Prognostic impact of pretreatment immunoglobulin clonal composition in pediatric B-lymphoblastic leukemia

Carol Fries,[1]*Lik Wee Lee,[2]* Meenakshi Devidas,[3] Yunfeng Dai,[4] Karen R. Rabin,[5] Sumit Gupta,[6] Mignon L. Loh,[7] Ilan R Kirsch,[2]# Brent Wood[8]# and Rachel E. Rau[5]#

[1]Department of Pediatrics, Hematology/Oncology, University of Rochester, Rochester, NY, USA; [2]Adaptive Biotechnologies, Inc., Seattle, WA, USA; [3]Department of Global Pediatric Medicine, St Jude Children's Research Hospital, Memphis, TN, USA; [4]Department of Biostatistics, College of Medicine and Public Health and Health Professions, University of Florida, Gainesville, FL, USA; [5]Department of Pediatrics, Texas Children's Cancer Center, Baylor College of Medicine, Houston, TX, USA; [6]Division of Hematology/Oncology, Hospital for Sick Children, Faculty of Medicine, University of Toronto, Toronto, Onatario, Canada; [7]Department of Pediatrics, Ben Towne Center for Childhood Cancer Research, Seattle Children's Hospital, Seattle, WA, USA and [8]Department of Pathology and Laboratory Medicine, Children's Hospital Los Angeles, University of Southern California, Los Angeles, CA, USA

*CF and LWL contributed equally as co-first authors.
#IRK, BW, and RER contributed equally as co-senior authors.

Correspondence:
C. FRIES - carol_fries@urmc.rochester.edu

SUPPLEMENTAL TABLE 1. Patient characteristics by status of V-DJ subclone evolution

		V-DJ Subclone Evolution		
	Entire Cohort N=430	Absent N=31	Present N=399	Significance (P-value)
Risk Group, n (%)				
Standard Risk: AALL0331	214 (49.8)	17 (54.8)	197 (49.4)	0.58
High Risk: AALL0232	216 (50.2)	14 (45.2)	202 (50.6)	
Age (y), mean ± SD	7.03 ± 5.13	6.48 ± 5.98	7.07 ± 5.06	0.2
WBC (x10³/µl), mean ± SD	39.8 ± 65.03	33.68 ± 51.25	40.27 ± 66.01	0.16
Sex, n (%)				
Female	192 (44.7)	10 (32.3)	182 (45.6)	0.19
Male	238 (55.3)	21 (67.7)	217 (54.4)	
CNS status, n (%)*				
CNS1	359 (83.5)	27 (87.1)	332 (83.2)	1
CNS2	65 (15.1)	4 (12.9)	61 (15.3)	
CNS3	6 (1.4)	0 (0)	6 (1.5)	
EOI MRD (FC) status, n (%)[†]				
<0.01%	354 (82.3)	24 (77.4)	330 (82.7)	0.5
0.01-<0.10%	54 (12.6)	6 (19.4)	48 (12)	
0.10-<1.0%	20 (4.7)	1 (3.2)	19 (4.8)	
≥1.0%	2 (0.5)	0	2 (0.5)	
Cytogenetics, n (%)[††]				
ETV6-RUNX1	38 (8.8)	0 (0)	38 (9.5)	0.04
Double trisomy (DT)	76 (17.7)	8 (25.8)	68 (17)	
Hypodiploid	2 (0.5)	0 (0)	2 (0.5)	
KMT2Ar	10 (2.3)	3 (9.7)	7 (1.8)	
BCR-ABL1	1 (0.2)	0 (0)	1 (0.3)	
Neutral	276 (64.2)	17 (54.8)	259 (64.9)	
Excluded	27 (6.3)	3 (9.7)	24 (6)	

*CNS status definitions: CNS1: absence of blasts in cerebrospinal fluid (CSF); CNS2: <5 WBC/µL CSF and cytospin positive for blasts or >5 WBC/µL but negative by Steinherz/Bleyer algorithm; CNS3: ≥5 WBC/µL CSF and cytospin positive for blasts and/or clinical signs of CNS leukemia

[†]IgH HTS analysis was limited to patients on AALL0232 with FC MRD <0.10%.

[††]Patients lacking complete cytogenetic data or with a combination of 2 cytogenetic lesions were excluded.

SUPPLEMENTAL FIGURE 1. Survival impact of IgH composition by cytogenetic group. 5-year EFS probability according to the number of dominant pre-treatment IgH sequences (IgH seq) (0, 1-2, or ≥3) is shown across 3 cytogenetic groups [*ETV6-RUNX1*, double trisomies (DT), other] for **A-C)** Patients with Standard Risk (SR) B-ALL treated on AALL0331 and **D-F)** Patients with High Risk (HR) B-ALL treated on AALL0232. The impact of IgH composition on prognosis is limited to patients with HR B-ALL who lack favorable cytogenetics.