



MLPA P335								MLPA P202																	
IKZF1- Exon								IKZF1-Exon																	
1	2	3	4	5	6	7	8	1	1	1	2	2	3	3	3	4	4	5	5	6	6	7	7	8	8
								a	b	c	a	b	a	b	In <sup>2</sup>	a	b	a	b	a	b	a	b	a	b
[Red grid representing deletion data for 84 patients]																									

Online Supplementary Figure S2. Results for all 84 *IKZF1* deleted patients as analyzed with MLPA kit P335 and validation with MLPA kit P202. \*MLPA kit P202-A1 contains additional markers, compared to kit P335-A3, identical markers are highlighted in bold. Each row represents one patient, each colored lane represents a deletion in the respective exon. Light red deletions are heterozygous, dark red deletions are homozygous and light pink deletions are subclonal. In one subclonal sample, results were discordant between P335 and P202, as indicated. Of the 6 un-validated samples 4 had a Δ1-8, one a Δ4-7 and one a Δ5-7 deletion in P335. <sup>2</sup>In: Intron.

**Online Supplementary Table 1.** Patients' characteristics and response to treatment in the study cohort of 694 pediatric patients with ALL, in comparison to the remaining ALL-BFM 2000 patient cohort that was not studied.

Feature	Cohort not studied (%) 2133 (100)	Study cohort (%) 694 (100)	P <sup>1</sup>
Sex			0.20
Male	1170 (54.9)	400 (57.6)	
Female	963 (45.1)	294 (42.4)	
Age at diagnosis (years)			0.90
1-9	1603 (75.2)	520 (74.9)	
± 10	530 (24.8)	174 (25.1)	
Presenting WBC count (x10 <sup>9</sup> /L)			<0.0001
<1	1091 (51.1)	257 (37.0)	
1-4.99	666 (31.2)	256 (36.9)	
5-9.99	175 (8.2)	97 (14.0)	
≥ 10	201 (9.4)	84 (12.1)	
Prednisone response <sup>2</sup>			0.005
Good	1920 (90.0)	601 (86.7)	
Poor	189 (8.9)	87 (12.5)	
No information	24 (1.1)	6 (0.8)	
MRD <sup>3</sup>			0.57
MRD-SR	687 (32.2)	249 (35.9)	
MRD-IR	847 (39.7)	276 (39.8)	
MRD-HR	132 (6.2)	46 (6.6)	
No information	467 (21.9)	123 (17.7)	
Immunology			0.03
Non-T-ALL	1787 (83.8)	572 (82.5)	
T-ALL	280 (13.1)	116 (16.6)	
No information	66 (3.1)	6 (0.9)	
<i>ETV6/RUNX1</i>			0.80
Negative	1488 (69.8)	498 (71.7)	
Positive	449 (21.0)	146 (21.1)	
No information	196 (9.2)	50 (7.2)	
<i>BCR/ABL</i>			0.58
Negative	2053 (96.2)	668 (96.2)	
Positive	39 (1.8)	15 (2.2)	
No information	41 (2.0)	11 (1.6)	
<i>MLL/AF4</i>			0.23
Negative	1979 (92.8)	651 (93.8)	
Positive	10 (0.5)	1 (0.1)	
No information	144 (6.7)	42 (6.1)	
Final risk group			0.003
SR	667 (31.3)	240 (34.6)	
IR	1167 (54.7)	331 (47.7)	
HR	299 (14.0)	123 (17.7)	

<sup>1</sup> $\chi^2$  test comparing study cohort and patients not studied, patients with no information excluded from test; <sup>2</sup>good: less than 1000 leukemic blood blasts/ $\mu$ L on treatment Day 8, poor: more than 1000/ $\mu$ L. <sup>3</sup>MRD risk groups<sup>17</sup>: MRD-SR: TP1+2 negative, MRD-IR: TP1 and/or TP2 <10<sup>3</sup>, MRD-HR: TP2  $\geq$ 10<sup>3</sup>.

**Online Supplementary Table 2.** Multivariate Cox's regression analysis for event-free survival, including all 694 patients.

Feature	Hazard ratio	95% CI	P
<i>IKZF1</i>	2.28	1.44-3.60	< 0.0001
Sex	0.91	0.62-1.33	0.62
SR	0.56	0.34-0.93	0.03
HR	1.91	1.20-3.03	0.006
<i>ETV6/RUNX1</i>	1.00	0.58-1.73	0.99
Immunology	0.99	0.59-1.67	0.97
WBC $\geq$ x10 <sup>9</sup> /L	1.46	0.89-2.39	0.14

**Online Supplementary Table 3.** Multivariate Cox's regression analysis for event-free survival, excluding 27 *P2RY8-CRLF2* positive patients from the cohort.

Feature	Hazard ratio	95% CI	P
<i>IKZF1</i>	1.94	1.19-3.16	0.008
Gender	0.91	0.61-1.34	0.62
SR	0.58	0.34-0.99	0.05
HR	1.98	1.24-3.17	0.004
<i>ETV6/RUNX1</i>	1.03	0.59-1.79	0.92
WBC $\geq$ x10 <sup>9</sup> /L	1.53	0.93-2.51	0.09

**Online Supplementary Table 4.** Multivariate Cox's regression analysis for event-free survival, including *P2RY8-CRLF2* status in the model.

Feature	Hazard ratio	95% CI	P
<i>IKZF1</i>	2.08	1.32-3.28	0.002
<i>P2RY8-CRLF2</i>	2.04	0.94-4.41	0.07
Gender	0.90	0.6s2-1.32	0.591
SR	0.54	0.33-0.91	0.02
HR	2.07	1.31-3.28	0.002
<i>ETV6/RUNX1</i>	1.07	0.60-1.85	0.81
WBC $\geq$ x10 <sup>9</sup> /L	1.44	0.89-2.32	0.14