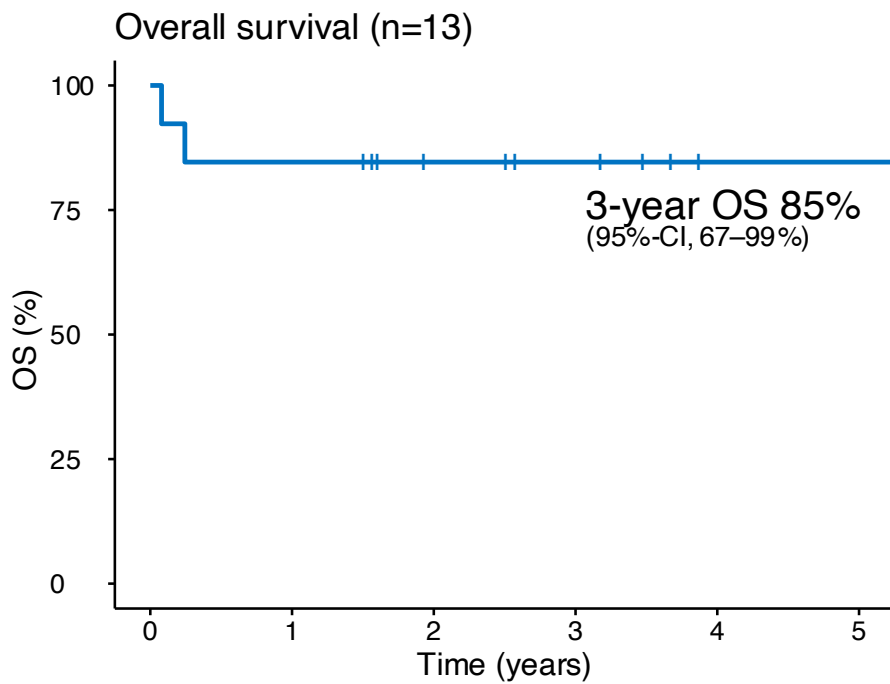
Patient	Initial Diagnosis			Relapse Diagnose			MRD*	Response	Outcome, last FU
	BM	CNS	MDD	BM	CNS	MDD			
TP1	pos.	neg.	n.d.	pos.	neg.	pos.	n.d.	Not evaluated	Died of infection (1 mo.)
TP2	neg.	neg.	pos.	neg.	n.d.	pos.	neg.	CR	FOP (18 mo.)
RP1	pos.	neg.	pos.	n.a.	pos.	pos.	pos.	PR (Sonography, 6 weeks)	Died of lymphoma (2,9 mo.)
RP2	neg.	neg.	neg.	n.d.	n.d.	pos.	neg.	PR (PET-CT, 6 weeks)	FOP (67,7 mo.)
RP3	neg.	neg.	pos.	pos.	neg.	pos.	neg.	n. a.	FOP after Relapse [#] (46,2 mo.)
RP4	neg.	neg.	pos.	neg.	neg.	pos.	neg.	unknown	FOP (44,1 mo.)
RP5	neg.	neg.	pos.	delayed neg.	neg.	pos.	n.d.	CR (MRI, 5 weeks)	FOP (41,7 mo.)
RP6	neg.	neg.	n.d.	pos.	neg.	n.d.	n.d.	CR (MRI, 8 weeks)	FOP (30,1 mo.)
RP7	neg.	neg.	pos.	neg.	neg.	n.d.	n.d.	CR (PET-CT, 8 weeks)	FOP (38,1 mo.)
RP8	neg.	neg.	neg.	neg.	neg.	neg.	n.d.	CR (MRI, 4 weeks)	FOP (18,8 mo.)
RP9	neg.	neg.	n.d.	neg.	neg.	pos.	n.d.	CR (Sonography, MRI, 12 weeks)	FOP (30,9 mo.)
RP10	neg.	neg.	pos.	neg.	n.a.	pos.	neg.	CR (MRI, 4 weeks)	FOP (23,1 mo.)
RP11	neg.	neg.	neg.	neg.	neg.	pos.	neg.	CR (MRI, CT, 8 weeks)	FOP (19,2 mo.)

BM, bone marrow involvement, CNS, central nervous system involvement, MDD, minimal disseminated disease, MRD, minimal residual disease, allo-SCT, allogeneic stem-cell transplantation, PR, partial response, CR, complete response, as defined by the International Pediatric Non-Hodgkin Lymphoma Response Criteria, n. d., not done, n. a., not available

* before allogeneic SCT or last MRD measurement after initiation of second line therapy



Supplementary Figure 1: Event-free survival of 13 patients treated with the combination of vinblastine and crizotinib. Event-free time is defined as time from first relapse to any event (Relapse, Progression, Secondary Malignancy, Death from any cause).



Supplementary Figure 2: Overall survival of 13 patients treated with the combination of vinblastine and crizotinib. Overall survival time is defined as time from first relapse to death of any cause.